

Appendix 11.13c Use in Patients with Autoimmune or Inflammatory Disorders (Autoimmune Hemolytic Anemia): Tables with cumulative literature for AIHA and mRNA vaccines and COVID-19 infection

Literature Review Tabulation

Table 20.11 Summary of Selected AIHA-Related Literature Reviews for mRNA COVID-19 Vaccines as of 18 Jun 2022

S/N	Literature Case Report	Age/ Gender Comorbidity Concomitant Medications (CM) History of COVID-19 infection (when known)	Vaccine & Dose No. Time to Onset (TTO) Presentation Diagnosis	Laboratory Diagnostics	AIHA Classification	Treatment /Outcomes	WHO-UMC Causality (MAH)
1	Fatima Z et al, 2022	Case: 66-year-old Female Med Hx: Long-term psoriatic arthritis CM: Adalimumab therapy	Vaccine: elasomeran Dose No.2 TTO: 3 months Presentation: Anemia Diagnosis: AIHA	IgG: C3: Hemoglobin: 9.9g/dL (11.1-15.9 g/dL) Hematocrit: 29.5% (34-46.6%) Bilirubin: 2.5mg/dL (0.2-1.2 mg/dL) Direct bilirubin: 0.6 mg/dL (<0.3 mg/dL) Lactate Dehydrogenase: 282 U/L:(120-246 U/L) Haptoglobin: <30 mg/dL (Reference Range provided: 30-200 mg/dL) Absolute reticulocyte count: 152000/ μ L: (50000-100000/ μ L)	Warm AIHA	Treatment: Prednisone : 60 mg/day Outcome: Hemoglobin and Hematocrit began to improve within 2 weeks of treatment and continued to improve with gradual prednisone tapering at the time of publication .	Unlikely: with a long time to onset (90days) of the events that make a relationship with the product improbable. Disease or other drugs provide a more plausible explanation. The patient's history of Psoriatic arthritis medication (adalimumab) is a confounder. Adalimumab has been associated with AIHA.
2	Gaignard M et al, 2021	56-year-old Male	Vaccine: elasomeran Dose No. 1	Thrombocytopenia: 3×10^9 /L (severe)	Flare (Evan's syndrom	Treatment: Dexamethasone: 40	Possible: Temporal association however, alternative

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		Med Hx: Evans Syndrome (since 2015), ITP, autosomal dominant polycystic kidney disease with hypertension CM: Antihypertensive drugs and aspirin	TTO: 3 days Presentation: Multiple painless petechia located on the oral mucous membranes of the lower lip and left upper arm Diagnosis: ITP (Relapse)	Hemoglobin: 151 g/L (normal) Leukocyte counts: $6.6 \times 10^9/L$ PTT, Fibrinogen, and D-dimer levels: Normal	e)	mg daily IVIg: 1 g/kg Prednisone : 1 mg/kg Thrombopoietin receptor agonist (TPO-RA) Outcome: Platelet count increased to $400 \times 10^9/L$; patient was discharged and was relapse-free at 3-month follow-up.	association of pre-existing Evan's syndrome provides a more plausible explanation.
3	Gaignard M et al, 2021	77-year-old Male Med Hx: Anemia CM: Unknown	Vaccine: elasomeran, Dose No. 1 TTO: 5 days Presentation: Weakness, fatigue and shortness of breath Diagnosis: AIHA	DAT: IgG: C3: Normochromic normocytic anemia: 86 g/L Reticulocytes: $310 \times 10^9/L$ Leukocytosis: $11.7 \times 10^9/L$ (mild) Platelets: $344 \times 10^9/L$ Haptoglobin: decreased Chest-abdomen CT scan: Normal	Warm AIHA	Treatment: Prednisone : 75 mg Outcome: Hemoglobin count increased to 112 g/L two weeks later. Reticulocytes, bilirubin, and LDH levels decreased. The patient's	Unclassifiable: due to insufficient evidence to assess for causality. This case is missing detailed information about medical history, & concomitant medication. This reported case is incomplete and cannot be complemented or verified

S/N o	Literature Case Report	Age/ Gender Comorbidity Concomitant Medications (CM) History of COVID-19 infection (when known)	Vaccine & Dose No. Time to Onset (TTO) Presentation Diagnosis	Laboratory Diagnostics	AIHA Classification	Treatment /Outcomes	WHO-UMC Causality (MAH)
				Bone marrow examination: Normal		hemoglobin level returned to almost normal after 10 weeks.	
4	Karabulut K et al, 2021	Case: 48-year-old Male Med Hx: Diabetes mellitus type 2, refractory thrombotic thrombocytopenic purpura, idiopathic thrombocytopenic purpura (ITP) CM: Insulin History of COVID-19: Positive via nasopharyngeal swab PCR 2 months prior to vaccination.	Vaccine: elasomeran Dose No. 1 TTO: 5 days Presentation: Paresthesia and acute-onset, transient right-sided weakness and slurred speech lasting Diagnosis: Thrombotic thrombocytopenic purpura (Recurrence)	Hemoglobin: 8.8 g/dL Peripheral blood smear: 2–3 schistocytes/hpf Haptoglobin: <10 mg/dL Total bilirubin: 5.0 with indirect bilirubin predominance Lactate dehydrogenase (LDH): 884 U/L D-dimer: 1.45 ug/mFEU Fibrinogen: 417 mg/dL Platelet count: 10×10^3 /dL (baseline platelet count of 130×10^3 /dL) ADAMTS13 inhibitor: 6.6 BEU (normal <0.4).	Not specified	Treatment: High-dose glucocorticoids, rituximab, fresh frozen plasma for bridging to urgent plasmapheresis. Outcome: Full recovery after a 10-day course of plasmapheresis, glucocorticoids and rituximab.	Unclassifiable: Insufficient evidence to assess for causality. Missing DAT, Ig serology report. The information in this reported case is incomplete and cannot be complemented or verified. The presence of alternative associations including TTP, ITP, T2DM, provide a more plausible explanation for the occurrence of the events.
5	Pérez-Lamas Let al, 2021	Case: 57-year-old Female Med Hx: Regenerative anemia, red	Vaccine: Unspecified mRNA COVID-19 vaccine Dose No. 1	Lab Parameters after Dose No. 1: Hemoglobin: 8.6 g/dl Reticulocyte	AIHA Flare	Treatment after Dose No. 1: Prednisone : 20 mg daily	Unlikely: with a short time to onset of the events that make a relationship with the product improbable.

S/N o	Literature Case Report	Age/ Gender Comorbidity Concomitant Medications (CM) History of COVID-19 infection (when known)	Vaccine & Dose No. Time to Onset (TTO) Presentation Diagnosis	Laboratory Diagnostics	AIHA Classification	Treatment /Outcomes	WHO-UMC Causality (MAH)
		blood cell agglutination on peripheral blood smear, elevated bilirubin and lactate dehydrogenase, DAT strongly positive for complement protein C3D and negative for IgG, cold agglutinin with anti-I specificity, serum monoclonal protein IgM lambda (352 mg/dl), a clonal lymphocyte population (0.4% of total leukocytes) and low titer antinuclear antibodies (1:80) CM: None reported History of COVID-19: Negative SARS-CoV2 test.	TTO: 2 days Presentation: Chills, weakness, shortness of breath upon exertion, and lumbar pain. Diagnosis: Jaundice and mild hemoglobinuria, AIHA Vaccine: Unspecified mRNA COVID-19 vaccine Dose No. 2 TTO for Dose No. 2: 7 days Diagnosis after Dose No. 2: AIHA exacerbation	count: increased Bilirubin: 2.9 mg/dl LDH: 462 U/L: Spherocytosis Ferritin: 426 or D-dimer were elevated at 426 and 726 ng/ml Antinuclear antibodies: Positive Cryoagglutinin titer: 256 (4°C) Lab Parameters after Dose No. 2: DAT: CD3: Cryoagglutinin titer: 512 with a wide range thermal amplitude.		Treatment after Dose No. 2: Prednisone : 20 mg daily.	Concurrent medical condition of AIHA provide plausible explanations.
6	Gadi SRV et	Case: 41-year-	Vaccine: elasomeran	Hemoglobin 7.1g/Dl (during	mixed warm/co	Treatment: Transfusio	Possible: due to temporal association.

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	al, 2021	old Female Med Hx: Central retinal Vein occlusion; hypertension. CM: Aspirin, metoprolol succinate	Dose No. 1 TTO- 7 days Presentation: Fatigue, dark urine, mild distress 7Temperature :96.9F, BP 133/78 mm Hg, Heart Rate 79 beats/min	initial presentation); 7.3 g/dL (Lab value during day of admission) MCV-(mean corpuscular volume)93 fl Reticulocyte count: 15.5% (upon initial presentation); and >30% (during admission) Total bilirubin 3.7mg/dl & 3.9 mg/Dl LDH 746 U/L, 3095 U/L (during admission): ¹⁰ Alanine aminotransferas e (U/L): 50 (during initial presentation); 139-(day of admission). Aspartate aminotransferas e (U/L): 40 (at initial presentation) and 181 (during admission). Direct Antiglobulin tests (DAT): negative for IgG and C3d	ld AIHA	n; required 13 units of RBC; Corticoster oids (Prednison e), rituximab, mycophen olate, mofetil and immuno globulin Outcome: Discharged after 14 days (49- days after receiving Vaccine). 4 weeks after Discharge Hemoglobi n = 10.9 g/dl and no RBC transfusion was required and LDH was 317 U/L.	however, the presence of alternative association, including cardiac disease and central retinal vein disease provide a more plausible explanation for the occurrence of the events.

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				although eluate prepared from Patient's RBC was reactive against all test cells. DAT (MTS gel cards): IgG: Presence of Cold autoantibody that was reactive at 37 degrees.			
7	Jaydev et al, 2022	42-year-old Female Med Hx: Hypertension, congenitally deaf and mute, Iron deficiency anemia due to menorrhagia, provoked venous sinus thrombosis. COVID-19 test: Negative by COVID-19 PCR test.	Vaccine: elasomeran Dose No. 1. TTO: 1 week Presentation: Worsening Dizziness, lightheadedness, progressive shortness of breath, palpitations, blurred vision, fatigue, generalized weakness, lack of energy.	Hemoglobin: 4.5g/dl Haptoglobin:<6 gm/dl LDH:4332 IU/L MCV: 90 fL Absolute reticulocyte count:19.9 ×10 ⁹ /L Indirect bilirubin: mildly elevated Peripheral blood smear: schistocytes, polychromasia and anisocytosis. Indirect and direct Coomb's test: IgG, C3 with identification of warm auto antibodies.	Warm AIHA	Treatment: IV steroids, methyl prednisone Cyanocobalamin injections Outcome: Week after discharge Hb 8.9g/dl and 9.6 g/dl (on second follow-up) with no Schistocytes. LDH was 540 IU/l and improved reticulocytes.	Possible: based on temporal association.

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				Low B12:<50 pg/ml.			
8	Brito S et al, 2021	88-year-old Female Med hx: Insomnia CM: Estazolam	Vaccine: Unspecified mRNA Vaccine Dose No. 2 TTO: 2 days Presentation: sudden onset of asthenia and jaundice, acute kidney injury Diagnosis: AIHA	Hematocrit: 13.8% Reticulocyte: 0.9% LDH: 1308 U/L Haptoglobins: <0.3 g/l Creatinine: 2.20 mg/dl Urea: 173 mg/dl Urinalysis: hemoglobinuria without bilirubinuria. DAT: Anti-erythrocyte IgG antibodies and high anti-C3d tiers.	Warm AIHA	Treatment: methyl prednisone Transfusion. Outcome: Improvement after 5 days, stable Hemoglobin levels, decreased LDH and decreased bilirubin. Acute kidney injury showed improvement without need for renal function replacement therapy after eight days	Unclassifiable: due to insufficient evidence to assess for causality. This case is missing detailed information about medical history, clinical course of the events. This reported case is incomplete and cannot be complemented or verified.
9	Jacobs JW et al, 2021	77-year-old-Male	Vaccine: elasomeran. TTO: 5 days	DAT: IgG: C3:	Warm AIHA	Treatment: Corticosteroid	Unclassifiable: Due to insufficient evidence on medical history, concomitant medication, to assess for causality. The information in this reported case is incomplete and cannot be

S/N o	Literature Case Report	Age/ Gender Comorbidity Concomitant Medications (CM) History of COVID-19 infection (when known)	Vaccine & Dose No. Time to Onset (TTO) Presentation Diagnosis	Laboratory Diagnostics	AIHA Classifi cation	Treatment /Outcomes	WHO-UMC Causality (MAH)
							complemented or verified.
10	Okuno S et al, 2021	75-year-old Female Med Hx: post operative chemotherapy for lung adenocarcino ma and idiopathic thrombocytop enic purpura.	Vaccine: BNT162B2 mRNA vaccine TTO: 2 weeks Diagnosis: AIHA.	Direct and indirect Coombs tests: Serum LDH & indirect bilirubin levels: high Reticulocytes: high.	AIHA	Prednisolo ne	Possible: Due to temporal association, however, the presence of alternative associations including lung adenocarcinoma and ITP, are strong cofounders that provide more plausible explanations for the occurrence of the events. Malignancies have been associated with secondary AIHA.
11	Aoun SA et al, 2021	45-year-old Female Med Hx: Not reported CM: Not reported	Vaccine: BNT162B2 mRNA vaccine Dose No. 1 Presentation: Tachycardia, jaundice, pallor TTO: 3 days Diagnosis: Cold agglutinin disease	DAT: C3: Hemoglobin: 57 g/l Reticulocytes: 10% LDH: 671 iu/l (normal range 125–220) Total bilirubin: 46.4 µmol/l (3– 20) Direct bilirubin 12.5 µmol/l (0.5–8.6) A peripheral blood film showed marked agglutination	Cold agglutini n disease	Treatment: Supportive blood transfusion and weekly rituximab for four cycles. Outcome: Complete remission 8 weeks after rituximab therapy	Unclassifiable: due to insufficient evidence to assess for causality. This case is missing medical history, & concomitant medication. This reported case is incomplete and cannot be complemented or verified

S/N o	Literature Case Report	Age/ Gender Comorbidity Concomitant Medications (CM) History of COVID-19 infection (when known)	Vaccine & Dose No. Time to Onset (TTO) Presentation Diagnosis	Laboratory Diagnostics	AIHA Classification	Treatment /Outcomes	WHO-UMC Causality (MAH)
12	Tomas M Murdych T et al. 2021	84-year-old Male Med Hx: Major depression, anxiety, prostate cancer (status post remote prostatectomy), colon cancer (status post remote laproscopic right hemicolectomy with patent anastomosis), nonocclusive coronary artery disease, hypertension, emphysema, trace cryoglobulinemia, evidence for duodenitis, chronic alcohol consumption and mild chronic anemia with baseline hemoglobin 123.3 g/dl 4 months prior to presentation.	Vaccine: BNT16B2b2 TTO: 19 Days Presentation: increased urinary frequency, dizziness, nausea, anorexia, shortness of breath, chest pain, palpitations, "ashen" appearance, and dark urine Diagnosis: AIHA.	DAT: IgG: AhG: C3: Urine analysis: small amount of bilirubin and few bacteria. Urine culture: + for 10 000-50 000 col/mL of Enterobacter cloacae. Hemoglobin: 8.8g/dL Reticulocyte count 0.163 mill/μL (0.010-0.110 mill/μL). LDH was elevated at 503 IU/L: Haptoglobin was less than 8.00 mg/dL (30-215 mg/dL). Total bilirubin was elevated at 3.3 mg/dL with indirect bilirubin of 2.8 mg/dL (0.2-1.2 mg/dL and 0.2-0.8 mg/dL, respectively).	Warm AIHA	Treatment: Ciprofloxacin, atorvastatin, cholecalciferol, cyanocobalamin, finasteride, metoprolol SR, sertraline and ocuvite capsule. Red cell transfused (2 units). Outcome: Hemoglobin increased to 7.7 g/dL and remained stable at discharge (7.3 g/dL, during follow up 8.2 g/dL and 9.0 g/dL week following discharge).	Possible: Due to temporal association, however, the presence of alternative associations including prostate and colon cancers, are strong cofounders that provide a more plausible explanation for the occurrence of the events. Malignancies have been associated with secondary AIHA.

Table 20.12 Summary of Literature review for COVID-19 Infection and Autoimmune Hemolytic Anemia

S/No	Author & Year	Patient Age & Sex	Comorbidity	DAT	Reported Diagnosis	AIHA Treatment	RBC Transfusion (No. of Units)	Outcome
1	Brazel et al -2021	51M	Unknown	IgG (+), C3(+)	Mixed AIHA	Steroids	Yes, 5	Alive
2	Arunpriyandanan et al -2021	23F	Unknown	DAT (+)	Warm AIHA	Steroids	Yes	Alive
3	Jacobs et al -2021	33F	Hypothyroidism. Covid-19: Positive	IgG (+), C3(+)	Mixed AIHA	Corticosteroids, rituximab	Yes, 11	Alive
4	Bae et al -2021	51M	None	IgG (-), C3(-)	Unknown	IVIG	Yes, 1	Alive
5	Huda et al -2021	54M	Diabetes	IgG (+)	AIHA	Steroids	Not reported	Not reported
6	Liput et al -2021	33F	None	IgG (-), C3(-)	Warm AIHA	Steroids	Yes, 1	Alive
7	Gupta et al -2021	77M	COPD, G6PD deficiency	C3(+)	Cold AIHA	Steroids	Yes, 3	Deceased
8	Renganathan et al -2021	42F	Not reported	+	Mixed AIHA	Steroids	No	Not reported
9	McGregor et al -2021	75M	HTN, CKD, Obesity	+	AIHA	Steroids	Not reported	Deceased
10	Nair et al -2021	23M	Asthma	IgG (+)	Warm AIHA	Steroids	Yes, 2	Alive
11	Saini et al -2021	94F	CKD, HFpEF	IgG (-), C3(+)	Cold AIHA	Not Reported	Yes, 6	Deceased
12	Hassanein et al -2021	48M	Not reported	IgG (-), C3(-)	Cold AIHA	Not Reported	Yes	Alive
13	Gruden et al -2021	83F	HTN	IgG (-), C3(-)		Steroids	Yes, 1	Alive

S/No	Author & Year	Patient Age & Sex	Comorbidity	DAT	Reported Diagnosis	AIHA Treatment	RBC Transfusion (No. of Units)	Outcome
14	Zama et al -2021	15M	None	IgG (+), C3(+)		Steroids	Yes,6	Alive
15	Zama et al -2021	2M	6 months after HSCT for B-thalassemia major	IgG (+), C3(+)	Cold AIHA	Steroids	Yes	Alive
16	Hasan et al -2021	45M	Hypothyroidism	+	AIHA	Steroids	Not reported	Alive
17	Hindilerden et al -2020	56M	HTN	IgG (+), C3(+)	Warm AIHA	None	Yes	Alive
18	Maslov et al -2020	48M	HTN, IDDM, ESRD, Obesity	+	Cold AIHA	Not Reported	Yes	Deceased
19	Lopez et al -2020	46F	Congenital thrombocytopenia	IgG (+), C3(+)	Warm AIHA	IVIG, steroids	Yes	Alive
20	Capes et al -2020	62 M	HTN	IgG (-), C3(-)	AIHA	Not Reported	Yes, 8	Alive

Appendix 11.13d Use in Patients with Autoimmune or Inflammatory Disorders (Autoimmune Hemolytic Anemia): Detailed review of fatal cases

Table 20.13 Summary of Five Reported Autoimmune Hemolytic Anemia (AIHA) Cases of Interest with Fatal Outcomes for elasmomeran (Cumulative to 18 June 2022)

S/ No	Case ID	Age(years) /Gender/Country	Dose Number/Manual reviewed Time to Onset	Hx of COVID-19/COVID-19 test	Intl Consensus Diagnostic Criteria for AIHA	Alternative Diagnostics	Classification/type of AIHA	WHO-UMC Causality Assessment
1		47/M/Spain	Day 4	No report	DAT:+	No report	AIHA	Unclassifiable

MAH Comments (based on medical review): This is a fatal case reported by a regulatory authority concerning a 47-year-old male patient with a past medical history of acute myocardial infarction (2001) and cardiac transplant (2011); concurrent medical conditions included hypercholesterolemia, atrial fibrillation, autoimmune thrombocytopenia and hypertension; concomitant medications included statins, eltrombopag, antihypertensives; who received dose 2 elasmomeran and 4 days post-vaccine experienced unspecified symptoms assessed as AIHA case of interest. Diagnostic results: Coombs direct test: positive. No reports of blood smears test, Ig serology and ID panels. Treatment given not provided. The patient died 24 days post-vaccine. The cause of death was not reported. An autopsy was not performed. This case is classified as Evan's syndrome (AIHA + Autoimmune thrombocytopenia [pre-existing condition]) based on positive Coombs test and history of autoimmune thrombocytopenia. This case is missing relevant information including clinical course, diagnostic results. Strong cofounders including cardiac transplant, autoimmune thrombocytopenia provide plausible explanations. According to the WHO-UMC causality assessment, this case is assessed as Unclassified, due to missing information that cannot be complemented.

2		57/M/Japan	Day 1	No report	Hb- 4.8 ↓	Stool culture: Campylobacter	AIHA flare	Conditional
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MAH Comments (based on medical review): This is a fatal case reported by a regulatory authority concerning a 57-year-old male patient living with HIV and autoimmune hemolytic anemia (2016, in remission), concomitant medications included abacavir and lamivudine (anti-HIV therapy, started 2012), who received dose 1 elasmomeran and 3 days post-vaccine, experienced progressive malaise, watery stool and anemia. Diagnostic panels: severe anemia (Hb: 4.8g/dL), repeat Hb: 10.6g/dL (6 weeks later); hyperbilirubinemia/T-Bilirubin: 5.0 mg/dL; stool culture: Campylobacter. Diagnosed with relapsed autoimmune hemolytic anemia./ Castleman's disease and Campylobacter gastroenteritis. Treated with steroids, antibiotics, RBC transfusion. 44 days post-vaccine, relapsed AIHA with Hb 3.1 g/dL, treated with pulsatile IV dose of steroids, red cell transfusion. Patient died 44 days post vaccine. Cause of death not reported, and autopsy not done. This case is confounded by HIV infection, Autoimmune haemolytic anaemia, and amoebic dysentery. This case is also missing information on Coombs test, and Ig serology. Though reported as relapsed AIHA, there is insufficient evidence to meet the case definition for AIHA for the reported event. Concurrent HIV infection and AIHA Flare provide plausible explanations. According to the WHO-UMC causality assessment, this case is considered Conditional, due to insufficient information for proper assessment. More data for proper assessment is needed.

S/ No	Case ID	Age(years) /Gender/Country	Dose Number/Manual reviewed Time to Onset	Hx of COVID-19/COVID-19 test	Intl Consensus Diagnostic Criteria for AIHA	Alternative Diagnostics	Classification/type of AIHA	WHO-UMC Causality Assessment
3		84/M/Italy	Unknown	No report	No report	No report	Insufficient evidence to meet the case definition for AIHA	Unclassifiable
MAH Comments (based on medical review): This regulatory authority reported case with a fatal outcome, concerns an 84-year-old male patient with no reported medical history and concomitant medications, who received an unknown dose of elasomeran and on the same day experienced dyspnea, thrombocytopenia and case of interest Coombs positive hemolytic anemia. No diagnostic results provided. The reported cause of death was thrombocytopenia, hemolytic autoimmune anemia DCP and Dyspnea. It is unknown if an autopsy was performed. This case is missing relevant information including medical history, concomitant medication, clinical course of events, and diagnostic reports. There is insufficient evidence to meet the case definition for AIHA. According to the WHO-UMC causality assessment, this case is assessed as Unclassifiable, due to missing information that cannot be complemented.								
4		73/M/USA	Day 2	No report	Hb- low (no value reported)	No report	Insufficient evidence to meet the case definition for AIHA	Unclassifiable
MAH Comments (based on medical review): This regulatory authority reported case with fatal outcome concerns a 73-year-old male patient with no report of medical history or concomitant medications; with discrepancies in vaccine dose numbers: report stated both dose 1 and dose 2 were given on the same day, and on the same day, the patient experienced dizziness, fatigue, and vomiting. Case of interest was autoimmune haemolytic anaemia, managed in intensive care, had blood transfusion, dialysis, multiple pharmaceutical treatments and a splenectomy. Diagnostic reports: No result of DAT provided, Hb-low, no value provided. The patient died 98 days post-dose 2 vaccine. The reported cause of death was autoimmune haemolytic anaemia. It is unknown if an autopsy was performed. This case is missing relevant information including medical history, concomitant medication, dose numbers, diagnostic reports, and so does not meet the case definition for AIHA. According to the WHO-UMC causality assessment, this case is assessed as Unclassifiable, due to missing information that cannot be complemented.								
5		35/F/USA	Day 2	SARS-CoV-2 test: positive	DAT: no result Elevated bilirubin, glucose, raised LFT	Hyponatremia, Hypoxia, Leukopenia, Pancytopenia. B-cell lymphoma	Evans syndrome Flare	Unlikely
MAH Comments (based on medical review): This case with a fatal outcome was reported by a regulatory								

S/ No	Case ID	Age(years) /Gender/C ountry	Dose Numb er/Ma nual revie wed Time to Onset	Hx of COVI D- 19/CO VID-19 test	Intl Consens us Diagnost ic Criteria for AIHA	Alternative Diagnostic s	Classificatio n/type of AIHA	WHO-UMC Causality Assessment
authority concerning a 35-year-old, female patient with a history of multiple comorbidities including Evans syndrome, Cytomegalovirus syndrome, B-cell lymphoma, Immune disorder, pneumonia and pneumothorax. No report of concomitant medications. The patient received dose 2 elasomeran and 94 days later reported fever, cough, dyspnea, Dehydration, splenomegal. Diagnostic results: Hyponatraemia, Hypoxia, Leukopenia, Pancytopenia. Diagnosis: Pneumonia, No diagnostic report for AIHA provided. Died 213 days (~7 months) post vaccine. The reported cause of death was Anaemia, B-cell lymphoma, covid-19 infection. It is unknown if an autopsy was performed. This case is missing diagnostic results for AIHA. There is insufficient evidence to meet the case definition for AIHA. According to WHO-UMC causality assessment, this case is assessed as Unlikely, due to a long latency time/time to onset of the events that make a relationship with the product improbable. The presence of multiple strong confounders including malignancy and COVID-19 infections provide plausible explanations.								

Appendix 11.13e Use in Patients with Autoimmune or Inflammatory Disorders (Autoimmune Hemolytic Anemia): Summary of 15 cases which met International Consensus case definition

Table 20.14 Summary of 15 Reported Cases of Interest Autoimmune Hemolytic Anemia (AIHA) for elasomeran (Cumulative to 18 June 2022)

S/No	Case ID	Age(years) / Gender / Country	Dose Number / Manual review / Time to Onset	Hx of COVID-19/COVID-19 test	Intl Consensus Diagnostic Criteria for AIHA	Alternative Diagnostics	Classification/type of AIHA	WHO-UMC Causality Assessment
1		77 / Male /	Dose 1 / 5 days	No report	DAT: + IDAT: + Blood LDH: 535 ↑	No report	AIHA	Unclassifiable
MAH Comments (based on medical review): This case is classified as AIHA based on the positive DAT but missing relevant information including serology result to determine the type of AIHA. The significantly raised LDH suggests intravascular hemolysis. According to the WHO-UMC causality assessment, this case is assessed as Unclassifiable, due to insufficient evidence to assess for causality. The information in this reported case is incomplete and cannot be complemented or verified.								
2		74 / Male /	Dose 2 / 34 days	No report	DAT: + IgG: + Thrombocytopenia (Platelet: 59 cells/mL)	No report	Warm AIHA (Evans syndrome)	Possible
MAH Comments (based on medical review): This is a case of warm AIHA + immune thrombocytopenia (Evan's syndrome) based on a positive DAT, positive IgG and thrombocytopenia. This case is considered WHO Possible due to temporal association, however, concurrent medical conditions, including prostate malignancy, are strong cofounders. Malignancies have been associated with secondary AIHA.								
3		53 / Female	Dose 2 / 1 day	No report	DAT: + IDAT: + C3: +	ID screening: negative. MRI: Ischemic Heart Disease	Warm AIHA (r/o CAD)	Unlikely
MAH Comments (based on medical review): This is a case of warm AIHA based on a positive DAT and positive anti-C3 Ab. However, cold agglutinin disease (CAD) should be excluded. This case is considered WHO Unlikely based on the short time to onset that makes relationship with the product improbable. Concurrent medical condition or other drugs provide plausible explanations.								
4		48 / Male /	Dose 2 / 4 days	No report	DAT: + LDH: ↑	No report	AIHA	Unclassifiable

S/No	Case ID	Age(years) /Gender/ Country	Dose Number /Manual review/ Time to Onset	Hx of COVID-19/COVID-19 test	Intl Consensus Diagnostic Criteria for AIHA	Alternative Diagnostics	Classification/type of AIHA	WHO-UMC Causality Assessment
					Bilirubin: ↑ Hb: ↓ Haptoglobin ↓ Reticulocytosis			
MAH Comments (based on medical review): This is a case of AIHA based on a positive DAT. No report of Ig serology to determine the type of AIHA. This case is considered WHO Unclassified, due to insufficient evidence to assess for causality. The information in this reported case is incomplete and cannot be complemented or verified.								
5		59 / Female	Dose 2 / 1 day	No report	DAT: + Hb: ↓ Ig: Unknown	No report	AIHA	Unclassifiable
MAH Comments (based on medical review): This is a case of AIHA based on a positive DAT. No serology Ig result to determine the type of AIHA. According to the WHO-UMC causality assessment, this case is assessed as Unclassifiable, due to insufficient evidence to assess for causality. The information in this reported case is incomplete and cannot be complemented or verified.								
6		41/Female	Dose 1 / Unknown	No report	DAT: + Blood smear: +	No report	AIHA	Unclassifiable
MAH Comments (based on medical review): This is a case of AIHA based on a positive DAT. No serology Ig result to determine the type of AIHA. According to the WHO-UMC causality assessment, this case is assessed as Unclassifiable, due to insufficient evidence to assess for causality. The information in this reported case is incomplete and cannot be complemented or verified.								
7		47 / Male	Dose 2 / 4 days	No report	DAT: +	No report	AIHA	Unclassifiable
MAH Comments (based on medical review): This case is classified as Evan's syndrome (AIHA +Autoimmune thrombocytopenia [pre-existing condition]) based on positive Coombs test and history of autoimmune thrombocytopenia. This case is missing relevant information including clinical presentations, diagnostic results. Strong cofounders including cardiac transplant, autoimmune thrombocytopenia) provide plausible explanations. According to the WHO-UMC causality assessment, this case is assessed as Unclassifiable, due to insufficient evidence to assess for causality. The information in this reported case is incomplete and cannot be complemented or verified.								

S/No	Case ID	Age(years) / Gender / Country	Dose Number / Manual reviewed Time to Onset	Hx of COVID-19/COVID-19 test	Intl Consensus Diagnostic Criteria for AIHA	Alternative Diagnostics	Classification/type of AIHA	WHO-UMC Causality Assessment
8		88 / Female	Dose 2 / 23 days	No report	DAT: + Hb: ↓ Troponin: 1284ng/L: ↑ Blood LDH: 645 ↑	CT Scan: hyperdense nodule in parotid gland. Multinodular goiter. Hepatic granulomas. Adrenal hyperplasia. Sigmoid colon diverticulosis	AIHA	Possible
MAH Comments (based on medical review): This case is classified as AIHA, however, missing Ig serology for typing, and is confounded by underlying comorbidities including breast malignancy and cardiac disease. This case is considered WHO Possible due to temporal association, however, the presence of alternative associations, including malignant breast metastasis and cardiac disease provide more plausible explanations.								
9		88 / Female /	Dose 2 / Unknown	SARS-CoV-2 test: negative	DAT: + IgG + anti-C3 titres ↑ Negative cold agglutinin. Severe anemia: Hb – 4.5g/dL. LDH: 1309 U/L ↑ 6	Normal	Warm AIHA	Unclassifiable
MAH Comments (based on medical review): This case is classified as Warm AIHA based on abnormal agglutination test, high titers of anti-erythrocyte IgG autoantibodies and high anti-C3d titers; with no cold agglutinins detected. Missing relevant information included event time to onset, detailed medical history with advanced age. According to the WHO-UMC causality assessment, this case is assessed as Unclassifiable, due to insufficient evidence to assess for causality. The information in this reported case is incomplete and cannot be complemented or verified.								
10		77 / Male /	Dose 1 / 5 days	No report	DAT: + IDAT: + IgG: +	Negative ID panels	Warm AIHA	Unclassifiable

S/No	Case ID	Age(years) /Gender/County	Dose Number /Manual reviewd Time to Onset	Hx of COVID-19/COVID-19 test	Intl Consensus Diagnostic Criteria for AIHA	Alternative Diagnostics	Classification/type of AIHA	WHO-UMC Causality Assessment
MAH Comments (based on medical review): This is a case of warm AIHA, but missing relevant information about medical history, concomitant medications to properly assess causality. This case is assessed as WHO Unclassifiable, due to insufficient evidence to assess for causality. The information in this reported case is incomplete and cannot be complemented or verified.								
11		41 / Female	Dose 1 / 7 days	SARS-CoV-2 test: negative	DAT: + IgG: + Cold autoantibody (3+) at 37 degrees LDH: 746U/L. ↑ Spherocytosis ↑	No report	Mixed AIHA	Possible
MAH Comments (based on medical review): This is a case of mixed AIHA (Warm & Cold) based on positive DAT (MTS get cards) and cold autoantibody (3+) at 37 degrees. This case is considered WHO Possible due to temporal association however, the presence of alternative associations, including cardiac disease and central retinal vein disease provide a more plausible explanation for the occurrence of the events.								
12		66 / Unknown /	Dose 2 / 90 days	No report	DAT: + IgG: +4 C3 -	No report	Warm AIHA	Unlikely
MAH Comments (based on medical review): This case is classified as warm AIHA based on a positive serology test for DAT, IgG. And considered 'WHO Unlikely', with a long time to onset of the events that make a relationship with the product improbable. Disease or other drugs provide plausible explanations. The patient's history of treatment of Psoriatic arthritis with adalimumab is a strong confounder/alternative association, that provide a more plausible explanation for the occurrence of the events. Adalimumab has been associated with AIHA.								
13		44 / Female	Dose 1 / Day 7	SARS-CoV-2 test: negative	DAT: + C3: + IgG: + LDH: 4332U/L. ↑ 16 Positive warm autoantibodies	No report	Warm AIHA	Possible

S/No	Case ID	Age(years) /Gender/County	Dose Number /Manual reviewd Time to Onset	Hx of COVID-19/COVID-19 test	Intl Consensus Diagnostic Criteria for AIHA	Alternative Diagnostics	Classification/type of AIHA	WHO-UMC Causality Assessment
MAH Comments (based on medical review): This is a case of warm AIHA based on a positive Coombs test and positive IgG and C3. According to WHO causality assessment, this case is considered Possible based on temporal association								
14		60 / Female	Dose 2 / Day 2	No report	DAT: + Reticulocytosis (15.3); Anemia (Hb- 6.6 g/dl)	No report	AIHA	Conditional
MAH Comments (based on medical review): This regulatory authority reported case concerns a 60-year-old female patient, with a past medical history of multiple sclerosis and osteoarthritis, concurrent medical conditions of allergy and concomitant medications included alemtuzumab, nirabegron, NSAIDs, supplements; who received dose 2 elasomeran, and 2 days post-vaccine, experienced progressive dyspnea, fatigue, pain, palpitations, pyrexia. She had significant anemia. Coombs test was positive. Case of interest was autoimmune hemolytic anemia. Treated with prednisone. Events had not resolved at the time of the report. This case is classified as AIHA based on the positive DAT but missing relevant information including serology result to determine the type of AIHA. According to the WHO-UMC causality assessment, this case is considered Conditional. More data for proper assessment is needed.								
15		28/ Male /	Dose 1 / Day 4	No report	DAT: +LDH: ↑ Hb- 8.4 ↓ Retics: 7.4 ↑ Leucocytosis	Lymphoma	AIHA	Possible
MAH Comments (based on medical review): This case reported by a regulatory authority concerns a 28-year-old male patient with a past medical history of COVID-19 infection, and concurrent medical conditions including mantle cell lymphoma and asthma, no relevant concomitant medications reported; who received dose 1 elasomeran and 4 days post vaccine experience anemia and unspecified symptoms. The case of interest was warm autoimmune hemolytic anemia based on a positive Coombs test. No serology results. Diagnostic results: and leukocytosis. This case is classified as AIHA based on positive DAT. According to the WHO-UMC causality assessment, this case is assessed as Possible based on temporal association.								

Appendix 11.14a Acquired haemophilia: Case listings

Case ID	Country	Report Type	Patient Age (Years)	Patient Gender	PT	Event Seriousness	ALL PTs	Case Seriousness	Event Outcome	Event Duration	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	TTO All Doses	Initial Receipt Date	Initial / Follow-up	WW Identifier
	SWITZERLAND	Literature-Non-Study	85.00	Male	Acquired haemophilia	Serious	Acquired haemophilia, Gallbladder rupture, Haemobilia	Serious	Fatal	27	Acute kidney injury(C); Anaemia(C); Coronary artery disease(C); Thrombocytopenia(C); Hypertension(C); Vascular graft; Peripheral arterial occlusive disease(C); Renal artery stenosis(C); Carotid artery stenosis(C)	ASPIRIN CARDIO; ATORVASTATIN; SPIRONOLACTONE; BISOPROLOL FUMARATE; EZETROL; ALDACTONE 50 HCT; CONCOR; FLUDEX [BROMHEXINE HYDROCHLORIDE; DEXTROMETHORPHAN HYDROBROMIDE]; TRIATEC [RAMIPRIL]; ZANIDIP; ZYLORIC	Dose 2	2	4/13/2021	Prior	
		Regulatory Authority	81.00	Male	Acquired haemophilia	Serious	Acquired haemophilia, Haematoma muscle	Serious	Recovering/Resolving		Acquired haemophilia(H)	COUMADIN	Dose 1	20	4/28/2021	Prior	
		Regulatory Authority	72.00	Female	Acquired haemophilia	Serious	Acquired haemophilia, Petechiae, Spontaneous haematoma	Serious	Unknown		Coronary artery disease(H); Colitis ischaemic(H); Colitis microscopic(H); Drug hypersensitivity; Arterial disorder(H); Drug hypersensitivity; Drug hypersensitivity; Drug hypersensitivity	ASPIRIN CARDIO; CLOPIDOGRELUM; TRIATEC [RAMIPRIL]; CONCOR; ROSUVASTATIN [ROSUVASTATIN]; PANTOPRAZOLUM	Dose 1	0	5/12/2021	Prior	
		Literature-Non-Study	86.00	Female	Acquired haemophilia	Serious	Acquired haemophilia, Contusion, Dyspnoea, Fall, Haemothorax, Rib fracture	Serious	Recovered/Resolved		Atrioventricular block complete(H); Hypertension(C); Skin ulcer(C); Traumatic haemothorax(C); Cardiac pacemaker insertion; Aortic valve stenosis(H); Drug hypersensitivity; Ulcer(C); Drug hypersensitivity; Drug hypersensitivity; Drug hypersensitivity	ASPIRIN CARDIO; AMLODIPIN AXAPHARM; AMLODIPIN-MEPHA; CONCOR; TRIATEC [RAMIPRIL]; PANTOZOL [PANTOPRAZOLE SODIUM SESQUIHYDRATE]	Dose 2	18	5/17/2021	Prior	
		Regulatory Authority	72.00	Female	Acquired haemophilia	Serious	Acquired haemophilia	Serious	Unknown				Dose 1	Unknown	7/1/2021	Prior	
		Literature-Non-Study	76.00	Female	Acquired haemophilia	Serious	Acquired haemophilia, Acquired Von Willebrand's disease, Blood loss anaemia, Ecchymosis, Melaena, Presyncope	Serious	Unknown		Asthma(C); Raynaud's phenomenon(C); Ecchymosis(H); Hiatus hernia(H); Oesophagogastric fundoplasty		Dose 2	4	7/20/2021	Prior	
		Regulatory Authority	88.00	Female	Acquired haemophilia	Serious	Acquired haemophilia	Serious	Recovering/Resolving		Dyslipidaemia(C); Hypertension(C); Herpes zoster(H); Depression(C); Gastric ulcer(C); Breast cancer(C); Anxiety(C); Drug hypersensitivity		Dose 2	67	7/28/2021	Prior	
		Regulatory Authority	63.00	Female	Acquired haemophilia	Serious	Acquired haemophilia, Incorrect route of product administration	Serious	Not Recovered/Not Resolved		Hypertension(C); Psoriatic arthropathy(C); HER2 positive breast cancer(H); Nephrectomy		Dose 2	2	9/17/2021	Prior	
		Regulatory Authority	59.00	Female	Acquired haemophilia	Serious	Acquired haemophilia, Factor VIII deficiency, Spontaneous haematoma	Serious	Recovering/Resolving		Essential hypertension(C)		Unknown	18	10/14/2021	Follow-up	
		Regulatory Authority	53.00	Female	Acquired haemophilia	Serious	Acquired haemophilia	Serious	Not Recovered/Not Resolved		Obstructive sleep apnoea syndrome(C); Large intestine polyp(C); Tachycardia(C); Carpal tunnel syndrome(C); Asthma(C); Mammoplasty; Intervertebral disc protrusion(C); Gastric ulcer(C); Rheumatoid arthritis(C)	PROCORALAN; TRAMADOL ACTAVIS; LYRICA; [REDACTED]	Dose 2	2	10/19/2021	Prior	
		Regulatory Authority	89.00	Female	Acquired haemophilia	Serious	Acquired haemophilia, Activated partial thromboplastin time prolonged, Ecchymosis	Serious	Recovered/Resolved		Osteoarthritis(C); Osteoporosis(C); Polymyalgia rheumatica(C); Chronic obstructive pulmonary disease(C); Hypertensive heart disease(C); Chronic kidney disease(C); Sinus bradycardia(C); Monoclonal B-cell lymphocytosis(C)	FUROSEMID; TRAZODONE HYDROCHLORIDE; LANSOPRAZOLE; ALLOPURINOL; RAMIPRIL; ACETYLSALICYLIC ACID; DIGOXIN	Unknown	82	10/21/2021	Follow-up	
		Regulatory Authority	90.00	Male	Acquired haemophilia	Serious	Acquired haemophilia	Serious	Recovering/Resolving		Systemic lupus erythematosus(C); Ischaemic stroke(C); Paraesthesia(H); Pain(H); Hypoaesthesia(H); Congestive cardiomyopathy(C); Atrioventricular block(C); Sympathectomy; Carotid artery stenosis(C); Type 2 diabetes mellitus(C); Renal failure(C); Tubulointerstitial nephritis(C); Nephroangiosclerosis(C); METFORMIN(H); Immune thrombocytopenia(C); Spinal osteoarthritis(C); Hypoaesthesia(C); Hearing aid user(C); Parapsoriasis(C); Osteoarthritis(C); Osteonecrosis(C); Cataract(H); Prostatic adenoma(C); Transurethral prostatectomy		Unknown	2	10/22/2021	Prior	
		Regulatory Authority	76.00	Male	Acquired haemophilia	Serious	Acquired haemophilia, Cerebral haematoma	Serious	Recovering/Resolving		Deep vein thrombosis(C); Hypertension(C)		Dose 1	63	11/26/2021	Prior	
		Literature-Non-Study	70.00	Male	Acquired haemophilia	Serious	Acquired haemophilia	Serious	Recovered/Resolved		Polymyalgia rheumatica(H); Hepatitis C(H)	SULFAMETHIZOLE; TRIMETHOPRIM	Dose 1	2	1/24/2022	Initial	

Case ID	Country	Report Type	Patient Age (Years)	Patient Gender	PT	Event Seriousness	ALL PTs	Case Seriousness	Event Outcome	Event Duration	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	TTO All Doses	Initial Receipt Date	Initial / Follow-up	WW Identifier
		Literature-Non-Study	77.00	Male	Acquired haemophilia	Serious	Acquired haemophilia, Inappropriate schedule of product administration, Pemphigoid, Underdose	Serious	Recovered/Resolved	162	Nasopharyngeal cancer(H); Hypertension(C); Dyslipidaemia(C); Diabetes mellitus(C)	AMLODIPINE; GLIMEPIRIDE; LINAGLIPTIN	Dose 2	27	3/28/2022	Initial	
		Literature-Non-Study	72.00	Male	Acquired haemophilia	Serious	Acquired haemophilia, Interchange of vaccine products, Pleomorphic malignant fibrous histiocytoma	Serious	Recovering/Resolving		Pleomorphic malignant fibrous histiocytoma(C); Benign prostatic hyperplasia(C); Carpal tunnel syndrome(H); Tobacco user(H)		Dose 3	Unknown	5/2/2022	Initial	
		Regulatory Authority	84.00	Female	Acquired haemophilia	Serious	Acquired haemophilia, Intra-abdominal haemorrhage, Skin haemorrhage	Serious	Recovering/Resolving		Obesity(C); Metabolic syndrome(C); Cardiac failure chronic(C); Cerebellar infarction(H); Lung disorder(C); Hypertension(C); Chronic kidney disease(C); Pulmonary hypertension(C)		Dose 3	11	5/18/2022	Initial	
		Regulatory Authority	61.00	Male	Acquired haemophilia	Serious	Acquired haemophilia	Serious	Recovering/Resolving		Hypertension(C); Gastrectomy; Urinary tract infection(C); Myocardial ischaemia(C); Bronchitis(H); Transient ischaemic attack(H); Pulmonary embolism(C)	LANSOPRAZOLE [REDACTED] ROSUVASTATINE CF	Dose 2	90	6/8/2022	Initial	
		Regulatory Authority	84.00	Male	Acquired haemophilia	Serious	Acquired haemophilia	Serious	Not Recovered/Not Resolved		Ischaemic stroke(H); Hypertension(C); Cerebrovascular stenosis(C); Diabetes mellitus(C); Cerebrovascular accident(H)	[REDACTED] PLAVIX; FUROSEMIDE	Unknown	10	6/9/2022	Initial	

Appendix 11.14b Acquired haemophilia: Case narratives

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This literature-non-study case was reported in a literature article and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired haemophilia A with anti factor VIII), HAEMOBILIA (gall bladder hemorrhage) and GALLBLADDER RUPTURE (gallbladder perforation) in an 85-year-old male patient who received mRNA-1273 (COVID-19 Vaccine Moderna) (batch nos. 3000496 and 300042460) for COVID-19 vaccination. LITERATURE REFERENCE: Cittone MG, Battagay R, Condoluci A, Terzi di Bergamo L, Fernandes E, Galfetti E, et.al. The statistical risk of diagnosing coincidental acquired hemophilia A following anti-SARS-CoV-2 vaccination. J Thromb Haemost. 2021;19:2360 The patient's past medical history included Bypass surgery. Concurrent medical conditions included Acute on chronic renal failure since 14-Mar-2021, Anaemia, Triple vessel disease, Thrombopenia, Arterial hypertension, Peripheral arterial disease, Renal artery stenosis and Carotid artery stenosis. Concomitant products included ACETYLSALICYLIC ACID (ASPIRIN CARDIO), ATORVASTATIN, SPIRONOLACTONE, BISOPROLOL FUMARATE, EZETIMIBE (EZETROL), HYDROCHLOROTHIAZIDE, SPIRONOLACTONE (ALDACTONE 50 HCT), BISOPROLOL FUMARATE (CONCOR), BROMHEXINE HYDROCHLORIDE, DEXTROMETHORPHAN HYDROBROMIDE (FLUDEX [BROMHEXINE HYDROCHLORIDE; DEXTROMETHORPHAN HYDROBROMIDE]), RAMIPRIL (TRIATEC [RAMIPRIL]), LERCANIDIPINE HYDROCHLORIDE (ZANIDIP) and ALLOPURINOL (ZYLORIC) for an unknown indication. On 12-Feb-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 12-Mar-2021, received second dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) dosage was changed to 1 dosage form. On 14-Mar-2021, after starting mRNA-1273 (COVID-19 Vaccine Moderna), the patient experienced ACQUIRED HAEMOPHILIA (Acquired haemophilia A with anti factor VIII) (seriousness criteria death, hospitalization and medically significant). On 10-Apr-2021, the patient experienced HAEMOBILIA (gall bladder hemorrhage) (seriousness criteria death, hospitalization and medically significant) and GALLBLADDER RUPTURE (gallbladder perforation) (seriousness criteria death, hospitalization and medically significant). The patient was treated with PREDNISONE for Adverse event, at a dose of 100 mg/d; RITUXIMAB for Adverse event, at an unspecified dose and frequency; Surgery for Haemobilia and Surgery for Gallbladder rupture. The patient died on 10-Apr-2021. The reported cause of death was gallbladder rupture, Gallbladder haemorrhage and Acquired haemophilia A with anti factor VIII. It is unknown if an autopsy was performed. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 14-Mar-2021, Computerised tomogram: arterial hemorrhage (abnormal) an arterial haemorrhage in the right psoas muscle. On 14-Mar-2021, Computerised tomogram abdomen: haematoma (abnormal) Haematoma in the iliac muscle and psoas on the right	Prolonged.	No report	Factor VIII: 29%(low). Factor VIII inhibitor: 2.2 bu/ml (abnormal)	1. Antiphospholipid antibodies: positive. 2) Hb: low(58g/l). 3) CTScan: haematoma abdomen, iliac muscle and psoas on the right. 4) SARS-CoV-2 antibody test: Positive.	Acquired Hemophilia A (AHA)	Possible	This literature-non-study case with fatal outcome in a 85-year-old male patient with multiple cardiac comorbidities including cardiac bypass surgery, coronary artery disorder, chronic renal failure, anemia, thrombopenia and concomitant medications included antihypertensive, diuretics, statins; who received dose 2 Spikevax and 2 days post vaccine experienced progressive lower abdomen pain, muscle pain, knee pain and swelling. Positive rechallenge. Post dose 1 Spikevax, patient reported "various hematomas and painful knee joint effusions on both sides and pain in the right leg". Diagnostic results: aPTT-elevated, low FVIII activity (29%), high FVIII inhibitor, positive antiphospholipid Ab. 29 days post dose 2, experienced gall bladder bleed and rupture and died. The reported cause of death was gallbladder rupture, gallbladder haemorrhage and Acquired haemophilia A with anti factor VIII. It is unknown if an autopsy was performed. This case is classified as Acquired hemophilia A based on diagnostic results. According to WHO-UMC causality assessment, this case is assessed as Possible based on temporal association.	

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	(approx. 400mL) active arterial bleeding most likely from muscular branches. On 14-Mar-2021, Haemoglobin: 58 (Low) 58 g/L. On 15-Mar-2021, Anti factor VIII antibody test: factor viii 29%, factor viii inhibitor: 2.2 hu/ml (abnormal) factor VIII 29%, factor VIII inhibitor: 2.2 BU/mL. On 15-Mar-2021, SARS-CoV-2 antibody test: 42.6 (Positive) 42.6 COI (Negative: COI < 0.7, borderline: COI 0.7-1.0, positive: COI > 1.0). On 16-Mar-2021, Activated partial thromboplastin time: elevated (High) isolated elevation. On 16-Mar-2021, Antiphospholipid antibodies: positive (Positive) Positive. On 16-Mar-2021, Cardiolipin antibody: very high (High) high. On 16-Mar-2021, Electrophoresis protein: inconspicuous (Inconclusive) inconspicuous. On 16-Mar-2021, Immunophenotyping: negative (Negative) Negative. On 17-Mar-2021, Prostatic specific antigen: normal (normal) normal. On 18-Mar-2021, Computerised tomogram: no indication of tumor (normal) No tumor. On 21-Mar-2021, Platelet count: low (Low) 60 x 10⁹. For mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular), the reporter considered ACQUIRED HAEMOPHILIA (Acquired haemophilia A with anti factor VIII), HAEMOBILIA (gall bladder hemorrhage) and GALLBLADDER RUPTURE (gallbladder perforation) to be possibly related. On 12-Feb-2021, patient reported various hematomas and painful knee joint effusions on both sides and pain in the right leg. On 12-Mar-2021 post vaccination, the symptoms of the patient had worsened and pain in lower abdomen was added. On 10-Apr-2021, due to severe bleeding risk and the critical condition, surgery was not possible and arterial coiling was performed which, however, transiently stopped bleeding. The patient refused further intervention and died shortly after that. Company comment: This is a case of death in a 85-year-old male subject with a medical history of Chronic renal failure, Acute blood loss anemia, Thrombopenia and Coronary artery disorder., who died 29 days after receiving the second dose of vaccine. Based on information received, death was due to gallbladder hemorrhage and perforation, hence the events and death are assessed as unlikely related to mRNA-1273. This case was linked to [REDACTED] (Patient Link). Most recent FOLLOW-UP information incorporated above includes: On 14-Jun-2021: Swiss affiliate comment added. On 17-Jun-2021: Full text article was received. On 26-Feb-2022: Follow up received by safety on 26-Feb-2022 included an Email from SARA team and contains non-significant information.								

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This regulatory authority case was reported by a physician (subsequently medically confirmed) and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired haemophilia) and HAEMATOMA MUSCLE (Haematoma muscle) in an 81-year-old male patient who received mRNA-1273 (COVID 19 Vaccine Moderna) (batch no. 3000494) for COVID-19 vaccination. The patient's past medical history included Acquired haemophilia. Concomitant products included WARFARIN SODIUM (COUMADIN) for an unknown indication. On 10-Mar-2021, the patient received first dose of mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular) 1 dosage form in total. On 30-Mar-2021, the patient experienced ACQUIRED HAEMOPHILIA (Acquired haemophilia) (seriousness criterion hospitalization) and HAEMATOMA MUSCLE (Haematoma muscle) (seriousness criterion hospitalization). At the time of the report, ACQUIRED HAEMOPHILIA (Acquired haemophilia) and HAEMATOMA MUSCLE (Haematoma muscle) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Anti factor VIII antibody positive: (Positive) positive. On an unknown date, Factor III deficiency: (Inconclusive) Factor III deficiency. The action taken with mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular) was unknown. For mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular), the reporter did not provide any causality assessments. Treatment information was not provided. Company comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. Most recent FOLLOW-UP information incorporated above includes: On 03-May-2021: Follow up report received on 03MAY2021 included no new information. On 06-May-2021: Follow up received contains NNI	No report	No report	1. Anti factor VIII antibody positive: 2. Factor III deficiency:	No result	AHA Flare	Conditional	This regulatory authority reported case concerns an 81-year-old male patient with past medical history including acquired haemophilia, concomitant medications included warfarin; who received dose 1 Spikevax and 20 days post vaccine, experienced haematoma muscle. Diagnostics: Anti factor VIII antibody positive, Factor III deficiency. No report of aPTT, PT, CBC, or inhibitor screen. Treatment information was not provided. At the time of the report, event was resolving. This case is missing diagnostic results for aPTT, however, classified as a flare of pre-existing AHA. According to WHO-UMC causality assessment, this case is assessed as Conditional. More information is needed for proper assessment. The use of warfarin is a strong confounder.	

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This literature-non-study case was reported in a literature article and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired hemophilia A), SPONTANEOUS HAEMATOMA (Spontaneous haematoma) and PETECHIAE (Petechiae) in a 72-year-old female patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for COVID-19 vaccination. LITERATURE REFERENCE: Cittone MG, Battegay R, Condoluci A, Gerber B. The statistical risk of diagnosing coincidental acquired hemophilia A following anti-SARS-CoV-2 vaccination.. J Thromb Haemost;19(9):2360 The patient's past medical history included Coronaropathy, Colitis ischemic, Colitis collagenous and Arterial disorder NOS (Taking low-dose aspirin for arterial disease). Concurrent medical conditions included Drug allergy (Chlorhexidine), Drug allergy (Articaine), Drug allergy (Lidocaine) and Drug allergy (Procaine). Concomitant products included ACETYLSALICYLIC ACID (ASPIRIN CARDIO), CLOPIDOGREL (CLOPIDOGRELUM), RAMIPRIL (TRIATEC [RAMIPRIL]), BISOPROLOL FUMARATE (CONCOR), ROSUVASTATINA [ROSUVASTATIN] and PANTOPRAZOLE (PANTOPRAZOLUM) for an unknown indication. On 09-Apr-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 09-Apr-2021, after starting mRNA-1273 (COVID-19 Vaccine Moderna), the patient experienced SPONTANEOUS HAEMATOMA (Spontaneous haematoma) (seriousness criterion hospitalization). On 19-Apr-2021, the patient experienced PETECHIAE (Petechiae) (seriousness criterion hospitalization). On an unknown date, the patient experienced ACQUIRED HAEMOPHILIA (Acquired hemophilia A) (seriousness criteria hospitalization prolonged and medically significant). The patient was hospitalized from sometime in 2021 to sometime in 2021 due to ACQUIRED HAEMOPHILIA and SPONTANEOUS HAEMATOMA. The patient was treated with TRANEXAMIC ACID for Adverse event, at an unspecified dose and frequency; PREDNISONE for Adverse event, at an unspecified dose and frequency and RITUXIMAB for Adverse event, at an unspecified dose and frequency. At the time of the report, ACQUIRED HAEMOPHILIA (Acquired hemophilia A) outcome was unknown and SPONTANEOUS HAEMATOMA (Spontaneous haematoma) and PETECHIAE (Petechiae) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 20-Apr-2021, Platelet count: normal (normal) normal, Piastrine 303 x 10E9/L. On 30-Apr-2021, Von Willebrand's factor activity test: decreased (Low) Possible Low Von Willebrand. On 03-May-2021, Von Willebrand's factor activity test: decreased (abnormal) Detection of Von Willebrand factor slightly decreased compared to reference values. On an unknown date, Activated partial thromboplastin time: prolonged (abnormal) prolonged 184 s, a delayed-acting inhibitor in the aPTT mixing study Normal range: 25-37s).	Prolonged 184 s.	Delayed-acting inhibitor in the aPTT mixing study	Factor VIII activity: non-detectable. Factor VIII inhibitor: high (12.4BU/ml). Von Willebrand's factor activity test: decreased	SARS-CoV-2 antibody test: 83 BAU/ml (High) Hb: 56g/l (Low)	AHA & vWD	Unlikely	This literature-non-study case concerns a 72-year-old female patient with past medical history including coronaropathy, ischemic colitis, arterial disease, concomitant medications included low dose ASA, clopidogrel; who received dose 1 Spikevax and few hours later experienced "spontaneous hematoma on both lower limbs and progressive petechiae the wrists and backs of hands. Diagnostic tests: FVIII deficiency, prolonged aPTT, Mixing test: delayed acting inhibitor. Screening for malignancy, chronic infectious diseases and autoimmune disorders was negative. Treatment included a rFVIIa, steroids. Event was resolving as at time of report. This case is classified as AHA based on prolonged aPTT, FVIII deficiency, weak aPTT correction. According to WHO-UMC causality assessment, this case is assessed as Unlikely related to the product due to the short latency time. The use of clopidogrel provides plausible explanation. Clopidogrel is associated with acquired hemophilia and this is stated in the manufacturer's leaflet.	

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	On an unknown date, Factor VIII inhibition: 5.6 (normal) factor VIII activity increased to 5% while factor VIII inhibitor decreased to 5.6 BU/ml and 12.4 (abnormal) a non-detectable factor VIII activity and a factor VIII inhibitor of 12.4BU/ml. On an unknown date, Haemoglobin: 56 (Low) 56g/l Normal range: 120g/l-160g/l. On an unknown date, SARS-CoV-2 antibody test: 83 (High) 83 BAU/ml. The action taken with mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) was unknown. For mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular), the reporter considered ACQUIRED HAEMOPHILIA (Acquired hemophilia A), SPONTANEOUS HAEMATOMA (Spontaneous haematoma) and PETECHIAE (Petechiae) to be related. The patient had history of lymphocytic colitis. Approximately 2-3 hours after the vaccine administration, the patient reported the onset of hematomas on both lower limbs, in the absence of trauma. Two weeks after the vaccine, the patient had the onset of petechiae on her wrists and backs of her hands. She went to the Emergency Room 09 April 2021. Screening for malignancy, chronic infectious diseases and autoimmune disorders was negative. Treatment also included a seven-day treatment with rFVIIa. The bleeding tendency improved remarkably one week after the first dose of rituximab abd after the third dose of rituximab, factor VIII activity increased to 5%. Based on the current available information which shows a temporal association between the use of mRNA-1273 and the onset of the reported events, a causal relationship cannot be excluded. The patient's comorbidities and concomitant product use of Aspirin, Clopidogrel remains as confounders. This case was linked to [REDACTED] (Patient Link). Most recent FOLLOW-UP information incorporated above includes: On 26-Feb-2022: Follow up received by safety 28-FEB-2022 has Email from SARA team and contain significant information: Reporter and Literature information were updated.								

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This literature-non-study case was reported in a literature article and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired haemophilia A with anti factor VIII), HAEMOTHORAX (Rght-sided hemothorax), RIB FRACTURE (fractures of ribs 9-11), FALL (incidental fall), DYSPNOEA (Increasing shortness of breath) and CONTUSION (chest and shoulder contusion) in an 86-year-old female patient who received mRNA-1273 (COVID-19 Vaccine Moderna) (batch nos. 300042723 and 300042460) for COVID-19 vaccination. LITERATURE REFERENCE: Cittone MG, Battagay R, Condoluci A, Terzi di Bergamo L, Fernandes E, Galfetti E et al. The statistical risk of diagnosing coincidental acquired hemophilia A following anti-SARS-CoV-2 vaccination. J Thromb Haemost. 2021 The patient's past medical history included Atrioventricular block third degree in 2017, Aortic valve stenosis (treated non-surgically) and Pacemaker insertion (cardiac) (placement of pacemaker (PM) due to atrioventricular block (AVB) grade III. in 2017. Concurrent medical conditions included Arterial hypertension (under treatment with drugs.), Chronic leg ulcer, Traumatic haemothorax (right haemothorax) since 16-Feb-2021, Drug allergy (allergic to piroxicam), Ulcer NOS since 2020, Drug allergy (allergic to acemetacin), Drug allergy (allergic to Bioflorin) and Drug allergy (allergic to biotin). Concomitant products included AMLODIPINE MESILATE (AMLODIPIN-MEPHA), BISOPROLOL FUMARATE (CONCOR) and RAMIPRIL (TRIATEC [RAMIPRIL]) for Arterial hypertension, ACETYLSALICYLIC ACID (ASPIRIN CARDIO) from an unknown date to 23-Apr-2021 for Arteriopathy, AMLODIPINE BESILATE (AMLODIPIN AXAPHARM) for Blood pressure high, PANTOPRAZOLE SODIUM SESQUIHYDRATE (PANTOZOL [PANTOPRAZOLE SODIUM SESQUIHYDRATE]) for Ulcer. On 27-Jan-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 24-Feb-2021, received second dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) dosage was changed to 1 dosage form. On 16-Feb-2021, the patient experienced RIB FRACTURE (fractures of ribs 9-11) (seriousness criteria hospitalization and life threatening). On 14-Mar-2021, after starting mRNA-1273 (COVID-19 Vaccine Moderna), the patient experienced DYSPNOEA (Increasing shortness of breath) (seriousness criterion hospitalization). On 24-Mar-2021, the patient experienced ACQUIRED HAEMOPHILIA (Acquired haemophilia A with anti factor VIII) (seriousness criteria hospitalization, medically significant and life threatening) and HAEMOTHORAX (Rght-sided hemothorax) (seriousness criteria hospitalization, medically significant and life threatening). In 2021, the patient experienced FALL (incidental fall) (seriousness criterion hospitalization). On an unknown date, the patient experienced CONTUSION (chest and shoulder contusion) (seriousness criterion hospitalization). The patient was hospitalized on sometime in February 2021 due to FALL and RIB FRACTURE, then on 24-Mar-2021 due to DYSPNOEA, then from 26-Mar-2021 to 13-Apr-2021 due to ACQUIRED HAEMOPHILIA and HAEMOTHORAX, and then on sometime in 2021 due to CONTUSION. The patient was treated with CORTISONE for Adverse event, at a dose of 50 mg; EPTACOG ALFA (ACTIVATED) (NOVOSEVEN) for Adverse event, at a dose of 5000 mcg; FACTOR VIII INHIBITOR BYPASSING FRACTION (FEIBA) for Adverse event, at a dose of 1 dosage form; PREDNISONE (oral) for	Prolonged aPTT, 75s	Delayed-acting inhibitor of coagulation.	Factor VIII level: Decreased, 23%. low-titer FVIII inhibitor of 1.01 BU/ml	chest CT scan: right-sided hemothorax and fractures of ribs 9-11. SARS-CoV-2 spike IgG titer: 150 BAU/ml. Negative screen test for ID, autoimmune diseases and cancers.	AHA	Possible	This literature-non-study case concerns a 86-year-old female patient with past medical history including aortic valve stenosis and pacemaker implantation for third-degree atrioventricular block. Concomitant medications included ASA, antihypertensive. 8 days prior to receiving dose 2 Spikevax, patient experienced an accidental fall with chest and shoulder contusion and ribs fracture. chest CT scan revealed right-sided hemothorax. treated with ASA and chest drain. 18 days post vaccine, experienced progressive dyspnea, and by day 28 post vaccine, daignostic hema tests showed a prolongation of the aPTT, with an APTT mixing study typical for a FVIII:C was 23%, and a low-titer FVIII inhibitor of 1.01 BU/ml was detected. An extensive screening for cancer, chronic infectious diseases, and autoimmune diseases was negative. Treated with steroids, rFVIIa, and APCC Events were resolving at report. This case is classified as AHA based on FVIII deficiency, prolonged aPTT and an APTT mixing study typical for a FVIII. According to WHO-UMC causality assessment, this case is assessed as Possible based on temporal association. However, the history of hemothorax and rib fracture are strong confounders.	

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	Adverse event, at a dose of 1 mg/kg and Surgery for Haemothorax. In April 2021, ACQUIRED HAEMOPHILIA (Acquired haemophilia A with anti factor VIII) and HAEMOTHORAX (Rght-sided hemothorax) had resolved. At the time of the report, RIB FRACTURE (fractures of ribs 9-11) and FALL (incidental fall) was resolving and DYSPNOEA (Increasing shortness of breath) and CONTUSION (chest and shoulder contusion) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 24-Mar-2021, Activated partial thromboplastin time: 44s (abnormal) Prolonged aPTT, 75s (abnormal) Prolonged aPTT, 34s (abnormal) Prolonged aPTT and 46s (abnormal) Prolonged aPTTv. On 24-Mar-2021, Coagulation factor VIII level: 27% (Low) Decreased, 23%. On 24-Mar-2021, Computerised tomogram: abnormal (abnormal) right-sided hemothorax and fractures of ribs 9-11. On 24-Mar-2021, Prothrombin time: regular (normal) regular PT. On 24-Mar-2021, SARS-CoV-2 antibody test: 150 bau/ml (High) 150 BAU/ml. On 26-Mar-2021, Anti factor VIII antibody test: 1.01 bc/ml (High) Increased. On 26-Mar-2021, Coagulation factor VIII level: <3.5% (Low) Decreased. On 26-Mar-2021, Haemoglobin: 113g/dl (Low) 113g/dl. On 12-Apr-2021, Coagulation factor VIII level: 175% (Low) Decreased 175%. For mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular), the reporter did not provide any causality assessments. On an unspecified date, a chest drain was placed leading to large subcutaneous effusion. Three-day treatment with Factor VIIIa, and with Argon plasma coagulation (aPCC) was needed to control local bleeding and to remove the chest drain. An extensive screening for cancer, chronic infectious diseases and autoimmune diseases. The patient received Novoseven and Feiba, and steroid therapy was initiated with prednisone 1 mg/kg, obtaining a rapid normalization of FVIII, a response maintained immediately despite the reduction in corticotherapy, currently at 5 mg/day. Company comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. Events FALL and RIB FRACTURE and concomitant medication with ACETYLSALICYLIC ACID could be potentially cofounders/cofactors to events HAEMOTHORAX and CONTUSION. Swiss affiliate comment: This spontaneous HCP report from [REDACTED] was retrieved from literature screening and concerns one 86-year-old woman whose case was initially received from [REDACTED]. The literature report provides significant follow-up information (Ref.: Cittone MG, Battagay R, Condoluci A, Terzi di Bergamo L, Fernandes E, Galfetti E, Nosedà R, Leuppi-Taegtmeier A, Drexler B, Ceschi A, Tsakiris DA, Berger CT, Favre G, Martin T, Korte W, Graf L, Martinez								

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	M, Gerber B. The statistical risk of diagnosing coincidental acquired hemophilia A following anti-SARS-CoV-2 vaccination. J Thromb Haemost. 2021 Jun 8. doi: 10.1111/jth.15421. Epub ahead of print. PMID: 34101973). The patient presented with increasing shortness of breath days after an incidental fall with chest and shoulder contusion. She had received the second dose of the Moderna COVID-19 (mRNA-1273) vaccine 3 weeks prior to the fall. Her past medical history was remarkable for moderate to severe aortic valve stenosis treated non-surgically and pacemaker implantation for third-degree atrioventricular block. The patient was treated with low-dose aspirin. A chest CT scan revealed right-sided hemothorax and fractures of ribs 9–11. A chest drain was placed leading to a large subcutaneous effusion. Laboratory hemostasis tests showed a regular PT but a prolongation of the APTT, with an APTT mixing study typical for a delayed-acting inhibitor of coagulation. FVIII:C was 23%, and a low-titer FVIII inhibitor of 1.01 BU/ml was detected. Anti-SARS-CoV-2 spike IgG titer was 150 BAU/ml. A 3-day treatment first with rFVIIa, and later with APCC was needed to control local bleeding and to remove the chest drain. The further course was uneventful and after 17 days of treatment with oral prednisone (1 mg/kg) FVIII:C increased to 178%. An extensive screening for cancer, chronic infectious diseases, and autoimmune diseases other than AHA was negative and the patient was discharged. Company's assessment: Based on current available information and temporal association between the use of the product and the start date of the event, a causal relationship cannot be excluded. Local [REDACTED] assessment: acquired hemophilia A (onset latency: less than a month after the first dose; no other identifiable causes of AHA) [unlabeled / missing information in patient with possible individual risk factors, personal or family history of blood clotting diseases not reported]. In the Moderna g								

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	This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired haemophilia) in a 72-year-old female patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for COVID-19 vaccination. No Medical History information was reported. On 30-Mar-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form. In April 2021, the patient experienced ACQUIRED HAEMOPHILIA (Acquired haemophilia) (seriousness criteria hospitalization and medically significant). The patient was hospitalized on sometime in April 2021 due to ACQUIRED HAEMOPHILIA. At the time of the report, ACQUIRED HAEMOPHILIA (Acquired haemophilia) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In April 2021, Acquired factor VIII deficiency: negative (Negative) Negative. In April 2021, Activated partial thromboplastin time: 184 Second (High) 184. The action taken with mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) was unknown. For mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular), the reporter considered ACQUIRED HAEMOPHILIA (Acquired haemophilia) to be unlikely related. Concomitant medication information was not provided. Treatment medication information was not provided. There is no translation making evaluation difficult and this has been requested. Based on current available information and the temporal association between product use and the start date of the event a causal relationship cannot be excluded. Most recent FOLLOW-UP information incorporated above includes: On 01-Jul-2021: Translation received on 06-JUL-2021 and updated lab result.	Prolonged: 184s	No result	Factor VIII deficiency: negative	No result	Insufficient evidence to meet case definition of AH	Conditional	This regulatory authority reported case concerns a 72-year-old female patient with no reported medical history and concomitant medication, who received dose 1 Spikevax and on an unknown day post vaccine, experienced unspecified symptoms and assessed as a case of interest AHA. Diagnostic results: prolonged aPTT, FVIII deficiency - negative. This case is missing relevant information including medical history and concomitant medication, and has insufficient evidence to meet case definition of AH. According to WHO-UMC causality assessment, this case is assessed as Conditional. More information needed for proper assessment	

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This literature-non-study case was reported in a literature article and describes the occurrence of ACQUIRED VON WILLEBRAND'S DISEASE (Recurrent AvWD), ACQUIRED HAEMOPHILIA (Acquired hemophilia A), BLOOD LOSS ANAEMIA (Admitted for Blood loss anemia) and MELAENA (On day 7, she developed persistently melanotic stool) in a 76-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. LITERATURE REFERENCE: Portuguese A J, Sunga C, Kruse-Jarres R, Gernsheimer T, Ahkowitz J. Autoimmune-and complement-mediated hematologic condition recrudescence following SARS-CoV-2 vaccination. Blood Adv. 2021;5(13):2794-8 The patient's past medical history included Ecchymoses (multiple episodes of large, upper extremity), Paraesophageal hiatal hernia and Nissen fundoplication (status post recent uncomplicated). Concurrent medical conditions included Asthma and Raynaud's phenomenon. On an unknown date, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On an unknown date, received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On an unknown date, the patient experienced ACQUIRED VON WILLEBRAND'S DISEASE (Recurrent AvWD) (seriousness criteria hospitalization and medically significant), ACQUIRED HAEMOPHILIA (Acquired hemophilia A) (seriousness criteria hospitalization and medically significant), BLOOD LOSS ANAEMIA (Admitted for Blood loss anemia) (seriousness criteria hospitalization and medically significant), MELAENA (On day 7, she developed persistently melanotic stool) (seriousness criterion medically significant), ECCHYMOSIS (After dose 2, On day 4 she developed large ecchymoses covering most of her upper extremities) and PRESYNCOPE (On day 15 she presented to the emergency department with presyncope). The patient was hospitalized for 28 days due to ACQUIRED HAEMOPHILIA, ACQUIRED VON WILLEBRAND'S DISEASE and BLOOD LOSS ANAEMIA. The patient was treated with METHYLPREDNISOLONE for Adverse event, at a dose of 125 milligram every six hours; METHYLPREDNISOLONE for Adverse event, at a dose of 125 milligram twice a day; PREDNISONE for Adverse event, at a dose of 50 milligram twice a day and PREDNISONE for Adverse event, at a dose of 50 milligram once a day. At the time of the report, ACQUIRED VON WILLEBRAND'S DISEASE (Recurrent AvWD), ACQUIRED HAEMOPHILIA (Acquired hemophilia A), BLOOD LOSS ANAEMIA (Admitted for Blood loss anemia), MELAENA (On day 7, she developed persistently melanotic stool), ECCHYMOSIS (After dose 2, On day 4 she developed large ecchymoses covering most of her upper extremities) and PRESYNCOPE (On day 15 she presented to the emergency department with presyncope) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In 2021, Activated partial thromboplastin time: 122 Second (High) 122 s; mildly prolonged.	aPTT: prolonged 122s	Factor VIII inhibitor: detected (11.2 Bethesda units (BUs)	Anti factor VIII antibody test: high. Von Willebrand's factor activity test: abnormal	SARS-CoV-2 test: negative	AHA & AvWD	Possible	This literature-non-study case concerns a 76-year-old female patient with past medical history including ecchymoses, concurrent medical conditions including Raynaud syndrome. Concomitant medications not provided. The patient received dose 2 Spikevax and 4 days post vaccine, experienced large ecchymoses covering most of her upper extremities and by day 7 had persistent melena and anemia. Diagnostic tests: prolonged aPTT, high anti factor VIII antibody test, Von Willebrand's factor activity test: abnormal. Assessed as recurrent acquired Von Willebrand's disease (AvWD) and acquired hemophilia A. Treated with IgG & vWF/FVIII replacement therapy and events improved. Outcome unknown. This case is classified as AHA/vWD complex based on abnormal anti FVIII and vWF. According to WHO-UMC causality assessment, this case is assessed as Possible based on temporal association. However, the history of ecchymoses and Raynaud syndrome are strong confounders that provide plausible explanations for alternative etiology.	

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
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	In 2021, Anti factor VIII antibody test: high (High) High; uprending and less than 3 (Inconclusive) less than 3 percent. In 2021, Coagulation time: prolonged (Inconclusive) abnormalities illustrates a durable immune response and highlights the utility of corticosteroids in eliminating an autoantibody inhibitor. In 2021, Electrophoresis protein: monoclonal protein was not detected (Inconclusive) Monoclonal protein was not detected. In 2021, International normalised ratio: 1.5 (Inconclusive) 1.5. In 2021, Platelet aggregation test: abnormal (abnormal) abnormal ristocetin. In 2021, SARS-CoV-2 test: negative (Negative) negative. In 2021, Von Willebrand's factor activity test: abnormal (abnormal) showed a normal pattern and distribution of bands, consistent with a quantitative vWF deficiency, high (High) High; uprending, 5 (Inconclusive) 5 percent and less than 3 percent (Inconclusive) less than 3 percent. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter considered ACQUIRED VON WILLEBRAND'S DISEASE (Recurrent AvWD), ACQUIRED HAEMOPHILIA (Acquired hemophilia A), BLOOD LOSS ANAEMIA (Admitted for Blood loss anemia), MELAENA (On day 7, she developed persistently melanotic stool), ECCHYMOSIS (After dose 2, On day 4 she developed large ecchymoses covering most of her upper extremities) and PRESYNCOPE (On day 15 she presented to the emergency department with presyncope) to be possibly related. Concomitant medications were not provided by the reporter. The patient was diagnosed with recurrent Acquired Von Willebrand's disease (AvWD) and acquired hemophilia A, presumed to be due to an antibody directed against the Factor (FVIII)/von Willebrand factor (vWF) complex. After dose 2 on days 17 to 19, vWF/FVIII replacement therapy was provided with Humate-P 2290 International unit (U) every 12 hours x 4 doses.Reduction of factor inhibitors was achieved using IV immunoglobulin (IVIg) and corticosteroids as follows: IVIg1g/kg on days 18 and19. On an unknown date lab test included were A factor VIII inhibitor was detected and quantified as 11.2 Bethesda units (BUs) also on days 19 and 26, levels were 1.6 BUs and 0.5 BUs respectively. It was thought to had triggered a flare of an underlying autoimmune- or complement-mediated hematologic condition.The rapid normalization of FVIII and vWF activity after administration of Intravenous immunoglobulin (IVIg) was suggestive of an IgG antibody-mediated process against endogenous and exogenous FVIII/vWF complex. This case was linked to [REDACTED] (Patient Link). Most recent FOLLOW-UP information incorporated above includes: On 26-Jul-2021: Email with FTA received from SARA team and does not contain any new information. On 28-Jul-2021: Email with FTA received from SARA team and does not contain any new information.								

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired hemophilia A with anti factor VIII) in an 88-year-old female patient who received mRNA-1273 (COVID 19 Vaccine Moderna) (batch nos. 3001653 and 3000493) for COVID-19 vaccination. The patient's past medical history included Zona. Concurrent medical conditions included Dyslipidemia, Hypertension arterial, Depression, Ulcer gastric, Breast cancer, Anxiety state and Penicillin allergy. On 12-Mar-2021, the patient received first dose of mRNA-1273 (COVID 19 Vaccine Moderna) (unknown route) 1 dosage form. On 09-Apr-2021, received second dose of mRNA-1273 (COVID 19 Vaccine Moderna) (intramuscular) dosage was changed to 2 dosage form. On 15-Jun-2021, after starting mRNA-1273 (COVID 19 Vaccine Moderna), the patient experienced ACQUIRED HAEMOPHILIA (Acquired hemophilia A with anti factor VIII) (seriousness criteria hospitalization and medically significant). At the time of the report, ACQUIRED HAEMOPHILIA (Acquired hemophilia A with anti factor VIII) was resolving. For mRNA-1273 (COVID 19 Vaccine Moderna) (Unknown), the reporter did not provide any causality assessments. No concomitant medications were given by the reporter. No Treatment information were provided by the reporter. This case concerns an 88-year-old female hospitalized with a serious unexpected event of acquired hemophilia A with anti-factor VIII. Event latency 95 days after first dose and 67 days after second dose mRNA-1273. Event resolving. Based on current available information and temporal association between the use of the product and the start date of the event, a causal relationship cannot be excluded.	No result	No result	No result	No result	Insufficient evidence to meet case definition of AH	Unassessable	This regulatory authority reported case concerns an 88-year-old female patient with concurrent medical conditions included breast cancer, no reported concomitant medication; who received dose 2 Spikevax and 67 days post vaccine, experienced unspecified symptoms and assessed as a case of interest AHA. Diagnostic results: none provided. No Treatment information were provided. Event was resolving at time of report. This case is missing relevant information including concomitant medication and diagnostic results. There is insufficient evidence to meet case definition of acquired hemophilia (AH). According to WHO-UMC causality assessment, this case is assessed as Unassessable due to insufficient information that cannot be supplemented. The history of breast cancer is a strong confounder.	

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 17-Sep-2021 and was forwarded to Moderna on 17-Sep-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA [REDACTED] in a 63-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included HER2 positive breast cancer in 2015 and Nephrectomy in 2018. Concurrent medical conditions included Hypertension and Arthropathy psoriatic. On 14-Jun-2021, the patient received second dose of mRNA-1273 (Spikevax) (Subcutaneous) 1 dosage form. On 14-Jun-2021, the patient experienced INCORRECT ROUTE OF PRODUCT ADMINISTRATION (Incorrect Route of Product administration). On 16-Jun-2021, the patient experienced ACQUIRED HAEMOPHILIA [REDACTED] (seriousness criterion medically significant). On 14-Jun-2021, INCORRECT ROUTE OF PRODUCT ADMINISTRATION (Incorrect Route of Product administration) had resolved. At the time of the report, ACQUIRED HAEMOPHILIA [REDACTED] had not resolved. The action taken with mRNA-1273 (Spikevax) (Subcutaneous) was unknown. For mRNA-1273 (Spikevax) (Subcutaneous), the reporter did not provide any causality assessments. No relevant concomitant and treatment medications were reported. Company Comment: This case concerns a 63 year-old female patient with history of nephrectomy, HER2 positive breast cancer and psoriatic arthropathy who experienced the unexpected event of Acquired haemophilia. The event occurred 2 days after the most recent unspecified dose of mRNA-1273 vaccine. Additional unexpected event of Incorrect Route of product administration was added. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 17-Sep-2021: Translation Received on 23 SEP 2021, includes Dose Information.	No result	No result	No result	No result	Insufficient evidence to meet case definition of AH	Unassessable	This regulatory authority reported case concerns a 63 year-old female patient with history of HER2 positive breast cancer, nephrectomy and psoriatic arthropathy; no reported concomitant medication; who received dose 2 Spikevax and 2 days post vaccine, experienced unspecified symptoms and assessed as a case of interest AHA. Diagnostic results: none provided. No Treatment information were provided. Event was resolving at time of report. This case is missing relevant information including concomitant medication and diagnostic results. There is insufficient evidence to meet case definition of acquired hemophilia (AH). According to WHO-UMC causality assessment, this case is assessed as Unassessable due to insufficient information that cannot be supplemented. The history of breast cancer is a strong confounder.	

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	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 14-Oct-2021. The most recent information was received on 13-Jan-2022 and was forwarded to Moderna on 13-Jan-2022. This regulatory authority case was reported by a physician and describes the occurrence of FACTOR VIII DEFICIENCY (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia), ACQUIRED HAEMOPHILIA (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia.) and SPONTANEOUS HAEMATOMA (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia.) in a 59-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3001943) for COVID-19 vaccination. Concurrent medical conditions included Essential hypertension. On 14-May-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 01-Jun-2021, the patient experienced FACTOR VIII DEFICIENCY (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia) (seriousness criterion hospitalization), ACQUIRED HAEMOPHILIA (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia.) (seriousness criterion hospitalization) and SPONTANEOUS HAEMATOMA (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia.) (seriousness criterion hospitalization). At the time of the report, FACTOR VIII DEFICIENCY (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia), ACQUIRED HAEMOPHILIA (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia.) and SPONTANEOUS HAEMATOMA (Spontaneous hematomas. Finding of factor VIII discovered on Aug 06, 2021, acquired hemophilia.) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 06-Aug-2021, Activated partial thromboplastin time: inconclusive (Inconclusive) Inconclusive. On 09-Aug-2021, Coagulation factor VIII level: inconclusive (Inconclusive) Inconclusive. On 05-Oct-2021, Coagulation factor VIII level: inconclusive (Inconclusive) Inconclusive. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Concomitant product use was not provided by the reporter. No treatment information was provided. Patient sent to the Emergency Room due to spontaneous hematomas in the likely clinical picture of acquired hemophilia. The blood tests performed in the ER showed neutrophilic leukocytosis. The chest X-ray was negative for pleural-parenchymal lesions. After performing a swab	aPTT: inconclusive	No result	Coagulation factor VIII level was inconclusive.	Neutrophilic leukocytosis. CXR:negative for pleural-parenchymal lesions.	Inconclusive evidence to meet case definition of AH	Conditional	This regulatory authority reported case concerns a 59 year-old female patient with no relevant medical history and no concomitant medications reported, who received an unknown dose of Spikevax and 18 days post vaccine experienced spontaneous hematomas. Diagnostic tests were inconclusive. Assessed as acquired haemophilia, . Treated with steroids. Outcome was resolving. This case is classified as inconclusive. According to WHO-UMC causality assessment, this case is assessed as Conditional. More information needed for proper assessment	

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	for SARS-Cov2, the patient was admitted to Internal Medicine for treatment and evaluation of the case. Upon admission to the department, oral corticosteroid therapy was commenced. Company Comment: This case concerns a 59 year-old female patient with no relevant medical history, who experienced the unexpected serious events of Factor VIII deficiency, Acquired haemophilia, and Spontaneous haematoma. The events occurred 19 days after an unspecified dose of mRNA-1273 vaccine. The patient was sent to the emergency room for spontaneous hematomas. The chest x-ray was negative for pleuroparenchymal injuries, Activated partial thromboplastin time, Coagulation factor VIII level, Coagulation factor VIII level was inconclusive. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 14-Oct-2021: Translated document received on 18-Oct-2021, added translated event verbatim. On 19-Oct-2021: Additional follow-up received, added medical history and outcome of the events was updated. On 19-Oct-2021: Translation received for FU on 21-Oct-2021, with translated event reported by primary source, reporter's comments and sender's comments. Narrative updated accordingly. On 13-Jan-2022: Added lab data with results as inconclusive and updated suspect indication.								

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	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 19-Oct-2021 and was forwarded to Moderna on 19-Oct-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired haemophilia) in a 53-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3003610) for COVID-19 vaccination. Co-suspect product included non-company product ADALIMUMAB (HUMIRA) for Arthritis rheumatoid. The patient's past medical history included Breast reduction. Concurrent medical conditions included Obstructive sleep apnea hypopnea syndrome, Polyp colorectal, Tachycardia, Carpal tunnel syndrome, Asthma, Lumbar disc herniation, Gastric ulcer and Arthritis rheumatoid since 2016. Concomitant products included IVABRADINE HYDROCHLORIDE (PROCORALAN), TRAMADOL HYDROCHLORIDE (TRAMADOL ACTAVIS), PREGABALIN (LYRICA) and FLECAINIDE ACETATE [REDACTED] for an unknown indication. In 2016, the patient started ADALIMUMAB (HUMIRA) (Subcutaneous) 400 milligram every two months. On 29-Jun-2021, the patient received second dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 01-Jul-2021, the patient experienced ACQUIRED HAEMOPHILIA (Acquired haemophilia) (seriousness criteria hospitalization and medically significant). At the time of the report, ACQUIRED HAEMOPHILIA (Acquired haemophilia) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 05-Jul-2021, Haemoglobin: 13.4 billion per litre (normal) 13.4 billion per litre. On 28-Sep-2021, Haemoglobin: 8 billion per litre (Low) 8 billion per litre. On 02-Oct-2021, Haemoglobin: 9 billion per litre (Low) 9 billion per litre. On 25-Oct-2021, Haemoglobin: 10 billion per litre (Low) 10 billion per litre. mRNA-1273 (Spikevax) (Intramuscular) was withdrawn on an unknown date. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No treatment information provided. Company comment: This case concerns a 53-year-old female patient with medical history of Rheumatoid Arthritis, who experienced the serious unexpected event of Acquired haemophilia. The event occurred approximately 2 days after the second dose of the mRNA-1273. The rechallenge was not applicable. The medical history of Rheumatoid Arthritis remains a confounder considering that this autoimmune	No result	No result	No result		Insufficient evidence to meet case definition of AH	Unassessable	This regulatory authority reported case concerns a 53 year-old female patient with medical history of rheumatoid arthritis, taking adalimumab, who received dose 2 Spikevax and 2 days post vaccine, experienced unspecified symptoms and assessed as a case of interest AHA. Diagnostic results: none provided. No Treatment information were provided. Event was resolved at time of report. This case is missing relevant information including concomitant medication and diagnostic results. There is insufficient evidence to meet case definition of acquired hemophilia (AH). According to WHO-UMC causality assessment, this case is assessed as Unassessable due to insufficient information that cannot be supplemented. The history of rheumatoid arthritis and concomitant medication of adalimumab are strong confounder. AH is associated with adalimumab and rheumatoid arthritis in 4% to 8% of cases.	

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	disorder can co exist with the event. The benefit-risk relationship of the mRNA-1273 is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 19-Oct-2021: Translation received on 20-Oct-2021 contains No New Information(NNI). On 02-Nov-2021: Follow up report received contains no new information.								

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This case was initially received via European Medicines Agency (Reference number: [REDACTED] on 21-Oct-2021. The most recent information was received on 13-Jan-2022 and was forwarded to Moderna on 13-Jan-2022. This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Ecchymosis on right hemithorax and right elbow, acquired haemophilia, prolonged aPTT,), ECCHYMOSIS (Ecchymosis on right hemithorax and right elbow, acquired haemophilia, prolonged aPTT,) and ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED (Ecchymosis in right hemithorax and right elbow, acquired hemophilia, prolonged aPTT) in an 89-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3002186-12) for COVID-19 vaccination. Concurrent medical conditions included Arthrosis, Osteoporosis, Polymyalgia rheumatica, Chronic obstructive bronchopneumopathy, Hypertensive heart disease, Renal failure chronic (IRC stadio 3b), Sinus bradycardia and Monoclonal B-cell lymphocytosis (Monoclonal B-cell lymphocytosis). Concomitant products included ACETYLSALICYLIC ACID from an unknown date to 12-Aug-2021 for Hypertensive heart disease, FUROSEMIDE, TRAZODONE HYDROCHLORIDE, LANSOPRAZOLE, ALLOPURINOL, RAMIPRIL and DIGOXIN for an unknown indication. On 22-May-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) .5 milliliter. On 12-Aug-2021, the patient experienced ACQUIRED HAEMOPHILIA (Ecchymosis on right hemithorax and right elbow, acquired haemophilia, prolonged aPTT,) (seriousness criterion hospitalization), ECCHYMOSIS (Ecchymosis on right hemithorax and right elbow, acquired haemophilia, prolonged aPTT,) (seriousness criterion hospitalization) and ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED (Ecchymosis in right hemithorax and right elbow, acquired hemophilia, prolonged aPTT) (seriousness criterion hospitalization). At the time of the report, ACQUIRED HAEMOPHILIA (Ecchymosis on right hemithorax and right elbow, acquired haemophilia, prolonged aPTT,), ECCHYMOSIS (Ecchymosis on right hemithorax and right elbow, acquired haemophilia, prolonged aPTT,) and ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED (Ecchymosis in right hemithorax and right elbow, acquired hemophilia, prolonged aPTT) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 20-Aug-2021, Activated partial thromboplastin time: negative (Negative) NEGATIVE. On 20-Aug-2021, C-reactive protein: negative (Negative) NEGATIVE. On 20-Aug-2021, Haematocrit: negative (Negative) NEGATIVE. On 20-Aug-2021, Haemoglobin: negative (Negative) NEGATIVE. On 21-Aug-2021, Fibrin D dimer: negative (Negative) NEGATIVE. On 23-Aug-2021, Coagulation factor VIII level: negative (Negative) NEGATIVE.	aPTT: prolonged	No result	Coagulation factor VIII level: negative	AHA	Unlikely	This regulatory authority reported case concerns an 89-year-old female subject, with a medical history of polymyalgia rheumatica, HHD, CKD and concomitant medication including ASA, and antihypertensive, who received an unknown dose of Spikevax and 89 post vaccine experienced ecchymosis in right hemithorax and assessed as acquired hemophilia. Diagnostic tests: prolonged aPTT, FVIII "negative". The event had resolved at the time of report. This case is classified as acquired hemophilia A (AHA) based on FVIII deficiency and prolonged aPTT. According to the WHO-UMC causality assessment, this case is assessed as Unlikely related to the product due to the long latency time. Comorbidities including Polymyalgia rheumatica, and the use of ASA are strong confounders and provides plausible explanation.		

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	For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No treatment information was provided. Company comment: This case concerns an 89-year-old female subject, with medical history of Polymyalgia rheumatica, Hypertensive heart disease, Renal failure chronic (IRC stadio 3b), Monoclonal B-cell lymphocytosis and user of polypharmacy, who experienced the serious unexpected events of ECCHYMOSIS in right hemithorax and ACQUIRED HAEMOPHILIA that lead to hospitalization. The events occurred approximately 3 months after the administration of a dose of Moderna COVID-19 vaccine (dose number unknown). The rechallenge was not applicable. Patient's medical history of elderly, Hypertensive heart disease, Renal failure chronic (IRC stadio 3b), Monoclonal B-cell lymphocytosis and user of polypharmacy, remains as confounders. The benefit-risk relationship of Moderna COVID-19 vaccine Vaccine is not affected by this report Most recent FOLLOW-UP information incorporated above includes: On 29-Oct-2021: Translated document received on 04 Nov 2021, contains no new information On 13-Jan-2022: Follow up received on 13Jan2022 which included lab data with results. Indication updated. Narrative updated.								

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 22-Oct-2021 and was forwarded to Moderna on 22-Oct-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired hemophilia) in a 90-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 3002616) for COVID-19 vaccination. The patient's past medical history included Paresthesia, Pain NOS (pain of deafferentation), Hypoesthesia (sequellar hypoesthesia), Bilateral cataracts (1998 bilaterally cataract) in 1998, Sympathectomy (ETS) and TURP (prostate TURP for adenoma: 2010) in 2010. Previously administered products included for Product used for unknown indication: Metformin from March 2019 to 2021. Past adverse reactions to the above products included No adverse event with Metformin. Concurrent medical conditions included Systemic lupus erythematosus (Acute Hexamine-induced disseminated lupus erythematosus in 1998) since 1998, Ischemic stroke (right middle cerebral artery 2007 ischemic stroke) since 2007, Dilated cardiomyopathy (dilated cardiomyopathy (Jul-2010)) since July 2010, Atrioventricular block (first degree AVB), Carotid artery stenosis (ETS a left internal carotid stenosis 65%. perfect on the right), Type 2 diabetes mellitus (type 2 diabetes discovered Jan-2012) since January 2012, Renal failure (severe renal failure failure: clearance 26 mL/min Aug-2014) since August 2014, Chronic interstitial nephritis (Chronic interstitial nephropathy), Nephroangiosclerosis, Idiopathic thrombocytopenic purpura (Idiopathic thrombocytopenic purpura 1994) since 1994, Osteoarthritis of lumbar spine (Long-duration condition lumbar osteoarthritis Sep-2017) since September 2017, Hypoacusis, Hearing aid user (Hypoacusis with hearing aid), Parapsoriasis (cutaneous parapsoriasis Nov-2013) since November 2013, Gonarthrosis (bilateral gonarthrosis predominantly to the left Apr-2019) since April 2019, Aseptic necrosis of head and neck of femur (Right THR: post-cortisone aseptic necrosis of the femoral head) and Prostate adenoma. On 04-Jun-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 06-Jun-2021, the patient experienced ACQUIRED HAEMOPHILIA (Acquired hemophilia) (seriousness criteria hospitalization and medically significant). At the time of the report, ACQUIRED HAEMOPHILIA (Acquired hemophilia) was resolving. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medication were provided. No treatment information were given. On an unspecified date lab tests included complete tBB, HBAG and ESV, however results were not provided. Patient had no allergies. This is a regulatory authority case concerning a 90-year-old male patient with relevant medical history of Systemic lupus erythematosus who experienced serious unexpected event of Acquired hemophilia. The event occurred approximately 3 days after a dose of mRNA-1273. it was not specified whether adverse events occurred after the first or second	No result	No result	No result		Insufficient evidence to meet case definition of AH	Unassessable	This regulatory authority reported case concerns a 90-year-old male patient with relevant medical history of Systemic lupus erythematosus and prostate cancer, with no reported concomitant medications, who received an unknown dose of Spikevax and 2 days post vaccine experienced unspecified symptoms and was assessed as a case of interest AHA . Diagnostic results: none provided. No Treatment information were provided. Event was resolving at the time of report. This case is missing relevant information including concomitant medication and diagnostic results. There is insufficient evidence to meet the case definition of acquired hemophilia (AH). According to WHO-UMC causality assessment, this case is assessed as Unassessable due to insufficient information that cannot be supplemented. The history of SLE and prostate cancer are strong confounder.	

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	dose. Rechallenge is not applicable since it cannot be assessed. Medical history of Systemic lupus erythematosus remains a confounder. The benefit-risk relationship of mRNA-1273 is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 22-Oct-2021: Translation received on 26-Oct-2021 included medical history and narrative information were updated.								

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 26-Nov-2021 and was forwarded to Moderna on 26-Nov-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired hemophilia A with anti factor VIII)) and CEREBRAL HAEMATOMA (Cerebral hematoma) in a 76-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. Co-suspect product included non-company product FLUINDIONE (PREVISCAN [FLUINDIONE]) for Thrombosis venous deep. Concurrent medical conditions included Deep vein thrombosis and Hypertension arterial. On 09-Aug-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On an unknown date, the patient started FLUINDIONE (PREVISCAN [FLUINDIONE]) (Oral) 10 milligram once a day. On 11-Oct-2021, after starting mRNA-1273 (Spikevax), the patient experienced CEREBRAL HAEMATOMA (Cerebral hematoma) (seriousness criteria hospitalization and life threatening). On 15-Oct-2021, the patient experienced ACQUIRED HAEMOPHILIA (Acquired hemophilia A with anti factor VIII)) (seriousness criteria hospitalization and life threatening). At the time of the report, ACQUIRED HAEMOPHILIA (Acquired hemophilia A with anti factor VIII)) and CEREBRAL HAEMATOMA (Cerebral hematoma) was resolving. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Treatment information was not provided. Company comment: This regulatory authority case concerns a 76-year-old male patient with a history of Deep vein thrombosis undergoing treatment with co-suspect Previscan (Fluinidione), who experienced the unexpected serious (life-threatening and hospitalization) events of Cerebral haematoma and Acquired haemophilia A with anti factor VIII after mRNA- 1273 Moderna vaccine. The event Cerebral haematoma occurred approximately 2 months and 2 days after the first dose of mRNA- 1273 vaccine and Acquired haemophilia A with anti factor VIII was diagnosed 4 days later. Very limited information is available regarding clinical course. The events could be in connection with each other. Moreover, co-suspect Previscan (Fluinidione) may have contributed to Cerebral haemorrhage. The rechallenge is not applicable since only information about the first dose was disclosed. The benefit-risk relationship of mRNA- 1273 vaccine is not affected by this report Most recent FOLLOW-UP information incorporated above includes: On 26-Nov-2021: Translated document received on 30 Nov 2021 include translated suspect medication information.	No result	No result	anti-factor VIII		Insufficient evidence to meet case definition of AH	Unlikely	his regulatory authority case concerns a 76-year-old male patient with a history of deep vein thrombosis been treated with Previscan (Fluinidione), who received dose 1 Spikevax and 63 days post vaccine, experienced cerebral haematoma and was assessed as acquired haemophilia A with anti-factor VIII 4 days later. Very limited information is available regarding the clinical course and diagnostic tests. This case has insufficient evidence to meet the case definition of AH. According to the WHO-UMC causality assessment, this case is assessed as Unlikely due to the long latency time. The use of Fluindione for DVT provides plausible explanations.	

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	This literature-non-study case was reported in a literature article and describes the occurrence of ACQUIRED HAEMOPHILIA (acquired haemophilia) in a 70-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. LITERATURE REFERENCE: Lemoine C, Giacobbe AG, Bonifacio E, Karapetyan L, Seaman C. A case of acquired haemophilia in a 70-year-old post COVID-19 vaccine. Haemophilia. 2022;28 (1):e15-7 The patient's past medical history included Polymyalgia rheumatica and Hepatitis C (hepatitis C virus with spontaneous clearance). Concomitant products included SULFAMETHIZOLE; TRIMETHOPRIM for Pneumocystis jirovecii prophylaxis. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, after starting mRNA-1273 (Moderna COVID-19 Vaccine), the patient experienced ACQUIRED HAEMOPHILIA (acquired haemophilia) (seriousness criteria hospitalization and medically significant). The patient was treated with PREDNISONE ongoing since an unknown date for Adverse event, at a dose of 1 milligram/kilogram once a day; PREDNISONE ongoing since an unknown date for Adverse event, at a dose of 10 milligram once a day; CYCLOPHOSPHAMIDE for Adverse event, at a dose of 2 milligram/kilogram once a day and ACETYLSALICYLIC ACID, CAFFEINE, PARACETAMOL (EXCEDRIN [ACETYLSALICYLIC ACID; CAFFEINE; PARACETAMOL]) for Adverse event, at a dose of 1500 milligram once a day. At the time of the report, ACQUIRED HAEMOPHILIA (acquired haemophilia) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Activated partial thromboplastin time (23-38): 57.5 seconds (High) 57.5 seconds. On an unknown date, Angiogram: arterial vasculature Upper extremity CT angiogram with and without intravenous contrast showed patent right upper extremity arterial vasculature without evidence of arterial injury. On an unknown date, Body temperature: afebrile Afebrile. On an unknown date, C-reactive protein: 3.2 mg/dl (High) 3.2 mg/dl. On an unknown date, Coagulation factor IX level (0.60-1.50): 1.5iu/ml 1.5IU/ml. On an unknown date, Coagulation factor VIII level (0.60-2.50): 0.03iu/ml 0.03IU/ml and 0.07 iu/ml FVIII activity was increased to .07 IU/ml. On an unknown date, Coagulation factor XI level (0.60-1.40): 0.85 iu/ml 0.85 IU/ml. On an unknown date, Coagulation factor XII level (0.40-1.40): 0.95 iu/ml 0.95 IU/ml. On an unknown date, Factor VIII inhibition: 39.9 bu 39.9 BU Normal: less than or equal to 0.4 and 11.4 bu FVIII inhibitor was decreased to 11.4 BU. On an unknown date, Neutrophil count: 79 percent 79 percent.	aPTT prolonged: 57.5 s	Factor VIII inhibition: high (39.9 bu)	Coagulation factor VIII deficiency	C-reactive protein: high, Prothrombin time: high	AHA	Possible	This literature non-study case concerns a 70-year-old male patient with a medical history of polymyalgia rheumatica, hepatitis c virus, concomitant medication included sulfamethizole; who received dose 1 Spikevax and day 2 post-vaccine experienced progressive extensive ecchymosis from his right shoulder to the elbow and extending to his hand. Diagnostic tests: prolonged aPTT, FVIII deficiency, high Factor VIII inhibition. Assessed as AHA and treated with steroids. At the time of reporting the event had resolved. This case is assessed as AHA based on prolonged aPTT and FVIII C deficiency. The patient's medical history of hepatitis c infection, Polymyalgia rheumatica are strong confounders. According to the WHO-UMC causality assessment, this case is assessed as Possible based on temporal association. However, the history of hepatitis c virus, use of sulfamethizole are strong confounders that provide plausible explanations for alternative etiology.	

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	On an unknown date, Physical examination: abnormal Physical examination was notable for extensive ecchymosis from his right shoulder to right hand with preserved range of motion and sensation. Distal pulses were present and symmetric in both extremities and swelling had markedly decreased from pictures taken earlier in the week. Ecchymoses were also noted on his left forearm (4 × 1 inches) and right lower extremity (3 × 3 inches). On an unknown date, Prothrombin time (9.4-11.2): 13.5 seconds (High) 13.5 seconds. On an unknown date, Red blood cell sedimentation rate: 75 mm/h (High) 75 mm/h. On an unknown date, White blood cell count: 22.2×10^9 per 122.2×10^9 per L. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered ACQUIRED HAEMOPHILIA (acquired haemophilia) to be related. Patient presented with extensive right upper extremity bruising. He was in his usual state of health when he received the vaccine. On the same day of vaccine, he developed arm soreness at the injection site, and 2 days after, he noticed an ecchymosis on his right shoulder. The ecchymosis progressed distally over the following days reaching his elbow on day four and extending to his hand on day five, despite no additional trauma to the area. The expanding ecchymosis was associated with right arm swelling, soreness, tightness, and limited range of motion. By day seven, the swelling and range of motion in his right hand started to improve, but he developed a new ecchymosis on his left forearm. CC: This literature non-study case concerns a 70-year-old male patient with medical history of Polymyalgia rheumatica, hepatitis c virus, experienced the unexpected serious event acquired haemophilia in association with mRNA-1273. The event occurred 8 days after the first dose of mRNA-1273. The patient had developed bruising in right upper extremity. Patient treated with PREDNISONE ,CYCLOPHOSPHAMID, ACETYLSALICYLIC ACID, CAFFEINE, PARACETAMOL. Activated partial thromboplastin was elevated , C-reactive protein was high, Prothrombin time was high , At the time of reporting the event had resolved. The patient's medical history of hepatitis c infection, Polymyalgia rheumatica could be contributory. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 27-Jan-2022: Follow up received by safety 27-Jan-2022 included an Email with FTA received from SARA team and contains Significant information regarding Lab data, medical history, treatment and event details								

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	This literature-non-study case was reported in a literature article and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired hemophilia A) and PEMPHIGOID (Bullous pemphigoid) in a 77-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 939599-CDC) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. LITERATURE REFERENCE: Fu PA, Chen CW, Hsu YT, Wei KC, Lin PC, Chen TY. A case of acquired hemophilia A and bullous pemphigoid following SARS-CoV-2 mRNA vaccination. J Formos Med Assoc:1-5 The patient's past medical history included Nasopharyngeal carcinoma (in complete remission) in 2015. Concurrent medical conditions included Hypertension, Dyslipidemia and Diabetes mellitus. Concomitant products included GLIMEPIRIDE and LINAGLIPTIN for Diabetes mellitus, AMLODIPINE for Hypertension. On 03-Jul-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) .5 milligram. On 17-Aug-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to .25 milligram. On 17-Aug-2021, the patient experienced UNDERDOSE (0.25ml administered as second dose) and INAPPROPRIATE SCHEDULE OF PRODUCT ADMINISTRATION (Inappropriate schedule of vaccine administered). On 07-Sep-2021, after starting mRNA-1273 (Moderna COVID-19 Vaccine), the patient experienced PEMPHIGOID (Bullous pemphigoid) (seriousness criterion medically significant). On 13-Sep-2021 at 12:06 PM, the patient experienced ACQUIRED HAEMOPHILIA (Acquired hemophilia A) (seriousness criteria hospitalization and medically significant). The patient was hospitalized from 14-Sep-2021 to 29-Sep-2021 due to ACQUIRED HAEMOPHILIA. The patient was treated with PREDNISOLONE for Acquired hemophilia, at a dose of 1 microgram/kilogram once a day; CYCLOPHOSPHAMIDE (oral) for Acquired hemophilia, at a dose of 100 microgram once a day; FACTOR VIII INHIBITOR BYPASSING FRACTION (FEIBA) for Adverse event, at a dose of 90 microgram/kilogram; IMMUNOGLOBULINS NOS (IMMUNOGLOBULIN I.V) (intravenous) for Adverse event, at an unspecified dose and frequency and RITUXIMAB for Adverse event, at an unspecified dose and frequency. On 14-Sep-2021, PEMPHIGOID (Bullous pemphigoid) had resolved. On 23-Feb-2022, ACQUIRED HAEMOPHILIA (Acquired hemophilia A) had resolved. At the time of the report, UNDERDOSE (0.25ml administered as second dose) and INAPPROPRIATE SCHEDULE OF PRODUCT ADMINISTRATION (Inappropriate schedule of vaccine administered) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Activated partial thromboplastin time (29.3 s-40.1 s): 97.3 s (High) severe prolongation of the activated partial thromboplastin time. On an unknown date, Anti-platelet factor 4 antibody test (Unknown-<0.4od): 0.745 optical density (od) (High) weak positive (0.745 optical density (OD) value..	aPTT prolongation	lupus anticoagulants (normal)	Coagulation factor VIII level: 0.6%	Skin biopsy: sub-epidermal blistering with fibrin and abundant neutrophils and linear deposition of IgG and C3 at the dermis-epidermis junction, consistent with bullous pemphigoid	AHA	Possible	This literature-non-study case concerns a 77-year-old male patient with a past medical history including nasopharyngeal carcinoma, and concurrent medical conditions including Hypertension, Dyslipidemia and Diabetes mellitus. Concomitant medication included GLIMEPIRIDE and LINAGLIPTIN and amlodipine, who received dose 2 Spikevax and 27 days post vaccine experienced unspecified symptoms of "acquired hemophilia A" and PEMPHIGOID (Bullous pemphigoid). Diagnostic tests: prolonged aPTT, FVIII C deficiency. This case is assessed as AHA based on prolonged aPTT, and FVIII C deficiency. According to WHO-UMC causality assessment, this case is assessed as Possible based on temporal association. However, a strong confounder includes nasopharyngeal carcinoma, that provides alternative etiology.	

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	On an unknown date, Biopsy skin: subepidermal blistering and abundant neutrophils (abnormal) subepidermal blistering with fibrin and abundant neutrophils. On an unknown date, Coagulation factor IX level: 117.6% 117.6%. On an unknown date, Coagulation factor VIII level: 0.6% 0.6%. On an unknown date, Factor VIII inhibition: 71.6bu 71.6BU. On an unknown date, Haemoglobin (13 g/dl-18 g/dl): 9.4 g/dl (Low) 9.4 g/dL (Normocytic anemia). On an unknown date, Immunology test: linear deposition of igg and c3 at the dermis epid (abnormal) Linear deposition of IgG and C3 at the dermis epidermis junction and negative (Negative) Negative for anti-ICS and anti-BMZ antibodies. On an unknown date, Mean cell volume (81 fl-98 fl): 91 fl (normal) 91 fL. On an unknown date, Physical examination: no relevant findings except for the ecchymoses (abnormal) No relevant findings except for the ecchymoses. On an unknown date, Platelet count (143 x10³/micro litre-349 x10³/micro litre): 200 x10³/micro litre (normal) 200x10³/micro litre. On an unknown date, Prothrombin time (9.4 s-12.5 s): 11.9 s (normal) 11.9 s. On an unknown date, Russell's viper venom time: did not show lupus anticoagulants (normal) Did not show lupus anticoagulants. On an unknown date, Von Willebrand's factor activity test: 230% (High) Elevated 230%. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter considered ACQUIRED HAEMOPHILIA (Acquired hemophilia A) and PEMPHIGOID (Bullous pemphigoid) to be related. No further causality assessments were provided for UNDERDOSE (0.25ml administered as second dose) and INAPPROPRIATE SCHEDULE OF PRODUCT ADMINISTRATION (Inappropriate schedule of vaccine administered). Company comment: This is a literature-non-study case concerning a 77-year-old male patient with no reported medical history, who experienced the serious unexpected events acquired hemophilia A (AHA) and bullous pemphigoid, three weeks after receiving the second dose of mRNA-1273. Patient presented with multiple ecchymoses at bilateral forearms and legs and hemorrhagic blisters and papules at this hands and trunk. Skin biopsy was performed, and was hospitalized due to progression of the ecchymoses and persistent bleeding from the skin biopsy site. Positive findings at laboratory included: severe prolongation of the aPTT (93 s), aPTT mixing study prolonged with incubation, von Willebrand factor function elevated (230%), FVIII activity lowered (0.6%)and FVIII inhibitor titer 71.6 BU. AHA was diagnosed and started treatment with prednisolone 1 mg/kg/day and two doses of FVIII inhibitor bypassing activity (FEIBA) of recombinant factor VII activated (rFVIIa) at the dose of 90 mcg/kg. There was no major bleeding after the start of prednisolone treatment. Oral Cyclophosphamide was added due to persisten aPTT prolongation after one week of prednisolone with an improvement after 4 weeks treatment. Skin biopsy showed sub-epidermal blistering with fibrin and abundant neutrophils and linear deposition of IgG and C3 at the dermis-epidermis junction, consistent with bullous pemphigoid diagnose. The benefit-risk relationship of mRNA-1273 is not affected by this report.								

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	The patient had bruises and ecchymosis on bilateral upper limbs (elbow and wrist) and lower limbs (ankle and toe) for around two weeks before the admission. Also noted some hemorrhagic bullae and trunk skin rash. Acquired hemophilia A was controlled from around Jan-2022. Currently there is no signs of disease recurrence. Meanwhile, during the use of prednisolone, there is no flare up of bullous pemphigoid. Most recent FOLLOW-UP information incorporated above includes: On 31-Mar-2022: Follow up received by safety on 01-APR-2022 has Email with FTA received from SARA team and contains significant information: Reporter information, Patient details, Lab data, Product and event details updated. On 09-Apr-2022: Follow up received by safety on 11-Apr-2022 from SARA team and contains significant information: reporter address, patient details (initials, height, weight, ethnicity and race), events, event outcome, dose details, medical history, concomitant medications, lab details and other treatment medications were updated.								

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	This literature-non-study case was reported in a literature article and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired Hemophilia A with anti factor VIII) and PLEOMORPHIC MALIGNANT FIBROUS HISTIOCYTOMA (Pleomorphic Dermal Sarcoma) in a 72-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. LITERATURE REFERENCE: Pluss M, Mitteldorf C, Szusies CJ, Tampe B. Case Report: Acquired haemophilia A following mRNA-1273 booster vaccination against SARS-CoV-2 with concurrent diagnosis of Pleomorphic dermal sarcoma. Front Immunol. 2022;13 The patient's past medical history included Carpal tunnel syndrome and Smoker (50 pack-year smoking history). Concurrent medical conditions included Pleomorphic sarcoma of skin and Benign prostatic hyperplasia. On an unknown date, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On an unknown date, the patient experienced ACQUIRED HAEMOPHILIA (Acquired Hemophilia A with anti factor VIII) (seriousness criteria hospitalization and medically significant), PLEOMORPHIC MALIGNANT FIBROUS HISTIOCYTOMA (Pleomorphic Dermal Sarcoma) (seriousness criterion medically significant) and INTERCHANGE OF VACCINE PRODUCTS (received homologous BNT162b2 vaccinations (05/2021 and 06/2021)). The patient was treated with CYCLOPHOSPHAMIDE (oral) for Immunosuppression, at a dose of 150 milligram once a day; PREDNISONE (oral) for Immunosuppression, at a dose of 100 milligram once a day and RITUXIMAB for Immunosuppression, at a dose of 375 milligram/sq. meter. At the time of the report, ACQUIRED HAEMOPHILIA (Acquired Hemophilia A with anti factor VIII) was resolving and PLEOMORPHIC MALIGNANT FIBROUS HISTIOCYTOMA (Pleomorphic Dermal Sarcoma) and INTERCHANGE OF VACCINE PRODUCTS (received homologous BNT162b2 vaccinations (05/2021 and 06/2021)) outcome was unknown. Related DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Activated partial thromboplastin time (25-37): 164.6 seconds (High) distinctly prolonged aPTT of 164.6 seconds and 130 seconds (High) severely prolonged at 130 seconds. On an unknown date, Antiphospholipid antibodies: normal (normal) normal. On an unknown date, Antithrombin III (83-128): 87percent (normal) 87percent. On an unknown date, Basophil count: 0.2% (normal) (0.2%, normal range: ≤2%). On an unknown date, Biopsy: a punch biopsy revealed a pleomorphic dermal sarco (abnormal) A punch biopsy revealed a pleomorphic dermal sarcoma (PDS). On an unknown date, Blood bilirubin (0.3-1.2): 1.4 mg/dl (High) slightly elevated bilirubin level (1.4 mg/dL).	aPTT prolonged: 164.6 s		Coagulation factor VIII C: <0.1%	CT scan : adenoma adrenal	AHA	Possible	This literature-non-study case concerns a 72-year-old male patient, with a medical history of Smoking (50 pack-year), concurrent medical conditions including pleomorphic sarcoma of skin and benign prostatic hyperplasia, who received heterologous dose 3 Spikevax (primary series with Pfizer), and 9 days post vaccine, experienced several bruises appearing on his arms, left leg and trunk. Diagnostic tests: prolonged aPTT, antiFVIII. Treated with steroid, rituximab. Event was resolving at time of the report. This case is classified as AHA based on prolonged aPTT, antiFVIII. According to WHO-UMC causality assessment, this case is assessed as Possible based on temporal association. However, strong confounders included sarcoma of the skin and benign prostatic hyperplasia, which provides alternative etiology.	

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	On an unknown date, Blood fibrinogen (200-393): 245.2 mg/dl (normal) (245.2 mg/dL,) and 355 mg/dl (normal) (355 mg/dL). On an unknown date, Blood lactate dehydrogenase (125-250): 299 u/l (High) Lactate dehydrogenase (LDH) was mildly increased 299 U/L.. On an unknown date, C-reactive protein: 18.5 mg/l (High) C-reactive protein (CRP) was moderately increased at 18.5 mg/L (normal range: ≤5 mg/L). On an unknown date, Cardiolipin antibody: normal (normal) Normal. On an unknown date, Coagulation factor (0.8-1.2): inr of 0.9 (normal) The coagulation profile revealed a normal international normalized ratio (INR) of 0.9. On an unknown date, Coagulation factor IX level (65-150): 48 percent (Low) 48 percent. On an unknown date, Coagulation factor V level (62-139): 144 percent (High) 144 percent. On an unknown date, Coagulation factor VII level (50-129): 88 percent (normal) 88 percent. On an unknown date, Coagulation factor VIII level (70-170): fviii (<0.1%) (abnormal) There was no measurable activity of FVIII (<0.1%). On an unknown date, Coagulation factor X level (77-131): 87percent (normal) 87percent. On an unknown date, Coagulation factor XI level (65-150): 35 percent (Low) 35 percent. On an unknown date, Coagulation factor XIII level (63-157): 40 percent (Low) 40 percent. On an unknown date, Computerised tomogram: abnormal (abnormal) A CT scan of the neck, chest, abdomen and pelvis was performed, which yielded a 4 cm mass on the left adrenal gland as the sole pathological finding. A dedicated adrenal CT with arterial and portalvenous contrast phase confirmed the mass to be a lipid adenoma.. On an unknown date, Eosinophil count: 0.5% (normal) (0.5%, normal range: ≤8%). On an unknown date, Flow cytometry: no pathological b cell population (normal) No pathological B cell population. On an unknown date, Free prostate-specific antigen: normal (normal) prostate-specific antigen was measured, which was within normal limits (3.14 µg/L,normal range: <4 µg/L) and hence gave no indication of prostatic cancer.. On an unknown date, Haemoglobin (13-18): 7.8 g/dl (Low) The patient's complete blood count showed anaemia (haemoglobin 7.8 g/dL) and 8.5 g/dl (Low) Upon admission, the complete blood count confirmed anaemia (Hb 8.5 g/dL, normal range: 13.5-17.5 g/dL). On an unknown date, Haptoglobin (0.14-2.58): 1.64 g/l (normal) there was no sign of intravascular haemolysis (haptoglobin 1.64 g/L). On an unknown date, Liver function test: normal (normal) Normal. On an unknown date, Lymphocyte count (20-45): 40% (normal) A differential blood count showed normal distribution of lymphocytes(40%). On an unknown date, Magnetic resonance imaging: normal (normal) MRI of the cranium was completed and showed no evidence of an intracranial lesion. On an unknown date, Monocyte count (3-13): 9.7 percent (normal) 9.7 percent. On an unknown date, Neutrophil count (40-76): 49.5 percent (normal) 49.5 percent.								

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	On an unknown date, Physical examination: abnormal (abnormal) The physical exam revealed generalized pallor of the skin and mucous membranes, as well as large ecchymosis on both forearms and elbows, the right trunk and flank as well as the left leg. and normal (normal) The in-depth physical exam was otherwise unremarkable, with no palpable lymphadenopathy or organomegaly.. On an unknown date, Platelet count: 320×1000 µl (normal) (320×1000 µL, normal range: 150-500×1000 µL). On an unknown date, Prothrombin level (79-131): 90 percent (normal) FII: 90 percent and 14.2 seconds (normal) prothrombin time (14.2 seconds). On an unknown date, Von Willebrand's factor activity test (66-176): high (High) Final tests revealed an elevated von Willebrand factor (vWF) activity (210%). On an unknown date, White blood cell count: 8.25×1000 µl (normal) (8.25×1000 µL, normal range: 4-11×1000 µL). For mRNA-1273 (Spikevax) (Unknown), the reporter considered ACQUIRED HAEMOPHILIA (Acquired Hemophilia A with anti factor VIII), PLEOMORPHIC MALIGNANT FIBROUS HISTIOCYTOMA (Pleomorphic Dermal Sarcoma) and INTERCHANGE OF VACCINE PRODUCTS (received homologous BNT162b2 vaccinations (05/2021 and 06/2021)) to be related. Patient received appropriate care including immunosuppression using glucocorticoids. The patient had no allergies, no history of immune deficiency, no recent infections or fevers, and no personal or family history of any bleeding disorders. As previously observed in AHA, MixCon-LA ratio was elevated because FVIII inhibitors are reported to interfere with LA assays, producing false-positive results for those tests. A very high FVIII inhibitor measured at 158.6 Bethesda units. Together with the fully eliminated FVIII activity, the diagnosis of AHA was confirmed. The patient had started on recombinant activated FVII (rFVIIa). A proton pump inhibitor (PPI), Vitamin D and trimethoprim sulfamethoxazole were given as adjunct treatment with the high corticosteroid doses for ulcer, osteoporosis and pneumocystis jirovecii prophylaxis, respectively. The aPTT gradually decreased with the rFVIIa treatment, which was tapered from Q3H to Q6H after four days of treatment, and after a further reduction to Q12H was discontinued after a total treatment duration of 10 days. Because of new ecchymosis within 48 hours, rFVIIa substitution was resumed at Q3H, with a careful taper after another four days and a longer course of Q12H treatment until day 23. FXIII was substituted three times. The FVIII inhibitor was shown to decrease from 158.6 BU on admis								

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	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 18-May-2022 and was forwarded to Moderna on 18-May-2022. This regulatory authority case was reported by a physician and describes the occurrence of SKIN HAEMORRHAGE (Extensive bleeding on both arms and legs), INTRA-ABDOMINAL HAEMORRHAGE (Haemorrhage intraabdominal) and ACQUIRED HAEMOPHILIA (Severe inhibitor hemophilia (factor VIII <1%)) in an 84-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The patient's past medical history included Cerebellar infarction in February 2022. Concurrent medical conditions included Adipositas, Metabolic syndrome, Heart failure NYHA class III, Pulmonary function impairment since February 2022, Arterial hypertension, Chronic renal insufficiency and Pulmonary hypertension. On 03-Feb-2022, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 3 dosage form. On 14-Feb-2022, the patient experienced SKIN HAEMORRHAGE (Extensive bleeding on both arms and legs) (seriousness criteria hospitalization and life threatening), INTRA-ABDOMINAL HAEMORRHAGE (Haemorrhage intraabdominal) (seriousness criteria hospitalization and life threatening) and ACQUIRED HAEMOPHILIA (Severe inhibitor hemophilia (factor VIII <1%)) (seriousness criteria hospitalization and life threatening). At the time of the report, SKIN HAEMORRHAGE (Extensive bleeding on both arms and legs), INTRA-ABDOMINAL HAEMORRHAGE (Haemorrhage intraabdominal) and ACQUIRED HAEMOPHILIA (Severe inhibitor hemophilia (factor VIII <1%)) was resolving. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. No concomitant and treatment medication details was reported. Company comment: This is a regulatory case reported by a physician, concerning a 84-year-old female patient with relevant medical history of Cerebellar Infarction and Concurrent medical conditions Obesity, Metabolic syndrome, Heart failure NYHA class III, Pulmonary function impairment, Arterial hypertension, Chronic renal insufficiency and Pulmonary hypertension, who experienced the unexpected serious (Hospitalization, Life threatening) events of skin haemorrhage (extensive bleeding on both arms and legs), intra-abdominal haemorrhage (haemorrhage intraabdominal) and acquired haemophilia (severe inhibitor hemophilia (factor viii <1%)), occurring 11 days after receiving the 3 dose of mRNA-1273 Vaccine in the covid 19 vaccination series. She had a strong feeling of illness, loss of appetite and severe drop in performance after the 3rd vaccination. 1st and 2nd vaccination against SARS-CoV2 were uncomplicated with other vaccines. Interechange of vaccine products was noted. Coagulation tests were unremarkable prior to the event. she was hospitalized and was treated with factor VIII substitution, prednisolone and cyclophosphamide. The events were resolving. Details of concomitant medications were not provided. Age of the subject, history of obesity, metabolic syndrome and hypertension are risk factors to the events skin	No result	No result	factor VIII <1%		AHA	Conditional	This is a regulatory case reported by a physician, concerning an 84-year-old female patient with concurrent medical conditions Obesity, Metabolic syndrome, Heart failure, Chronic renal insufficiency and hypertension, who received heterologous dose 3 Spikevax and 11 days post vaccine, experienced skin hemorrhage (extensive bleeding on both arms and legs), intra-abdominal hemorrhage.No concomitant and treatment medication details were reported. Assessed as acquired hemophilia (factor viii <1%). Diagnostic tests: no result of aPTT, antiFVIII. Event was resolving at the time of the report. This case is classified as AHA based on antiFVIII. According to WHO-UMC causality assessment, this case is assessed as Conditional based on missing relevant information including aPTT result. More information needed to make proper assessment. Strong confounders included Obesity, Metabolic syndrome, which provides alternative etiology.	

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	Haemorrhage and Intraabdominal Haemorrhage. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Events' seriousness assessed as per Regulatory Authority's report.								

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	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 08-Jun-2022 and was forwarded to Moderna on 08-Jun-2022. This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired haemophilia) in a 61-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 006G21A) for COVID-19 vaccination. Co-suspect products included non-company products RAMIPRIL (RAMIPRIL-DP) for Arterial hypertension, ACETYLSALICYLIC ACID, CLOPIDOGREL BISULFATE (CLOPIDOGREL PLUS) for Ischemic cardiomyopathy, PIPERACILLIN SODIUM, TAZOBACTAM SODIUM [REDACTED] for Shock septic, HEPARIN SODIUM (HEPARINE LEO) for Embolism pulmonary, APIXABAN (ELIQUIS) for Embolism pulmonary, CEFUROXIME for Bronchial superinfection, ALFUZOSIN HYDROCHLORIDE (XATRAL) for Benign prostatic hyperplasia, BISOPROLOL for Arterial hypertension and EZETIMIBE for Ischemic cardiomyopathy. The patient's past medical history included Bronchial superinfection from 25-Nov-2021 to 01-Mar-2022, TIA and Partial gastrectomy. Concurrent medical conditions included Arterial hypertension, Urinary infection since 23-Mar-2022, Ischaemic heart disease since 2017 and Embolism pulmonary since 30-Nov-2021. Concomitant products included LANSOPRAZOLE (LANSOPRAZOLE [REDACTED]) and ROSUVASTATIN CALCIUM (ROSUFASTATINE CF) for an unknown indication. In 2017, the patient started ACETYLSALICYLIC ACID, CLOPIDOGREL BISULFATE (CLOPIDOGREL PLUS) (Oral) 75 milligram once a day. On 19-May-2021, the patient started ALFUZOSIN HYDROCHLORIDE (XATRAL) (Oral) 2.5 milligram once a day, BISOPROLOL (Oral) 10 milligram once a day and EZETIMIBE (Oral) 10 milligram once a day. On 29-Nov-2021, the patient started APIXABAN (ELIQUIS) (Oral) 10 milligram once a day. On 30-Dec-2021, the patient received second dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 22-Feb-2022, the patient started CEFUROXIME (Intravenous) 500 milligram once a day. On 16-Mar-2022, the patient started HEPARIN SODIUM (HEPARINE LEO) (Subcutaneous) according to anti-Xa. On 24-Mar-2022, the patient started PIPERACILLIN SODIUM, TAZOBACTAM SODIUM [REDACTED] (Intravenous) 16 gram once a day. On an unknown date, the patient started RAMIPRIL (RAMIPRIL-DP) (Oral) 5 milligram once a day. On 30-Mar-2022, the patient experienced ACQUIRED HAEMOPHILIA (Acquired haemophilia) (seriousness criteria hospitalization and medically significant). At the time of the report, ACQUIRED HAEMOPHILIA (Acquired haemophilia) was resolving. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments.	No result	No result	No result		Insufficient evidence to meet case definition of AH	Conditional	This is a regulatory authority case concerning a 61-year-old, male patient with medical history including bronchial TIA and Partial gastrectomy. Concomitant medications included ASA and clopidogrel; who received dose 2 Spikevax, and 90 days post vaccine, experienced "acquired hemophilia". No report of clinical course and diagnostics. This case is missing relevant information to classify for AH. According to the WHO-UMC causality assessment, this case is assessed as Conditional based on missing relevant information including aPTT AND FVIII results. More information is needed to make a proper assessment. Strong confounders including medications of Clopidogrel, Heparin, Piperacillin + Tazobactam [REDACTED] and Cefuroxime provide a plausible explanation.	

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		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	No treatment drug details was reported. Company comment: This is a regulatory authority case concerning a 61-year-old, male patient with no relevant medical history and with relevant co-suspect medications of Clopidogrel bisulfate (Clopidogrel Plus), Heparin sodium (Heparine Lco), Piperacillin + Tazobactam () and Cefuroxime, who experienced the unexpected serious (hospitalization and medically significant according to regulatory authority) event of acquired haemophilia. The event occurred 90 days after the second dose of mRNA-1273 vaccine administration. No other information surrounding the event was reported. The outcome of the event was reported as resolving. The co-suspect medications of Clopidogrel bisulfate (Clopidogrel Plus), Heparin sodium (Heparine Leo), Piperacillin + Tazobactam () and Cefuroxime, remain confounders for the event. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.								

Case ID	Narrative (Complete)	Diagnostic Parameters			Other Diagnostic	Type of Acquired hemophilia	WHO-UMC Causality Assessment	MAH Comment	WW Identifier
		Activated partial thromboplastin time (aPTT)	Inhibitor screen/ Mixing test	FVIII / FIX					
	This case was received via European Medicines Agency (Reference number: [REDACTED] on 09-Jun-2022 and was forwarded to Moderna on 09-Jun-2022. This regulatory authority case was reported by a physician and describes the occurrence of ACQUIRED HAEMOPHILIA (Acquired haemophilia) in an 84-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The patient's past medical history included Ischaemic stroke and CVA (En 2017). Concurrent medical conditions included Arterial hypertension, Cerebrovascular stenosis (Sylvian stenosis) and Diabetes mellitus. Concomitant products included PROCAINE HYDROCHLORIDE [REDACTED], CLOPIDOGREL BISULFATE (PLAVIX) and FUROSEMIDE for an unknown indication. On 07-Apr-2022, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) .25 milliliter. On 17-Apr-2022, the patient experienced ACQUIRED HAEMOPHILIA (Acquired haemophilia) (seriousness criterion hospitalization). At the time of the report, ACQUIRED HAEMOPHILIA (Acquired haemophilia) had not resolved. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Dose text was reported as R1. No treatment medication were provided. Company Comment: This regulatory authority case concerns an 84-year-old male patient, with relevant concomitant use of Clopidogrel, who experienced unexpected, serious (hospitalization) event Acquired Hemophilia, around 10 days after receiving a dose of mRNA-1273. Clinical course, labs, and treatment details not reported. The outcome was not recovered. The concomitant use of Clopidogrel could be a confounding factor for the event. The benefit risk relationship of mRNA-1273 is not affected by this report. Event seriousness is assessed as per regulatory authority's report.	No result	No report	No result	No result	Insufficient evidence to meet case definition of AH	Unassessable	This regulatory authority reported case concerns an 84-year-old male patient, with past medical history including ischaemic stroke and CVA, concurrent medical conditions included hypertension, cerebrovascular stenosis and diabetes mellitus, and relevant concomitant use of Clopidogrel, who received an unknown dose of Spikevax and 10 days post vaccine experienced unspecified symptoms and assessed as acquired Hemophilia. ,Clinical course, labs, and treatment details not reported. The events had not resolved at time of report. This case is missing relevant diagnostic results, and has insufficient evidence to meet case definition for acquired hemophilia. The concomitant use of Clopidogrel is a strong confounder for the event. According to WHO-UMC causality assessment, this case is assessed as Unassessable.It cannot be judged because information is insufficient,The use of clopidogrel provides plausible explanation. Clopidogrel is associated with acquired hemophilia and this is stated in the manufacturer's leaflet	

Appendix 11.14c Acquired haemophilia: Literature Search Methodology

((("Acquired Hemophilia") AND ("mrna vaccines"[MeSH Terms] OR "2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "mRNA 1273"[All Fields] OR "mRNA 1273"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "mrna1273"[All Fields]) OR ("modernatx"[All Fields] AND "1273"[All Fields]) OR "1273"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "m 1273"[All Fields]) OR "m 1273"[All Fields] OR ("moderna"[All Fields] AND ("covid 19 vaccines"[MeSH Terms] OR ("covid 19"[All Fields] AND "vaccines"[All Fields]) OR "covid 19 vaccines"[All Fields] OR ("covid19"[All Fields] AND "vaccine"[All Fields]) OR "covid19 vaccine"[All Fields])) OR "moderna covid 19 vaccine"[All Fields] OR "moderna covid 19 vaccine"[All Fields] OR "moderna covid 19 vaccine"[All Fields] OR "Spikevax"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "elasomeran"[All Fields]) OR "CX-024414"[All Fields] OR "tak 919"[All Fields] OR "tak 919"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] OR (SARS-CoV-2 vaccination) AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields]))) AND ("2020/12/18"[Date - Publication] : "2022/06/18"[Date - Publication]))))

Appendix 11.14d Acquired haemophilia: Literature articles/Abstracts

PMID	Title	Authors	Link	Type of vaccine	Class of Vaccine	Type of Study (Case Report/ Cohort)	Due to Infection	MOA	Refers to	Comment	Citation	First Author	Journal/Book	Publication Year	Cover Date	PMCID	NIDDK ID	DOI
	A case report of acquired hemophilia following COVID-19 vaccine	Rahai M, Puri S.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8259362/	Plasmer	m-RNA	Case Report	No	The pathophysiology of AHA is unclear, although it is thought that T-lymphocytes and certain genetic polymorphisms may play a role. A Vaccine have been implicated in generating autoantibodies. It has been suggested that vaccination may trigger an autoimmune response due to antigenic mimicry as well as due to activation of quiescent auto-reactive T and B cells.	Yes	A 69-year-old male received COVID-19 Vaccine premixed with salt buffer 9 days after the vaccination. The patient has no personal or family history of bleeding disorders. Following the second dose of COVID-19, he noticed several new bruises appearing on his arms and legs. His physical exam revealed large ecchymosis on his left forearm and elbow, as well as his right thigh. The coagulation profile reveals a normal prothrombin time at 10.8 s (normal range =9.4–12.5 s) and a severely prolonged activated partial thromboplastin time (APTT) at 115.2 s (normal range = 25.1–36.5 s). Further testing revealed elevated von Willebrand antigen/functional, FVIII level at 1% using APTT-based assay, and PVIII inhibitor titer at 80 Bethesda units, which were consistent with the diagnosis of AHA. The patient was given high dose of prednisone only (1 mg/kg) as corticosteroid treatment. After 4 weeks of treatment with corticosteroids, PVIII level increased to 5% and FVIII inhibitor titer decreased to 2 Bethesda units.	J Thromb Haemost. 2021 Jun;19(6):1515–1518. doi: 10.1111/jth.15291. Epub 2021 May 10.	Rahai M	J Thromb Haemost	2021	3/30/2021	PMC8259362		10.1111/jth.15291
	Autoimmune- and complement-mediated hematology conditions exacerbation following SARS-CoV-2 vaccination	AJ, Sanga C, Kone-Bekele A, Girma D, Girma T, Aklonis J.	https://pubmed.ncbi.nlm.nih.gov/3435503/	Modernia	m-RNA	Case Report	No	Acquired hemophilia A, presumed to be due to an antibody directed against the FVIII-WF complex.	Yes	Patient 3 was a 76-year-old woman with a history of severe Raynaud's phenomenon, multiple episodes of large, upper extremity ecchymoses, and a parasitological bacteria status post recent uncomplicated Nausea fluoroquinolone. She tolerated dose 1 of the Moderna SARS-CoV-2 vaccine. After dose 2, on day 4 she developed large ecchymosis involving most of her upper extremities. A VWF multimer analysis showed a normal pattern and distribution of bands, consistent with a quantitative VWF deficiency. A factor VIII inhibitor was detected and quantified as 11.2 Bethesda units (BIU). The patient was diagnosed with recurrent AAVD and acquired hemophilia A, presumed to be due to an antibody directed against the FVIII-WF complex.	Blood Adv. 2021 Jul 13;5(13):2794–2798. doi: 10.1182/bloodadvances.2021004957.	Portuguese AJ	Blood Adv	2021	7/13/2021	PMC8276576		10.1182/bloodadvances.2021004957
	Acquired Autoimmune Hemophilia Following SARS-CoV-2 Vaccine: Dual-Drug Effects on Blood Coagulation and the Bgla and Ccrp Levels Phenomenon	Hersberg J, Marchetti M, Falanga A.	https://pubmed.ncbi.nlm.nih.gov/3459277/	Autismax, m-RNA	Viral vector, m-RNA	Case Report	No	Acquired hemophilia A, presumed to be due to an antibody directed against the FVIII-WF complex.	Yes	The first cases of bleeding complications were reported 15 to 19 days (or later) after vaccination with adenoiral vector vaccine ChAdOx1 [18]. Fitch et al report on a case of acquired hemophilia with a large hematoma of his left posterior leg extending from his heel to below his left knee, 19 days after the second dose of BNT162B2 Pfizer-BioNTech vaccine. Laboratory values revealed a two to tenfold prolongation of the activated partial thromboplastin time (APTT), decrease of prothrombin to 10 g/dL, lower VIII activity <1%, and 110 Bethesda Units/mL of factor VIII inhibitor. Fibrinogen, creatinine, and other laboratory parameters were in the normal range. The patient had no personal and family history of hemostatic disorders. The patient recovered without sequelae after adequate treatment.	Thromb Haemost. 2021 Dec;121(12):1555–1557. doi: 10.1055/s-10058-4852. Epub 2021 Sep 30.	Hersberg J	Thromb Haemost	2021	9/30/2021			10.1055/s-10058-4852
	The statistical risk of diagnosing coincidental acquired hemophilia A following anti-SARS-CoV-2 vaccination	Chen M, Jiang Y, R. Conditio A, Tosi di Bagnolo L, Fernandez R, Gelfand R, Nanda R, Longo-Tegoni A, Drexler B, Candi A, Tackis DA, Berger CT, Fene O, Martin T, Kone W, Gelfand, Martin M, Gelfand R.	https://pubmed.ncbi.nlm.nih.gov/3410197/	Modernia	m-RNA	Case Report	No	Not mentioned	Yes	Three case reports of patients who developed acquired hemophilia after 2nd dose of Moderna vaccine.	J Thromb Haemost. 2021 Sep;19(9):2366–2368. doi: 10.1111/jth.15421. Epub 2021 Jun 26.	Chen M	J Thromb Haemost	2021	6/26/2021			10.1111/jth.15421
	Acquired Hemophilia A Post-COVID-19 Vaccination: A Case Report and Review	AJ Hossaini R, AJ Hossaini M, Bakir M, Alharbi M, Jazari F, Alharbi TN, Shouni S, Boudak ABB, Taha A, Khan MK, Zaki H.	https://pubmed.ncbi.nlm.nih.gov/3526543/	Plasmer	m-RNA	Case Report	No	Acquired hemophilia A, presumed to be due to an antibody directed against the FVIII-WF complex.	Yes	The patient developed multiple sites of cutaneous hematomas. Corticosteroid treatment was given with IFV. Followed by prednisone 80 mg daily for 3 days, rituximab 375 mg/m ² , cryoprecipitate 750 mg/mL, cryoprecipitate 25 mg.	Cureus. 2022 Feb 4;14(2):e21909. doi: 10.7759/cureus.21909. eCollection 2022 Feb 4.	AJ Hossaini R	Cureus	2022	3/10/2022	PMC8896468		10.7759/cureus.21909
	Autoimmunity after Coronavirus Disease 2019 (COVID-19) Vaccine A Case of Acquired Hemophilia A	Foley S, Ouley R, Van Wagoner N, Patel F.	https://pubmed.ncbi.nlm.nih.gov/3435291/	Plasmer	m-RNA	Case Report	No	While the exact mechanisms responsible for these immunohematologic complications are unknown, there is increasing concern that antibodies against SARS-CoV-2 spike protein S1 could be responsible for autoimmunity [2]. In support of this, similar presentations have been reported after COVID-19 vaccination, such as proteinuria [17] and vasculitis [18]. Therefore, as COVID-19 infection and current available vaccines may share the S1 spike protein in common, it is suspected that an immune response against this protein is responsible for autoimmune conditions observed.	Yes	The patient, a 67-year-old African American male with a history of hypertension and asymptomatic pulmonary sarcoidosis not receiving any pharmacological treatment, began to experience left thigh tightness and cramping pain at day -19 after his second dose of the Pfizer-BioNTech COVID-19 vaccine. Physical exam was otherwise unremarkable. His activated partial thromboplastin time (APTT) was 72 seconds (normal 25–35 seconds). Review of prior medical records showed normal APTT in 2013 and 2014, but no more recent coagulation laboratory. His was transferred to [redacted] for further evaluation. His hemoglobin level was 10.2 g/dL (from 11.4 g/dL 2 days prior and down from a baseline of 11.5 g/dL in September 2020).	Thromb Haemost. 2021 Dec;121(12):1674–1676. doi: 10.1055/s-10055-1579-5396. Epub 2021 Aug 5.	Foley S	Thromb Haemost	2021	8/5/2021			10.1055/s-10055-1579-5396
	A Case of Acquired Hemophilia A Following SARS-CoV-2 Infection	Habibi H, McGuire C, Harad A.	https://pubmed.ncbi.nlm.nih.gov/3443467/	NA	NA	Case Report	Yes	Not mentioned	Yes	A 73-year-old developed acquired hemophilia post SARS-CoV-2 infection. The testing showed factor VIII activity of <1% (normal range 56–141) and an extremely elevated Bethesda assay of 70.4 Bethesda units (BU).	Cureus. 2021 Jul 23;13(7):e16579. doi: 10.7759/cureus.16579. eCollection 2021 Jul 23.	Habibi H	Cureus	2021	8/26/2021	PMC8380307		10.7759/cureus.16579

PMID	Title	Authors	Link	Type of vaccine	Class of Vaccine	Type of Study (Case Report/Cohort)	Due to Infection	MOA	Relevant	Comment	Citation	First Author	Journal/Book	Publication Year	Create Date	PMCID	NIHMS ID	DOI
	Illustrated State-of-the-Art Capsules of the ISTH 2022 Congress	Ariens RA, Hunt BJ, Agnani HO, Alnasser J, Ahrends R, Alkhalil A, Asinger A, Bagoly Z, Balduini A, Barbon E, Barrott CD, Batty P, Carneiro JDA, Chan WS, de Maat M, de Wit K, Denis C, Ellis MH, Eikelink R, Fu H, Hayward CPM, Ho-Yin-Noé B, Klok FA, Kumar R, Leidekker K, Litvinov RJ, Mackman N, McQuillan Z, Neil MD, Parker WAE, Preston RJS, Rayes J, Renzie AR, Roberts LN, Rocca B, Shapiro S, Siegel DM, Soave LF, Suzuki-Inoue K, Zafar T, Zhou J.	https://pubmed.ncbi.nlm.nih.gov/35814801/	NA	NA	NA	No	NA	No	Highlights of the different states	Res Pract Thromb Haemost. 2022 Jul 6;6(5):e12747. doi: 10.1002/rth2.12747. eCollection 2022 Jul.	Ariens RA	Res Pract Thromb Haemost	2022	7/11/2022	PMC9257378		10.1002/rth2.12747
	Consumption of complement in a 26-year-old woman with severe thrombotic thrombocytopenia after ChAdOx1 nCoV-19 vaccination	Cugno M, Macor P, Giordano M, Manfredi M, Griffini S, Grovetto E, De Masi L, Mellone S, Valenti L, Prati D, Bonato S, Comi G, Artoni A, Meroni PL, Peyvandi F.	https://pubmed.ncbi.nlm.nih.gov/34592707/	NA	NA	NA	No	NA	No	The article talks about a different condition.	J Autoimmun. 2021 Nov;124:102728. doi: 10.1016/j.jaut.2021.102728. Epub 2021 Sep 27.	Cugno M	J Autoimmun	2021	9/30/2021			10.1016/j.jaut.2021.102728
	Case of acquired haemophilia a in Southeast Asia following COVID-19 vaccine	Ai Vuen L, Ann Su-Vin E, Nalla Kori A, Shah TM.	https://pubmed.ncbi.nlm.nih.gov/35264381/	Pfizer	m-RNA	Case Report	No	Not mentioned	Yes	A man in his 80s developed multiple bruises 2 weeks after his first dose of the COVID-19 vaccine. Diagnosis was delayed due to his cognitive impairment and low clinical suspicion. This led to a representation with worsening ecchymosis, a left thigh haematoma and symptomatic anaemia. Laboratory testing was notable for an isolated prolongation of the activated partial thromboplastin time, which remained uncorrected in the mixing test. Further testing confirmed the presence of factor VIII (FVIII) inhibitors and low FVIII titres of 6.7%. He responded to treatment with intravenous methylprednisolone and recombinant activated FVII. Screening for autoimmune diseases and malignancies was negative.	BMJ Case Rep. 2022 Mar 9;15(3):e246922. doi: 10.1136/bcr-2021-246922.	Ai Vuen L	BMJ Case Rep	2022	3/10/2022	PMC8915366		10.1136/bcr-2021-246922
	A case of acquired haemophilia A in a 70-year-old post COVID-19 vaccine	Lemoine C, Giacoble AG, Benfaisano E, Karpotyan L, Sosman C.	https://pubmed.ncbi.nlm.nih.gov/34708828/	Moderna	m-RNA	Case Report	No	Not mentioned	Yes	A 70 year male patient developed eight days after the first dose, he developed extensive ecchymosis on the right upper limb, ecchymosis on the left forearm and right lower extremity. Oral prednisone 1 mg/kg daily Cyclophosphamide 2 mg/kg daily	Haemophilia. 2022 Jan;28(1):e15-e17. doi: 10.1111/hae.14442. Epub 2021 Oct 28.	Lemoine C	Haemophilia	2022	10/28/2021	PMC8652744		10.1111/hae.14442

Appendix 11.14e Acquired haemophilia: Various Synonyms of SPIKEVAX

("mrna vaccines"[MeSH Terms] OR "2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "mRNA 1273"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "mrna1273"[All Fields]) OR ("modernatx"[All Fields] AND "1273"[All Fields]) OR "1273"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "m 1273"[All Fields]) OR "m 1273"[All Fields] OR ("moderna"[All Fields] AND ("covid 19 vaccines"[MeSH Terms] OR ("covid 19"[All Fields] AND "vaccines"[All Fields]) OR "covid 19 vaccines"[All Fields] OR ("covid19"[All Fields] AND "vaccine"[All Fields]) OR "covid19 vaccine"[All Fields])) OR "moderna covid 19 vaccine"[All Fields] OR "moderna covid 19 vaccine"[All Fields] OR "moderna covid 19 vaccine"[All Fields] OR "SPIKEVAX"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields] OR "elasomeran"[All Fields]) OR "CX-024414"[All Fields] OR "tak 919"[All Fields] OR "tak 919"[All Fields] OR ("2019 ncov vaccine mrna 1273"[MeSH Terms] OR ("2019 ncov"[All Fields] OR (SARS-CoV-2 vaccination) AND "vaccine"[All Fields] AND "mRNA 1273"[All Fields]) OR "2019 ncov vaccine mrna 1273"[All Fields]))))

**Appendix 11.15a Thrombosis with Thrombocytopenia Syndrome (TTS):
Reporting Period Case Listings According to The Brighton Collaboration Case
Definitions**

Case ID	Country	Report Type	PT	ALL PT'S	Case Seriousness	Age	Gender	Event Outcome	Medical History	Concomitant Medications	Dose #	TTO	Brighton Def.	CDC Def.	WHO Causality	WW Identifier
		Regulatory Authority	Thrombosis with thrombocytopenia syndrome	Cerebral venous sinus thrombosis, Thrombosis with thrombocytopenia syndrome	Serious	57	Male	Recovering/Resolving	Not reported	COMIRNATY	Dose 3	15	Level 4	Not a case	Unassessable	
		Regulatory Authority	Platelet count decreased	Cerebral infarction, Platelet count decreased	Serious	78	Female	Recovering/Resolving	COMIRNATY; COMIRNATY	Not reported	Unknown		Level 3	Not a case	Unassessable	
		Regulatory Authority	Thrombocytopenia	Cerebral infarction, Deep vein thrombosis, Dyspnoea, Hemiparesis, Pelvic venous thrombosis, Pulmonary embolism, Thrombocytopenia	Serious	73	Male	Recovered/Resolved with Sequelae	Chronic kidney disease(C); Type 2 diabetes mellitus(C); Vitamin D deficiency(C); Anti-platelet factor 4 antibody positive(C); Hyperlipidaemia(C); COVID-19(C); Hypertension(C)	Not reported	Unknown		Level 4	Not a case	Unassessable	
		JAPAN	Spontaneous	Thrombosis with thrombocytopenia syndrome	Serious	77	Female	Fatal	Cerebral infarction(C); Osteoporosis(C); Constipation(C); Glaucoma(H)	LIXIANA	Dose 3	1	Level 4	Not a case	Unassessable	
		Regulatory Authority	Thrombocytopenia	Deep vein thrombosis, Thrombocytopenia	Serious	72	Male	Unknown	Non-tobacco user(H)	Not reported	Unknown		Level 1	Not a case	Possible	
		Regulatory Authority	Thrombosis with thrombocytopenia syndrome	Anaemia, Diarrhoea, Malaise, Myalgia, Thrombosis with thrombocytopenia syndrome, Vomiting	Serious	79	Female	Recovered/Resolved	SPIKEVAX(H); SPIKEVAX(H)	Not reported	Unknown		Level 4	Not a case	Possible	
		Regulatory Authority	Thrombocytopenia	Gingival bleeding, Thrombocytopenia, Thrombotic thrombocytopenic purpura	Serious	76	Female	Not Recovered/Not Resolved	Hypertension(C); Type 2 diabetes mellitus(C)	COMIRNATY	Unknown		Level 4	Not a case	Unassessable	
		Spontaneous	Thrombosis with thrombocytopenia syndrome	Deep vein thrombosis, Penile oedema, Thrombosis with thrombocytopenia syndrome	Serious	81	Male	Unknown	Benign prostatic hyperplasia(C)	Not reported	Dose 3	25	Level 1	Not a case	Possible	
		Literature-Non-Study	Thrombosis with thrombocytopenia syndrome	Blood potassium decreased, Loss of personal independence in daily activities, Seizure, Thrombosis with thrombocytopenia syndrome, Walking aid user	Serious	56	Female	Recovered/Resolved with Sequelae	Hypothyroidism(C); Hyperlipidaemia(C); Thrombectomy; Obesity(C); Endotracheal intubation	LEVOTHYROXINE; ATORVASTATIN	Unknown		Level 1	Tier 1	Possible	
		JAPAN	Spontaneous	Thrombotic thrombocytopenic purpura	Serious	24	Female	Fatal	Obesity(C); Intellectual disability(H); Cleft palate(H)	Not reported	Unknown		Level 5	Not a case	N/A	
		Regulatory Authority	Thrombocytopenia	Drug reaction with eosinophilia and systemic symptoms, Pulmonary embolism, Thrombocytopenia	Serious	68	Male	Recovering/Resolving	Not reported	Not reported	Dose 3	14	Level 3	Not a case	Unlikely	
		Regulatory Authority	Thrombocytopenia	Deep vein thrombosis, Thrombocytopenia	Serious	83	Female	Unknown	Thrombosis(C); Cognitive disorder(C); Non-tobacco user(C)	Not reported	Unknown		Level 1	Not a case	Possible	
		Literature-Non-Study	Thrombosis with thrombocytopenia syndrome	Thrombosis with thrombocytopenia syndrome	Serious	34	Female	Recovered/Resolved	Hypothyroidism(H); LEVOTHYROXINE(H)	Not reported	Unknown		Level 5	Not a case	N/A	
		Regulatory Authority	Petechiae	Antiphospholipid syndrome, Immune thrombocytopenia, Petechiae	Serious	38	Female	Recovered/Resolved	Not reported	Not reported	Dose 2	7	Level 5	Not a case	N/A	
		Spontaneous	Thrombosis with thrombocytopenia syndrome	Deep vein thrombosis, Pulmonary embolism, Syncope, Thrombosis with thrombocytopenia syndrome	Serious	80	Male	Unknown	COMIRNATY; COMIRNATY	Not reported	Dose 3	3	Level 1	Not a case	Unassessable	
		Regulatory Authority	Thrombocytopenia	Thrombocytopenia, Venous thrombosis limb	Serious	74	Male	Unknown	Not reported	Not reported	Dose 3	41	Level 1	Not a case	Unlikely	
		Regulatory Authority	Petechiae	Eye haemorrhage, Injection site swelling, Petechiae, Thrombophlebitis	Non Serious	55	Female	Recovered/Resolved with Sequelae	Not reported	Not reported	Unknown		Level 5	Not a case	N/A	
		Regulatory Authority	Thrombocytopenia	Haemolytic uraemic syndrome, Renal disorder, Thrombocytopenia, Thrombotic microangiopathy	Serious	38	Female	Recovering/Resolving	Not reported	Not reported	Dose 1	6	Level 5	Tier 1	Unlikely	

Case ID	Country	Report Type	PT	ALL PT'S	Case Seriousness	Age	Gender	Event Outcome	Medical History	Concomitant Medications	Dose #	TTO	Brightou Def.	CDC Def.	WHO Causality	WW Identifier
		Spontaneous	Thrombosis with thrombocytopenia syndrome	Pancytopenia, Thrombosis with thrombocytopenia syndrome, Vaccination site pain	Serious	84	Male	Recovered/Resolved	Type 2 diabetes mellitus(H); Hypertension(H)	TAMSULOSIN HYDROCHLORIDE; DUTASTERIDE; LOSARTAN POTASSIUM; ONGLYZA [SAXAGLIPTIN]; NEXIUM EBB	Unknown		Level 5	Not a case	N/A	
		Spontaneous	Thrombosis with thrombocytopenia syndrome	Thrombosis with thrombocytopenia syndrome	Serious	Unknown	Unknown	Not Recovered/Not Resolved	Not reported	Not reported	Unknown		Level 4	Not a case	Unassessable	
		Regulatory Authority	Thrombotic thrombocytopenic purpura	ADAMTS13 activity decreased, Thrombotic thrombocytopenic purpura	Serious	28	Female	Recovering/Resolving	Not reported	Not reported	Dose 1	64	Level 5	Not a case	N/A	
		Spontaneous	Thrombosis with thrombocytopenia syndrome	Brain stem infarction, Cerebrovascular accident, Thrombosis with thrombocytopenia syndrome	Serious	68	Male	Recovering/Resolving			Dose 3	1	Level 4	Unassessable	Unassessable	
		Literature-Non-Study	Thrombotic thrombocytopenic purpura	Condition aggravated, Thrombotic thrombocytopenic purpura	Serious	50	Female	Recovered/Resolved	Cerebrovascular accident(H); Thrombocytopenia(H); Haemolytic anaemia(H); Schistocytosis(H); Plasmapheresis; Apheresis; Thrombotic thrombocytopenic purpura(C)	OCTAPLAS	Unknown		Level 5	Not a case	Unlikely	
		Spontaneous	Thrombosis with thrombocytopenia syndrome	Cerebral infarction, Cerebrovascular accident, Deep vein thrombosis, Pulmonary embolism, Thrombosis with thrombocytopenia syndrome	Serious	58	Female	Unknown			Dose 3	7	Level 4	Unassessable	Unassessable	
	NETHERLANDS	Regulatory Authority	Thrombocytopenia	Mesenteric vein thrombosis, Portal vein thrombosis, Thrombocytopenia	Serious	62	Male	Fatal	Type 2 diabetes mellitus(C); Diverticulitis(H); Incision site haemorrhage(H); Haemorrhoids thrombosed(H); Rectal haemorrhage(H); Hypertension(C); COVID-19 VACCINE ASTRAZENECA; COVID-19 VACCINE ASTRAZENECA	METFORMINE [METFORMIN]; AMLODIPINE	Dose 2	1	Level 5	Not a case	Unlikely	
		Literature-Non-Study	Thrombosis with thrombocytopenia syndrome	Interchange of vaccine products, Pulmonary embolism, Thrombosis with thrombocytopenia syndrome	Serious	83	Female	Recovering/Resolving	Transient ischaemic attack(H); Hypertension(C); PFIZER BIONTECH COVID-19 VACCINE; CLOPIDOGREL(H)		Dose 3	20	Level 1	Tier 2	Unlikely	
		Regulatory Authority	Platelet count decreased	Ischaemic cerebral infarction, Platelet count decreased	Serious	71	Male	Recovering/Resolving	COMIRNATY; COMIRNATY; COMIRNATY		Dose 4	Unknown	Level 4	Unassessable	Unassessable	
		Regulatory Authority	Thrombocytopenia	Headache, Ischaemic stroke, Nausea, Sensory disturbance, Thrombocytopenia, Visual impairment, Vomiting	Serious	51	Female	Unknown	Haemochromatosis(C); Non-tobacco user(H); Amblyopia(H)		Dose 3	0	Level 5	Not a case	Unlikely	
		Regulatory Authority	Thrombocytopenia	Pulmonary embolism, Thrombocytopenia	Serious	29	Male	Recovering/Resolving	Chronic hepatitis(C); Splenomegaly(C); Hepatic steatosis(H); PFIZER BIONTECH COVID-19 VACCINE; PFIZER BIONTECH COVID-19 VACCINE; Tobacco user(C); Alcohol use(C); Hypersensitivity		Dose 3	8	Level 4	Unassessable	Unlikely	
		Regulatory Authority	Thrombocytopenia	Dyspnoea, Peripheral swelling, Pulmonary embolism, Thrombocytopenia	Serious	95	Female	Unknown	Pulmonary embolism(C); Non-tobacco user(H); COVID-19(H)	COMIRNATY; VAXZEVRIA	Dose 4	6	Level 4	Unassessable	Unlikely	
		Literature-Non-Study	Thrombotic thrombocytopenic purpura	Thrombotic thrombocytopenic purpura	Serious		Female	Recovered/Resolved	Chronic myeloid leukaemia(C); Hyperlipidaemia(C); Tobacco user(C)	DASATINIB	Dose 3	2	Level 5	Not a case	Unlikely	
		Literature-Non-Study	Thrombosis with thrombocytopenia syndrome	Cerebral haemorrhage, Pulmonary embolism, Thrombosis with thrombocytopenia syndrome, Venous thrombosis limb	Serious	38	Female	Unknown	Stasis dermatitis(C); Anaemia(C)		Unknown		Level 4	Unassessable	Unassessable	
		Regulatory Authority	Ecchymosis	Ecchymosis, Eczema, Eye oedema, Pruritus, Thrombosis	Serious	50	Female	Recovered/Resolved with Sequelae			Unknown	0	Level 5	Not a case	Unlikely	

Case ID	Country	Report Type	PT	ALL PT'S	Case Seriousness	Age	Gender	Event Outcome	Medical History	Concomitant Medications	Dose #	TTO	Brighton Def.	CDC Def.	WHO Causality	WW Identifier
		Spontaneous	Thrombosis with thrombocytopenia syndrome	Deep vein thrombosis, Feeding disorder, Gait disturbance, Metabolic acidosis, Pulmonary embolism, Thrombosis with thrombocytopenia syndrome	Serious	70	Female	Recovered/Resolved			Dose 3	1	Level 4	Unassessable	Unassessable	
		Regulatory Authority	Petechiae	Fatigue, Hypoaesthesia, Peripheral swelling, Petechiae, Pruritus, Telangiectasia, Thrombosis	Serious	63	Male	Recovered/Resolved	Chronic lymphocytic leukaemia(H)		Dose 1	0	Level 4	Unassessable	Unlikely	
		Literature-Non-Study	Thrombotic thrombocytopenic purpura	Thrombotic thrombocytopenic purpura	Serious	57	Male	Recovered/Resolved	Thrombotic thrombocytopenic purpura(H); RITUXIMAB(H); ECULIZUMAB(H); MYCOPHENOLATE MOFETIL(H); BORTEZOMIB(H)		Unknown		Level 5	not a case	N/A	
		Spontaneous	Platelet count decreased	Cerebrovascular accident, Contusion, Headache, Hypokinesia, Influenza like illness, Peripheral swelling, Platelet count decreased, Platelet disorder, Pyrexia, Rash, Vaccination complication, Vision blurred	Serious	69	Female	Unknown		NASONEX; AMLODIPINE	Dose 2	0	Level 5	not a case	N/A	
		Regulatory Authority	Thrombocytopenia	Asthenia, Fibrin D dimer increased, Hemiparesis, Ischaemic stroke, Thrombocytopenia	Serious	69	Male	Recovered/Resolved with Sequelae		TRIAEC-8;	Unknown		Level 5	not a case	N/A	
		Regulatory Authority	Thrombocytopenia	Abdominal pain, Intestinal ischaemia, Mesenteric vein thrombosis, Portal vein thrombosis, Pulmonary embolism, Splenic vein thrombosis, Thrombocytopenia, Vena cava thrombosis, Vomiting	Serious	53	Male	Recovered/Resolved	Non-tobacco user(H)	LEVOTHYROXINE; SIMVASTATIN	Unknown		Level 1	Tier 1	Possible	
		Regulatory Authority	Thrombocytopenia	Myalgia, Thrombocytopenia, Transient ischaemic attack	Non Serious	78	Female	Unknown	Chronotropic incompetence(H); Cardiac pacemaker insertion; Atrioventricular block second degree(H); Cardiac pacemaker replacement; Hysterectomy; Endometrial cancer(C); Neurolysis; Temporal lobe epilepsy(H); Hypertension(C); PFIZER BIONTECH COVID-19 VACCINE; PFIZER BIONTECH COVID-19 VACCINE	LEVETIRACETAM; CLOPIDOGREL; AMLODIPINE; FENOTEROL HYDROBROMIDE; IPRAFATROPIUM BROMIDE; BECLOMETASONE; FORMOTEROL; OMEPRAZOLE [OMEPRAZOLE SODIUM]; CARBAMAZEPINE; ROSUVASTATIN EC; LOSARTAN; DOXAZOSIN	Unknown		Level 5	not a case	N/A	
		Regulatory Authority	Thrombocytopenia	Cough, Electrolyte imbalance, Pulmonary embolism, Pyrexia, Thrombocytopenia	Serious	83	Female	Recovered/Resolved	COMIRNATY; COMIRNATY; Fond poisoning(H); Essential hypertension(C); Hyperventilation(H); Supraventricular tachycardia(H); Osteoporosis(H); (H); (H)	PERINDOPRIL; GA; COLECALCIFEROL; VERAPAMILA	Unknown		Level 1	not a case	Conditional	
		Regulatory Authority	Thrombosis with thrombocytopenia syndrome	Pulmonary embolism, Thrombocytopenia, Thrombosis with thrombocytopenia syndrome	Serious	83	Female	Not Recovered/Not Resolved	Obesity(C); Transient ischaemic attack(H); PFIZER BIONTECH COVID-19 VACCINE(H); PFIZER BIONTECH COVID-19 VACCINE(H)	BUMETANIDE; LEVOTHYROXINE; CLOPIDOGREL; LOSARTAN	Unknown		Level 1	Tier 2	Possible	
	SPAIN	Regulatory Authority	Thrombocytopenia	Cardio-respiratory arrest, Pulmonary thrombosis, Thrombocytopenia	Serious	48	Male	Fatal	Obesity(C); Sleep apnoea syndrome(C); Deep vein thrombosis(C); Factor V Leiden mutation(C); Migraine(C)	LIXIANA; COMIRNATY	Dose 1	9	Level 3	not a case	Conditional	
		Spontaneous	Thrombocytopenia	Fibrin D dimer increased, Inappropriate schedule of product administration, Influenza, Muscle spasms, Paraesthesia, Thrombocytopenia, Thrombosis, Vaccination site erythema, Vaccination site pain	Serious	37	Unknown	Unknown	Systemic lupus erythematosus(C); Autoimmune thyroiditis(C); Asthma(C); Drug hypersensitivity; Drug hypersensitivity; Food allergy; Seasonal allergy		Dose 2	Unknown	Level 5	Not a case	not assessed because this was not a case of TTS	

**Appendix 11.15b Thrombosis with Thrombocytopenia Syndrome (TTS):
Reporting Period Case Narratives According to The Brighton Collaboration Case
Definitions**

Case ID	Narrative	MAH Comment	WW Identifier
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 17-Feb-2022 and was forwarded to Moderna on 17-Feb-2022. This regulatory authority case was reported by a pharmacist and describes the occurrence of CEREBRAL VENOUS SINUS THROMBOSIS (Trombosis cerebral) and THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Prothrombotic immune thrombocytopenia) in a 57-year-old male patient who received mRNA-1273 (Spikevax) (batch no. :EY3014) for COVID-19 vaccination. Concomitant products included TOZINAMERAN (COMIRNATY) from 09-May-2021 to an unknown date for COVID-19. On 19-Dec-2021, the patient received third dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 03-Jan-2022, the patient experienced THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Prothrombotic immune thrombocytopenia) (seriousness criterion hospitalization). On an unknown date, the patient experienced CEREBRAL VENOUS SINUS THROMBOSIS (Trombosis cerebral) (seriousness criterion hospitalization). At the time of the report, CEREBRAL VENOUS SINUS THROMBOSIS (Trombosis cerebral) had resolved and THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Prothrombotic immune thrombocytopenia) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 17-Jan-2022, Anti-platelet antibody: negative (Negative) NEGATIVE. mRNA-1273 (Spikevax) (Intramuscular) was withdrawn on 19-Dec-2021. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Date and time of last administration vaccine was on 19-Dec-2021. Treatment information was not provided. Company comment: This regulatory case concerns a 57-year-old, male patient with no medical history reported and with Interchange of vaccine products (Tozinameran, pfizer biontech covid-19 vaccine), who experienced unexpected serious AESI events of cerebral venous sinus thrombosis and thrombosis with thrombocytopenia syndrome (seriousness criterion: Hospitalisation). Thrombosis with thrombocytopenia syndrome occurred after 16 days and cerebral thrombosis unspecified days after receiving third dose of mRNA-1273 Vaccine. Antiplatelet antibody test was negative. At the time of the report, cerebral venous sinus thrombosis had resolved and thrombosis with thrombocytopenia syndrome was resolving. The benefit-risk relationship of mRNA-	Negative laboratory result for anti-platelet antibody is not consistent with TTS. Very limited clinical information.	

Case ID	Narrative	MAH Comment	WW Identifier
	1273 Vaccine is not affected by this report. Events seriousness assessed as per Regulatory Authority reporting.		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 18-Feb-2022. The most recent information was received on 02-Mar-2022 and was forwarded to Moderna on 02-Mar-2022. This regulatory authority case was reported by a consumer and describes the occurrence of CEREBRAL INFARCTION (cerebral infarction) in a 78-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 094F21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Previously administered products included for Product used for unknown indication: BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0,3ML on 19-Mar-2021, BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0 and3ML on 19-Apr-2021. Past adverse reactions to the above products included No adverse event with BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0,3ML, BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0 and3ML. On 16-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 21-Dec-2021, the patient experienced CEREBRAL INFARCTION (cerebral infarction) (seriousness criterion hospitalization) and PLATELET COUNT DECREASED (platelets lowered). At the time of the report, CEREBRAL INFARCTION (cerebral infarction) and PLATELET COUNT DECREASED (platelets lowered) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Platelet count: 120 /nl (per nanolitre) 120 /nL (per nanolitre), 160 /nl (per nanolitre) 160 /nL (per nanolitre) and 70 /nl (per nanolitre) 70 /nL (per nanolitre). No concomitant medication was provided. No Treatment medication was provided. Company comment: This regulatory case concerns a 78-year-old female patient no reported medical history, who experienced the unexpected serious AESI of ischemic cerebral infarction and non-serious, unexpected AESI of platelet count decreased. The events occurred 5 days after the 3rd dose of the mRNA-1273 Vaccine. Additionally, there was an	Consumer report with limited clinical information. Stroke not uncommon at age 78 years.	[REDACTED]

Case ID	Narrative	MAH Comment	WW Identifier
	interchange of vaccine products as the patient received Comirnaty for the first two doses. No further details regarding the events were provided. The patient's advanced age is a possible confounder. The benefit-risk relationship of mRNA-1273 is not affected by this report. The seriousness assessment as per regulatory authority. Most recent FOLLOW-UP information incorporated above includes: On 02-Mar-2022: Follow up received included updated lab investigations and new event "platelet count decreased" was added. On 02-Mar-2022: Translation received on 04-Mar-2022: Event verbatim (Cerebral infarction) updated, Lab data updated		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 22-Feb-2022. The most recent information was received on 22-Feb-2022 and was forwarded to Moderna on 25-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of DYSPNOEA (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis), PELVIC VENOUS THROMBOSIS (4-level pelvic venous thrombosis), CEREBRAL INFARCTION (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis), THROMBOCYTOPENIA (Thrombocytopenia), DEEP VEIN THROMBOSIS (4-level pelvic venous thrombosis), HEMIPARESIS (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis) and PULMONARY EMBOLISM (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis) in a 73-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. Concurrent medical conditions included Chronic renal insufficiency, Type 2 diabetes mellitus, Unspecified vitamin D deficiency, Anti-platelet factor 4 antibody positive, Hyperlipidaemia, COVID-19 since April 2021 and Arterial hypertension. On 22-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 23-Dec-2021, the patient experienced DYSPNOEA (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis) (seriousness criterion hospitalization), PELVIC VENOUS THROMBOSIS (4-level pelvic venous thrombosis) (seriousness criterion hospitalization), CEREBRAL INFARCTION (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis)	Lack of platelet count and diagnostic test results. Pelvic vein thrombosis (unusual site) diagnosed 2 weeks after initial thrombotic events at common sites. Multiple serious chronic disease risk factors and prior Covid disease. Anti-platelet factor 4 antibody positive.	

Case ID	Narrative	MAH Comment	WW Identifier
	(seriousness criterion hospitalization), THROMBOCYTOPENIA (Thrombocytopenia) (seriousness criterion hospitalization), DEEP VEIN THROMBOSIS (4-level pelvic venous thrombosis) (seriousness criterion hospitalization), HEMIPARESIS (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis) (seriousness criterion hospitalization) and PULMONARY EMBOLISM (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis) (seriousness criterion hospitalization). At the time of the report, DYSPNOEA (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis), PELVIC VENOUS THROMBOSIS (4-level pelvic venous thrombosis), CEREBRAL INFARCTION (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis), THROMBOCYTOPENIA (Thrombocytopenia), DEEP VEIN THROMBOSIS (4-level pelvic venous thrombosis), HEMIPARESIS (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis) and PULMONARY EMBOLISM (Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis) had resolved with sequelae. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. Concomitant medications were not provided by the reporter. Patient did not had any known allergies. Pre-existing conditions included, arterial hypertension with hypertensive derailment, hyperglycaic derailed (insulin & OAD, HbA1c 8.8%), hypercholesterolemia, chronic renal failure stage IIIa, SARS-CoV-2 infection with dehydration, without pneumonic infiltrate in April 2021. Patient took booster vaccination with Moderna (unknown whether 1st, 2nd or 3rd vaccination, patient was ill with Covid -19 in April 2021. On 23 Dec 21 morning, patient experienced pulmonary embolism on both sides, systemic lysis, evening of 23 Dec 21 media infarction on the right, undergone intubation, ITS, extubation, neurological normal station. No, TVT detected when taken, in control sono was done after 2 weeks, 4-level pelvic leg vein thrombosis was detected. For intake		

Case ID	Narrative	MAH Comment	WW Identifier
	thrombocytopenia, detection of platelet factor-4-AK. No heparins were given previously (outpatient) Treatment information was not provided. Acute admission with acute dyspnea on the morning of Dec 23, 2021, pulmonary embolism detected on both sides with cor pulmonale, systemic Thrombolysis occurs, afternoon development hemiparesis left, mediainfarction on the right. Most recent FOLLOW-UP information incorporated above includes: On 22-Feb-2022: Translation document received on 25-Feb-2022 was significant included Event Verbatim was updated. Company Comment : This regulatory case concerns a 73-year-old, male patient with relevant medical history of Type 2 diabetes mellitus, Anti-platelet factor 4 antibody positive, Hyperlipidemia, COVID-19 and Arterial hypertension, who experienced serious (hospitalisation) unexpected events of Dyspnoea, Hemiparesis and serious (hospitalisation) unexpected AESI events of Pelvic venous thrombosis, Cerebral infarction, Thrombocytopenia, Deep vein thrombosis and Pulmonary embolism, a day after receiving booster dose of mRNA-1273 Vaccine. On the day of booster vaccination, in the morning patient developed pulmonary embolism on both sides, systemic lysis and by evening media infarction on the right, intubation, ITS, extubation, neurological normal station. TVT was not detected when taken in control but after 2 weeks patient had 4-level pelvic venous thrombosis. For intake thrombocytopenia, detection of platelet factor-4- AK. Patient was not on heparin previously. In causal diagnosis for thrombosis in the thrombophilia laboratory, only borderline antithrombin III deficiency was detected (75%), no evidence of malignancy. Clinically patient had dysphagia, anarthria, hemiplegia on the left. Before the event, the Patient was self-sufficient. At the time of the report, events had resolved with sequelae. Elderly age and medical history of Type 2 diabetes mellitus, Anti-platelet factor 4 antibody positive, Hyperlipidemia, COVID-19 and Arterial hypertension could be contributory factors for all the events. The benefit-risk relationship of mRNA-1273 is not affected by this report. Event seriousness assessed as per Regulatory Authority reporting.		
	This case was initially received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 21-Feb-2022. The most recent information was received on 15-Mar-2022 and was forwarded to Moderna on 23-Mar-2022. This case, initially reported to the Pharmaceuticals and Medical Devices Agency (PMDA) by a (physician), was received via the PMDA ([REDACTED]). On 15-Mar-2022, follow-up information was received from a physician. Arteriosclerosis of the base of the brain and hyperkalaemia was assessed as serious by the MAH. The vaccine recipient had a history of treatment for left brain infarction two years ago. The patient was under treatment with edoxaban tosilate hydrate as anticoagulant agent, but no cardiac disease had been found. On an unknown date, the patient received the 1st dose of a COVID-19 vaccine (unknown product name). On an unknown date, the patient received the 2nd dose of a COVID-19 vaccine (unknown product name). On	Lack of platelet count and diagnostic test results. Death and its prodrome were not witnessed. Autopsy final report pending. Elderly patient with prior stroke.	

Case ID	Narrative	MAH Comment	WW Identifier
	18-Feb-2022, around 15:00, the patient received the 3rd vaccination with this vaccine. The patient had no symptoms on the day of the vaccination. On 19-Feb-2022, during the day, the patient complained of mild malaise. Around 17:00, the family member confirmed that the patient was alive. Around 18:30, the patient took a bath. The patient experienced thrombosis with thrombocytopenia. Around 19:25, the family member found the patient in a cardio-respiratory arrest state in the bathtub. An ambulance call was made, and cardiopulmonary resuscitation was performed by the family member. Around 19:40, an ambulance team confirmed that the patient was in asystole. Resuscitative measures were taken. Around 20:30, the patient arrived at a hospital. At 21:01, the patient continued to be in asystole status. Blood sampling and other tests revealed thrombocytopenia, elevated D-dimer, hepatic function disorder, hyperkalaemia, and acidosis. Resuscitation was judged to be difficult, and the patient was confirmed dead. The cause of death was near drowning. Autopsy imaging did not show cerebral hemorrhage and new-onset cerebral infarction. No appreciable findings were obtained except for the findings which could be considered as changes after death or cardiopulmonary resuscitation including gases in the hepatic portal. It cannot be ruled out that the patient experienced ischemic cerebral infarction or brain-stem infarction caused by disseminated intravascular coagulation syndrome or thrombus. On an unknown date, an autopsy was performed. The left lung weighed 320 g and the right lung weighed 506 g. Intrabronchial foam, pleural effusions, and arteriosclerosis of the base of the brain were seen. The outcome of thrombosis with thrombocytopenia, cardio-respiratory arrest, possibility of disseminated intravascular coagulation syndrome, possibility of ischemic cerebral infarction, possibility of brain-stem infarction, and near drowning was reported as fatal. The outcome of malaise, hepatic function disorder, hyperkalaemia, acidosis, pleural effusions, and arteriosclerosis of the base of the brain was unknown. No follow-up investigation will be made. Reporter's comment: At present, the cause of death is unknown, and a judicial autopsy was conducted to consider the possibility of abnormal death while taking a bath. Acute cardiac death and choking death due to aspiration may be other possible factors. The relationship between the cause of death and the adverse events is under forensic investigation. Looking back over the interview with the family members, it is difficult to believe that the patient had chronic thrombocytopenia of up to 57,000, even though the patient was seen by the nearby primary physician for underlying diseases. Although platelet decrease can be caused by a variety of factors, it was too soon to cause drug-induced platelet decrease. There was no bleeding, and unless the patient originally had idiopathic thrombocytopenic purpura, it is reasonable to consider that disseminated intravascular coagulation syndrome would have occurred. It is unclear whether a sudden decrease in platelet count may occur as a postmortem change; however, if blood clots were formed in association with immune response following administration of this vaccine on the previous day, the occurrence of adverse events may be temporally related to and the timing of administration of this vaccine. Since concomitant drugs have been used without change in the past and are unlikely to be associated with acute diseases such as platelet decrease, thrombus formation, and		

Case ID	Narrative	MAH Comment	WW Identifier
	cerebral infarction, the occurrence of adverse events is not associated with concomitant drugs. Atherosclerosis can be considered as one of the factors of the development of cerebral infarction. Narrowing of the vessel lumen due to the atherosclerosis increases the risk of occlusion when a thrombus is produced; therefore, it is difficult to consider that the events in this case were not related to the pathological factors of the underlying old cerebral infarction. This case is currently being analyzed by the forensic medicine course of a medical institution after the autopsy was performed, and the causal relationship between vaccination with this vaccine and death is under investigation with forensic medicine. Therefore, nothing definitive can be said at this time. At the time of the initial diagnosis, cerebral hemorrhage or cerebral infarction was considered based on the patient's history, but autopsy imaging revealed no cerebral hemorrhage. In addition, because the changes were noted about three hours after the patient was found in cardio-respiratory arrest, no CT imaging changes suggesting cerebral infarction were observed. It is notable that no increase in the shadow of asymptomatic cerebral infarction was observed compared to the CT image at the time of previous cerebral infarction several years earlier. Anticoagulants were taken, and the daily life was considered to have been appropriately controlled. Thus, if a cerebral infarction accidentally occurred near the brain stem on the day after the vaccination, it must have been a rather unfortunate situation. In addition, platelet decrease, elevated D-dimer, and hepatic function disorder may occur even as changes after death, but the time for the changes were too brief. It seemed more reasonable to assume that the onset had begun several hours before the time of near drowning based on the test values. It is regrettable that treatments could not have been given when the patient complained of malaise. However, at the daytime of the day following the administration, thrombosis was caused by a mechanism similar to disseminated intravascular coagulation syndrome, and ischaemic enterocolitis and hepatic function disorder due to intrahepatic vascular occlusion developed gradually. Eventually, thrombosis developed within the basilar arteriosclerosis when the patient was taking a bath, resulting in cerebral infarction. The possibility that the patient had difficulty moving and experienced near drowning cannot be ruled out. Although there is no clue of examination that would raise the possibility of this hypothesis, it is desirable, in this case, to avoid concluding easily that a coincidental event developed. It is hoped that investigation with forensic medicine will clarify whether or not there was a causal relationship. Follow-up received on 15-MAR-2022 Updated: Patient Information, Other Relevant History, Lab Data, Product Information, Event Information, Narrative, Reporter Comments LP Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship. Company comment: This spontaneous case report concerns a 77-year-old female patient with relevant medical history of previous cerebral infarction, who experienced serious unexpected		

Case ID	Narrative	MAH Comment	WW Identifier
	events of Thrombosis with thrombocytopenia syndrome, Cardiorespiratory arrest, Disseminated intravascular coagulation, Ischaemic cerebral infarction, Brain stem infarction and Near drowning which ended with fatal outcome. In addition, the patient also experienced serious unexpected events of Hyperkalaemia and Cerebral arteriosclerosis, as well as non-serious unex		
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 27-Feb-2022 and was forwarded to Moderna on 27-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of DEEP VEIN THROMBOSIS (Deep vein thrombosis leg) and THROMBOCYTOPENIA (platelet count <150 Å— 109/L) in a 72-year-old male patient who received mRNA-1273 (Moderna CoviD-19 Vaccine) for an unknown indication. Nil relevant to VTE Patient has not had symptoms associated with COVID-19 Not had a COVID-19 test. The patient's past medical history included Non-smoker since an unknown date. On 02-Nov-2021, the patient received third dose of mRNA-1273 (Moderna CoviD-19 Vaccine) (unknown route) 1 dosage form. On 12-Nov-2021, the patient experienced DEEP VEIN THROMBOSIS (Deep vein thrombosis leg) (seriousness criterion medically significant). On an unknown date, the patient experienced THROMBOCYTOPENIA (platelet count <150 Å— 109/L) (seriousness criterion medically significant). At the time of the report, DEEP VEIN THROMBOSIS (Deep vein thrombosis leg) was resolving and THROMBOCYTOPENIA (platelet count <150 Å— 109/L) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Fibrin D dimer: d-dimer was more than 4000 D-dimer was more than 4000. On an unknown date, Platelet factor 4: anti-pf4 antibodies were not identified (normal) Anti-PF4 antibodies were not identified. The action taken with mRNA-1273 (Moderna CoviD-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna CoviD-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. No Concomitant medications were reported but had previous 2 AZ vaccines. The Patient had Moderna booster vaccine 02-Nov-2021 and then he flew to [REDACTED] in 1.5 hours. Patient leg became painful and swollen and then waited for 10 days before	72yo man with DVT at a common site (leg), anti-PF4 antibodies were not identified	

Case ID	Narrative	MAH Comment	WW Identifier
	seeing it. Patient was diagnosed with L CFV/SFV/popliteal vein when returned from his holiday. Patient had no discernible risk factors for VTE. This report was related to possible blood clots or low platelet counts. This report was not related to possible myocarditis or pericarditis. Relevant investigations or tests conducted include bloods and doppler USS. On 22/11/2022, platelet count was measured and on the same day, lowest platelet count measured after vaccine was 138. On 22/11/2022, D-dimer was measured, and patient was diagnosed on 23/11/2022 with doppler USS. There was no medical history of previous venous or arterial thromboses. The Patient had no previous reactions to medications, especially heparin or anticoagulants. Patient had quiescent Bronchiectasis only and no other suspected autoimmune or inflammatory disease, including vasculitis. Patient had no current or any history of malignancy. Patient had no concurrent or historical intracranial malignancy and intracranial infections. Patient had no hemorrhage. Patient had no recent surgical or medical interventions to the central nervous system (including lumbar puncture) and trauma/head injury. Patient had PT-13; Fibrinogen-2.9; Activated Partial Thromboplastin Clotting Time (aPTT) -26. Thrombophilia screen, Infectious screen (eg HIV, hepatitis C/B, herpes zoster/ CMV), Blood film findings and Autoimmune screen were not indicated. PF4 HIT assay optical density was not done and HIT assay was not used. Patient was not tested positive for COVID-19 since vaccination and not enrolled in clinical trials. No Treatment information was reported. Company comment: This regulatory authority case concerns a 72-year-old male patient, with no relevant medical history, who experienced the unexpected AESI of deep vein thrombosis and AESI of thrombocytopenia, which were considered as medically significant. The events occurred approximately 10 days after the third dose of mRNA-1273. As reported, the patient had Moderna booster vaccine and then he flew to Norway in 1.5 hours. Patient leg became painful and swollen and then he waited for 10 days before seeing it. Patient was diagnosed with L CFV/SFV/popliteal vein when returned from his holiday. Patient had no discernible risk factors for VTE, as reported. Patient flying on an airplane may have increased the risk and remains a confounder for DVT. The benefit-risk relationship of mRNA-1273 is not affected by this report.		
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 25-Feb-2022 and was forwarded to Moderna on 25-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of DIARRHOEA (diarrhea), VOMITING (vomit), ANAEMIA (anaemia during hospitalisation), MYALGIA (muscle pain), MALAISE (general malaise) and THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (OBS suspicion of vaccine-induced thrombotic thrombocytopenia, no other symptoms hereto) in a 79-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3004954) for COVID-19 immunisation.	No diagnostic evidence of thrombosis: "In December 2021, Computerised tomogram thorax: nb. lung embolism: not found nb. lung embolism: not found." No anti-PF4 results. Patient had multiple symptoms not part of usual TTS clinical picture: diarrhea, vomiting, malaise, myalgia, anemia	

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	Previously administered products included for COVID-19 immunisation: SPIKEVAX on 18-Mar-2021 and SPIKEVAX on 15-Apr-2021. Past adverse reactions to the above products included No adverse event with SPIKEVAX and SPIKEVAX. On 30-Nov-2021, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. In December 2021, the patient experienced ANAEMIA (anaemia during hospitalisation) (seriousness criterion hospitalization) and THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (OBS suspicion of vaccine-induced thrombotic thrombocytopenia, no other symptoms hereto) (seriousness criteria hospitalization and medically significant). On an unknown date, the patient experienced DIARRHOEA (diarrhea) (seriousness criterion hospitalization), VOMITING (vomit) (seriousness criterion hospitalization), MYALGIA (muscle pain) (seriousness criterion hospitalization) and MALAISE (general malaise) (seriousness criterion hospitalization). In December 2021, ANAEMIA (anaemia during hospitalisation) and THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (OBS suspicion of vaccine-induced thrombotic thrombocytopenia, no other symptoms hereto) had resolved. At the time of the report, DIARRHOEA (diarrhea), VOMITING (vomit), MYALGIA (muscle pain) and MALAISE (general malaise) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In December 2021, Blood test: liver bile count increased (abnormal) liver bile count increased. In December 2021, C-reactive protein: slightly increased: 55 unit not specified (High) slightly increased: 55 unit not specified. In December 2021, Coagulation test: too low antithrombin (abnormal) too low antithrombin. In December 2021, Computerised tomogram: without malignant (normal) without malignant. In December 2021, Computerised tomogram thorax: nb. lung embolism: not found nb. lung embolism: not found. In December 2021, Echocardiogram: good function, without valvulopathy (normal) good function, without valvulopathy. In December 2021, Fibrin D dimer: increased (High) increased. In December 2021, Platelet count: thrombocytopenia, down to 65 unit not specified (abnormal) thrombocytopenia, down to 65 unit not specified. In December 2021, Reticulocyte count: reticulocytopenia, followed by an increased count (abnormal) reticulocytopenia, followed by an increased count. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments.		

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	No concomitant medication were provided. No treatment information were given. Company comment: This regulatory authority case concerns a 79-year-old female patient, with no medical history reported, who experienced the unexpected events of anemia, diarrhoea, vomiting, myalgia, malaise and AESI of thrombosis with thrombocytopenia syndrome, which all required hospitalization. The events of anemia and thrombosis with thrombocytopenia syndrome occurred in the month after the third dose of mRNA-1273, while the rest of the events occurred on unknown date. Laboratory findings included thrombocytopenia and reticulocytopenia, followed by an increased count. As reported, OBS suspicion of vaccine-induced thrombotic thrombocytopenia, no other symptoms hereto. The benefit-risk relationship of mRNA-1273 is not affected by this report.		
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 25-Feb-2022 and was forwarded to Moderna on 25-Feb-2022. This regulatory authority case was reported by a pharmacist and describes the occurrence of GINGIVAL BLEEDING (gingivorrhagia) and THROMBOCYTOPENIA (Thrombocytopenia) in a 76-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 091F21A) for Revaccination with different COVID-19 vaccine. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Hypertension arterial and Type 2 diabetes mellitus. Concomitant products included TOZINAMERAN (COMIRNATY) from 19-May-2021 to an unknown date for COVID-19 vaccination. On 15-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. In December 2021, the patient experienced THROMBOCYTOPENIA (Thrombocytopenia) (seriousness criterion hospitalization). On 21-Dec-2021, the patient experienced GINGIVAL BLEEDING (gingivorrhagia) (seriousness criterion hospitalization) and THROMBOTIC THROMBOCYTOPENIC PURPURA (Thrombocytopenic purpura). At the time of the report, GINGIVAL BLEEDING (gingivorrhagia), THROMBOCYTOPENIA (Thrombocytopenia) and THROMBOTIC THROMBOCYTOPENIC PURPURA (Thrombocytopenic purpura) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, SARS-CoV-2 test: negative (Negative) NEGATIVE. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown.	Limited clinical information. Age 76 years, hypertension and Type 2 diabetes are risk factors for thrombosis.	

Case ID	Narrative	MAH Comment	WW Identifier
	For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Treatment information was not provided. Company comment. This regulatory case concerns a 76 – year – old, female patient with no relevant medical history, and past drug history of administration of two doses of Comirnaty COVID-19 vaccine, who experienced the unexpected, serious (hospitalization) AESI of Thrombocytopenia and unexpected serious event of gingival bleeding. The unexpected AESI thrombotic thrombocytopenic purpura occurred 6 days after the administration of a dose of mRNA-1273 vaccine, considered as third dose of her COVID – 19 immunization schedule. No details regarding hospitalization, laboratory data, or clinical course were available for medical reviewing. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.		
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 22-Feb-2022 and was forwarded to Moderna on 01-Mar-2022. This case, initially reported to the [REDACTED] by a (physician), was received via the [REDACTED]. On an unknown date, the patient received the 1st dose of a COVID-19 vaccine (product name unknown). On an unknown date, the patient received the 2nd dose of a COVID-19 vaccine (product name unknown). On an unknown date, body temperature before the vaccination: 35.4 degrees Celsius. On 24-Jan-2022, at 14:19, the patient received the 3rd vaccination with this vaccine. On 14-Feb-2022, the patient experienced deep venous thrombosis in the right lower limb. The patient noticed pain in the right lower limb. On 15-Feb-2022, the patient visited an orthopedic surgeon with a chief complaint of pain in the lower limb. The cause was not identified, and the patient received symptomatic therapy with acetaminophen and pregabalin. On 18-Feb-2022, the patient visited a urological physician for penile oedema. Coagulation abnormality (PT-INR: 1.59, fibrinogen: 46.2, and FDP-D: 386.2) with decreased platelet count of 43,000/mcL was noted. In addition, the patient was diagnosed with deep venous thrombosis in the right lower limb based on the image findings. The patient was suspected to have thrombosis with thrombocytopenia due to the vaccination with this vaccine and was admitted to the hospital. The outcome of deep venous thrombosis in the right lower limb, penile oedema, and suspected thrombosis with thrombocytopenia was unknown. Follow-up investigation will be made. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.	3 week TTO, lack of anti-PF4 antibody studies	
	This literature-non-study case was reported in a literature article and describes the occurrence of THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Thrombosis with thrombocytopenia syndrome), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (She can now perform activities of daily living with moderate assistance), WALKING AID USER (Walks using a cane) and SEIZURE (Seizure) in a 56-year-old female patient who received mRNA-1273	obese, hypothyroid, hyperlipidemia, TTO 8 wks from dose 2, PLT 139, D-Dimer high, PF-4 antibody negative, CVST,	

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	(Spikevax) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. LITERATURE REFERENCE: Gurjar H, Dhallu M, Lvovsky D, Sadullah S, Chilimuri S. A rare case of coronavirus disease 2019 vaccine-associated cerebral venous sinus thrombosis treated with mechanical thrombectomy. Am J Case Rep. 2022;23:e935355 The patient's past medical history included Thrombectomy (Patient was referred to endovascular mechanical thrombectomy. Subsequently, she underwent thrombectomy, with successful restoration of venous blood flow.) and Intubation (patient was intubated in the ED for airway protection.). Concurrent medical conditions included Hypothyroidism, Hyperlipidemia and Obesity. Concomitant products included ATORVASTATIN for Hyperlipidemia, LEVOTHYROXINE for Hypothyroidism. On an unknown date, the patient received second dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On an unknown date, received first dose of mRNA-1273 (Spikevax) (unknown route) dosage was changed to 1 dosage form. On an unknown date, the patient experienced THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Thrombosis with thrombocytopenia syndrome) (seriousness criteria hospitalization, medically significant and life threatening), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (She can now perform activities of daily living with moderate assistance) (seriousness criterion medically significant), WALKING AID USER (Walks using a cane) (seriousness criterion medically significant), SEIZURE (Seizure) (seriousness criterion medically significant) and BLOOD POTASSIUM DECREASED (Blood potassium decreased). The patient was treated with WARFARIN for Cerebral venous sinus thrombosis, at an unspecified dose and frequency; LEVETIRACETAM for Epilepsy, at an unspecified dose and frequency; HEPARIN for Cerebral venous sinus thrombosis, at an unspecified dose and frequency and Surgery (thrombectomy, mechanically ventilated) for Thrombosis with thrombocytopenia syndrome. At the time of the report, THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Thrombosis with thrombocytopenia syndrome) had resolved with sequelae, LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (She can now perform activities of daily living with moderate assistance) and WALKING AID USER (Walks using a cane) had not resolved and SEIZURE (Seizure) and BLOOD POTASSIUM DECREASED (Blood potassium decreased) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Activated partial thromboplastin time (27.2-39.6): 30.8 s (normal) 30.8 s. On an unknown date, Anti-platelet factor 4 antibody test: negative (Negative) negative.		

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	On an unknown date, Antinuclear antibody: positive (Positive) positive in a nucleolar pattern at low titers of 1: 80. On an unknown date, Antiphospholipid antibodies: negative (Negative) negative. On an unknown date, Antithrombin III (80-135): 105 % (normal) 105 %. On an unknown date, Blood creatinine (0.5-1.5): 0.6 mg/dl (normal) 0.6 mg/dL. On an unknown date, Blood potassium (3.5-5): 2.7 meq per (Low) 2.7 meq per. On an unknown date, Blood pressure measurement: 126/67 mmhg 126/67 mmHg. On an unknown date, Blood sodium (135-145): 136 milliequivalent per liter (normal) 136 milliequivalent per liter. On an unknown date, Blood thyroid stimulating hormone (0.4-4.5): 4.05 miu/l (normal) 4.05 mIU/L. On an unknown date, Body temperature: 37°c 37°C. On an unknown date, C-reactive protein: 56.48 mg/l (High) 56.48 mg/L (reference range, less than 5). On an unknown date, Cardiolipin antibody: negative (Negative) negative. On an unknown date, Chest X-ray: normal (normal) The initial chest X-ray did not show any infiltrates. On an unknown date, Computerised tomogram head: abnormal (abnormal) underwent a CT scan of the head, which showed scattered hemorrhages and infarcts in both right and left cerebral hemispheres.. On an unknown date, Drug screen: negative (Negative) urine drug screen was negative.. On an unknown date, Fibrin D dimer (0-230): 16666 nanograms per (High) 16666 nanograms per milliliter. On an unknown date, Glycosylated haemoglobin (4.7-6.4): 5.5% (normal) 5.5%. On an unknown date, Haemoglobin (12.0-16.00): 12.8 g/dl (normal) 12.8 g/dL. On an unknown date, Heart rate: 67 beats per minute 67 beats per minute. On an unknown date, International normalised ratio (0.85-1.14): 1.04 (normal) 1.04. On an unknown date, Lipids: normal (normal) normal. On an unknown date, Liver function test: normal (normal) normal. On an unknown date, Magnetic resonance imaging head: cerebral venous sinus thrombosis (abnormal) She underwent MRI brain with angiogram (MRA) and venogram (MRV), which confirmed infarcts in watershed areas, along with foci of hemorrhages, and signal void in superior sagittal and inferior sagittal sinuses, left transverse sinus, left sigmoid sinus, and left internal jugular, suggestive of CVSST. On an unknown date, Physical examination: abnormal physical examination were notable for confusion and restlessness with the patient being non-communicative and with predominant left-side weakness. On an unknown date, Platelet count (150 000-400 000): 139000 per ml (Low) 139000 per mL. On an unknown date, Prothrombin time (9.9-13.3): 12.0 s (normal) 12.0 s. On an unknown date, Respiratory rate: 17 per minute 17 per minute. On an unknown date, SARS-CoV-2 antibody test: 1726 units per milliliter (Positive) antibodies against Spike protein for severe acute respiratory syndrome coronavirus-2		

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	(SARS-CoV-2) were 1726 units per milliliter (reference range, non-reactive), signifying an adequate immune response to the vaccine and negative (Negative) antibodies against nucleocapsid protein were negative, signifying absence of prior SARS-CoV-2 infection. On an unknown date, SARS-CoV-2 test: negative (Negative) Patient tested negative for COVID-19 based on reverse transcription polymerase chain reaction (RT-PCR) of a nasopharyngeal swab.. On an unknown date, Urine analysis: normal (normal) Urinalysis did not show any signs of infection.. On an unknown date, Venogram: abnormal (abnormal) Confirmed infarcts in watershed areas, along with foci of hemorrhages, and signal void in superior sagittal and inferior sagittal sinuses, left transverse sinus, left sigmoid sinus, and left internal jugular, suggestive of CVST.. On an unknown date, White blood cell count (4800-10800): 10100 per cubic millimeter (normal) 10100 per cubic millimeter. For mRNA-1273 (Spikevax) (Unknown), the reporter considered THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Thrombosis with thrombocytopenia syndrome), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (She can now perform activities of daily living with moderate assistance), WALKING AID USER (Walks using a cane), SEIZURE (Seizure) and BLOOD POTASSIUM DECREASED (Blood potassium decreased) to be related. Postmenopausal patient presented with fluctuating sensorium for 5 days and left-side weakness of 1-day duration. Patient was otherwise well until her daughter noticed a sudden onset of confusion, when patient was found to be mumbling incomprehensibly. Patient daughter reported the symptoms to be fluctuating. On the day of presentation, patient was noted to have sensory symptoms with a funny feeling in her left arm when she tried to open the door with her left hand. Patient received first dose around 12 weeks before presentation and the second dose 8 weeks before presentation. Patient was found to be restless, non-communicative, afebrile and confused, with left upper- and lower-extremity weakness. Patient antibodies against Spike protein for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) were 1726 units per mL, signifying an adequate immune response to the		
	This case was initially received via Takeda Pharmaceuticals (Reference number [REDACTED]) on 07-Mar-2022. The most recent information was received on 07-Apr-2022 and was forwarded to Moderna on 15-Apr-2022. This case, initially reported to the Pharmaceuticals and Medical Devices Agency (PMDA) by a physician, was received via the PMDA (Ref, [REDACTED]). On 07-Apr-2022, follow-up information was received from a physician. The vaccine recipient had a history of regular visits to a hospital for mental retardation in childhood. On an unknown date, the patient received the 1st dose of a novel coronavirus vaccine (product name unknown). On an unknown date, the patient received the 2nd dose of a	marked decrease in ADAMTS 13 activity, acute leukemia, diagnosis of thrombotic thrombocytopenic purpura (different from TTS), PLT 9K,	

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	novel coronavirus vaccine (product name unknown). On 04-Feb-2022, the patient received the 3rd vaccination with this vaccine. On 16-Feb-2022, thrombotic thrombocytopenic purpura developed. Impaired appetite and respiratory discomfort were noted. Disturbed consciousness and light-headedness also developed. On an unknown date, black stool, difficulty in moving the body, and subcutaneous petechiae were observed. On 21-Feb-2022, at 10:25, the patient visited the outpatient department of internal medicine at the reporting hospital. There were significant conjunctival anaemia and mildly disturbed consciousness with E4V4M5 based on the Glasgow Coma Scale. Body temperature was 38.1 degrees Celsius. Drip infusion of ringer's solution was started. Blood count and coagulation test were performed. There was no aggregation finding in the smear. Blood tests revealed marked thrombocytopenia at 9,000/mcL, marked leukocytosis at 36,830, marked anemia, hemolytic findings, and mild renal impairment. Drip infusion of meropenem hydrate 0.5 g plus normal saline 100 mL was performed. Drip infusion of methylprednisolone sodium succinate 1,000 mg plus normal saline 100 mL was performed. LDH was 2,445 U/L, and indirect bilirubin was 5.3 mg/dL. SARS-CoV-2 test was performed with quantitative antigen test to be negative. Other clinical symptoms included headache, decreased blood pressure, tachycardia, cyanosis, tachypnea, redness/dyscoloration/warmth/pitting edema of the extremities, and petechiae/subcutaneous hemorrhage/purpura/bleeding tendency. Transthoracic echocardiography showed no findings of myocardial infarction or cardiac tamponade. Chest X-ray showed findings suggestive of thrombus and embolism, cardiomegaly, and image of pulmonary congestion. At 11:29, chest and abdominal CT scan was performed. There were findings of suspected thrombus and embolism. Pulmonary congestion was suspected. Enlarged chest lymph nodes, increased concentration of fatty tissue in the mediastinum, suspected soft tissue shadow, and mild enlarged spleen were noted. Malignant lymphoma was considered in the differentiation. The diagnosis was suspected haemorrhage of digestive tract. At 14:54, biopsy of bone marrow and pathological test was performed. Acute leukaemia was diagnosed. There were no findings of thrombus or embolism. The possibility of hemolytic anemia was suggested, and the possibility of complication of idiopathic thrombocytopenic purpura (Evans syndrome) could not be ruled out. At 15:00, disturbed consciousness gradually worsened. Respiratory condition also worsened. The PLASMIC score was as high as six points, and thrombotic thrombocytopenic purpura was suspected. Treatments such as fluid replacement and steroid administration were started. At 15:04, the patient stopped breathing. At 15:09, the patient was in cardio-respiratory arrest. Cardiopulmonary resuscitation, including endotracheal intubation, chest compression, and administration of adrenaline, was started. The patient was observed to resume spontaneous heartbeat once but soon in asystole. Thereafter, the patient did not resolve. At 16:14, the patient's death was confirmed. The cause of death was thrombotic thrombocytopenic purpura. No autopsy was performed. On 21-Feb-2022, blood tests revealed marked decrease in ADAMTS 13 activity to less than 1% (0.01 IU/mL). Direct coombs test, antinuclear antibody, and anticardiolipin antibody showed no significant abnormalities, and the patient was diagnosed with thrombotic thrombocytopenic purpura. Heparin-induced		

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	thrombocytopenia, immune thrombocytopenia, disseminated intravascular coagulation syndrome, and antiphospholipid syndrome were excluded. The outcome of disturbed consciousness, cardiomegaly, congestion in lung, enlarged spleen, suspected haemorrhage of digestive tract, and acute leukaemia was unknown. The outcome of Thrombotic thrombocytopenic purpura and cardio-respiratory arrest was reported as fatal. No follow-up investigation will be made. 【CT scan of the chest and abdomen】 (date of exam:21-Feb-2022) Findings: • Interlobular septal wall thickening and bronchial wall thickening were observed in both lungs, and pulmonary congestion was suspected. • Band-like opacity was observed in the right middle lobe of the lung, and scarring and collapse after inflammation were suspected. • Cardiomegaly, pericardial effusion, and enlarged left supraclavicular lymph nodes were observed. • Mediastinal lymph nodes also appeared enlarged, and there appeared to be increased concentration of fatty tissue in the mediastinum and soft tissue shadow. • Caudate lobe of the liver was enlarged, but there was no gross mass in the liver. • Enlarged spleen was observed, and accessory spleen was suspected. Ureterohydronephrosis could not be pointed out. • Malignant lymphoma was considered in the differentiation. 【Bone marrow biopsy】 (date of exam:21-Feb-2022) Collection site: iliac bone Clinical diagnosis: acute leukaemia Cytological findings and consideration: bone marrow showed hyperplasia with marked predominance of erythroblasts and marked decrease of megakaryocytes. No increase in myeloblasts was observed. Around 10% of the granulocytic and erythroblastic series showed the above dysplasia. Megakaryocytic series were difficult to be judged as dysplasia because of marked decrease. The large number of polychromatophilic erythroblasts in erythroblastic cells suggested increased production of erythroblastic cells. There were no findings suggestive of bone marrow infiltration, such as tumor cells. There were no special findings in the result of flow cytometry analysis and leukemia-associated chimeric gene analysis. In the peripheral blood, marked decreases were observed with white blood cell count of 36,830/mcL, Hb of 5.3 g/dL, and platelet count of 9,000/L. Other findings included reticulocytosis, elevated CRP and indirect bilirubin, and elevated LD. Based on the above, hemolytic anemia was suggested, and the possibility of idiopathic thrombocytopenic purpura (Evans syndrome) could not be ruled out. Reporter comments continuation: There are no complications, and although the patient had mild mental retardation as an underlying disease, which is not considered related to thrombotic thrombocytopenic purpura; therefore, the occurrence of adverse events is not related to pathological factors of underlying diseases and complications. Since several cases of thrombotic thrombocytopenic purpura after the vaccination with this vaccine have been reported, the cause of death is related to adverse events. The patient, a young female who had no underlying medical condition other than mild mental retardation and worked, experienced impaired appetite and respiratory discomfort 12 days after the vaccination with this vaccine. The patient visited the reporting hospital 17 days later, but the clinical course was rapid, and the patient died. Although the cause could not be determined at that time, marked decrease in ADAMTS 13 activity was found later, confirming the diagnosis of thrombotic thrombocytopenic purpura. Although		

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	autoantibodies to ADAMTS 13 have not been determined, it is reasonable to assume that this case is acquired thrombotic thrombocytopenic purpura. Several cases of acquired thrombotic thrombocytopenic purpura after the vaccination with this vaccine have been reported including cases in Japan. Therefore, the vaccination with this vaccine was considered to be related to thrombotic thrombocytopenic p		
	This regulatory authority case was reported by a physician and describes the occurrence of DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (suspected DRESS syndrome), PULMONARY EMBOLISM (pulmonary embolism) and THROMBOCYTOPENIA (thrombopenia) in a 68-year-old male patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for COVID-19 vaccination. No Medical History information was reported. On 18-Nov-2021, the patient received third dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 20-Nov-2021, after starting mRNA-1273 (COVID-19 Vaccine Moderna), the patient experienced DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (suspected DRESS syndrome) (seriousness criteria hospitalization and medically significant). On 29-Nov-2021, the patient experienced PULMONARY EMBOLISM (pulmonary embolism) (seriousness criteria hospitalization and medically significant). On 02-Dec-2021, the patient experienced THROMBOCYTOPENIA (thrombopenia) (seriousness criteria hospitalization and medically significant). At the time of the report, DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (suspected DRESS syndrome), PULMONARY EMBOLISM (pulmonary embolism) and THROMBOCYTOPENIA (thrombopenia) was resolving. For mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular), the reporter considered DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (suspected DRESS syndrome), PULMONARY EMBOLISM (pulmonary embolism) and THROMBOCYTOPENIA (thrombopenia) to be possibly related. Company comment: This regulatory authority case concerns a 68-year-old male patient, with described medical history of an asymptomatic Covid-19 infection (positive rapid test) approximately 18 days prior to vaccination with mRNA-1273, who experienced the unexpected AESI of DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (suspected DRESS syndrome), pulmonary embolism, thrombocytopenia, which required hospitalization and were considered as medically significant. The event of suspected DRESS occurred approximately 2 days after the third dose of mRNA-1273, pulmonary embolism occurred 11 days after 3rd dose while thrombocytopenia 14 days after 3rd dose. As	This case was diagnosed as DRESS, not TTS.	

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	reported, 2 days after booster first symptoms began and diagnosis of a DRESS Syndrome. was suspected. There was eosinophilia and suberythroderma with maculopapular sometimes pityriasiform, sometimes eczematous dermatitis, acute renal insufficiency, decreased spontaneous quick and hepatic value increase. Further, an unclear inflammatory state picture was revealed, which was most likely to be interpreted as part of DRESS. Segmental and subsegmental pulmonary embolism with signs of right heart strain was also revealed and severe acute thrombopenia was shown in the laboratory. Later oral thrush and labial herpes were added- complicated, as reported. As stated, in combination of the clinic, the temporal connection with the Covid-19 booster vaccination, histology, and 8 points according to the RegisCar scoring system, the treating team of doctors most likely anticipated a DRESS syndrome with renal, cardiac and hepatic organ involvement and overlapping unclear inflammatory condition and started a high-dose steroid therapy, whereby the condition improved rapidly both clinically and laboratory-chemically. Above mentioned medical history remains a confounder. The benefit-risk relationship of mRNA-1273 is not affected by this report.		
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 15-Mar-2022 and was forwarded to Moderna on 15-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of DEEP VEIN THROMBOSIS (Deep vein thrombosis leg) and THROMBOCYTOPENIA (platelet count <150 Å— 109/L) in an 83-year-old female patient who received mRNA-1273 (Moderna CoviD-19 Vaccine) for an unknown indication. Concurrent medical conditions included Thrombosis leg, Cognitive impairment and Non-smoker. On 16-Oct-2021, the patient received third dose of mRNA-1273 (Moderna CoviD-19 Vaccine) (unknown route) 1 dosage form. On 04-Nov-2021, the patient experienced DEEP VEIN THROMBOSIS (Deep vein thrombosis leg) (seriousness criterion medically significant). On an unknown date, the patient experienced THROMBOCYTOPENIA (platelet count <150 Å— 109/L) (seriousness criterion medically significant). At the time of the report, DEEP VEIN THROMBOSIS (Deep vein thrombosis leg) was resolving and THROMBOCYTOPENIA (platelet count <150 Å— 109/L) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Platelet factor 4: anti-pf4 antibodies were not identified Anti-PF4 antibodies were not identified. The action taken with mRNA-1273 (Moderna CoviD-19 Vaccine) (Unknown) was unknown.	83yo woman, TTO 18 days after 3rd dose. "On an unknown date, Platelet factor 4: anti-pf4 antibodies were not identified Anti-PF4 antibodies were not identified."	

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	For mRNA-1273 (Moderna Covid-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Concomitant product use was not provided by the reporter. Patient had 2 initial Astra Zeneca vaccines without incident but had Moderna booster vaccine on 16/10/21. Daughter noted left leg to be swelling on 4/11/22 and was diagnosed with entire left leg clot on 6/11/22. No other obvious provoking factors in history. Patient was admitted and had CT chest/abdo/pelvis showing no malignancy. Has been treated with apixaban with good effect. Patient has not tested positive for COVID-19 since having the vaccine and was not enrolled in clinical trial. This report was related to possible blood clots or low platelet counts and not related to possible myocarditis or pericarditis. On 6/11/21, doppler ultrasound revealed thromboembolic event / thrombocytopenia. On 4/11/21, platelet count and D-dimer was measured. There was no additional medical history, that relates to previous venous or arterial thromboses. The patient does not have any previous reactions to medications, especially heparin or anticoagulants. The patient had not confirmed or suspected autoimmune or inflammatory disease, including vasculitis. The patient does not have history of, or current, malignancy. On 4/11/21, lowest platelet count after vaccine (usual normal range 150-450) was 130. On 27/9/21, last platelet count before vaccine (usual normal range 150-450) was 200. The patient was not reviewed by a haematologist. Haemorrhage was not identified. The patient does not have a history of, or concurrent, intracranial malignancy, concurrent or recent intracranial infections and recent surgical or medical interventions to the central nervous system (including lumbar puncture). Patient's PT, Aactivated Partial Thromboplastin Clotting Time (aPTT) and fibrinogen were clotted. Thrombophilia screen, infectious screen (eg HIV, hepatitis C/B, herpes zoster/ CMV) and Autoimmune screen were not indicated. Blood film findings, PF4 HIT assay optical density and HIT assay used were not done.		

Case ID	Narrative	MAH Comment	WW Identifier
	This literature-non-study case was reported in a literature article and describes the occurrence of THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-Induced Thrombotic Thrombocytopenia) in a 34-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. LITERATURE REFERENCE: Chittal A, Rao S, Lakra P, Nacu N, Haas C. A case of COVID-19 vaccine-induced thrombotic thrombocytopenia. J Community Hosp Intern Med Perspect. 2021;11(6):776-8 The patient's past medical history included Subclinical hypothyroidism. Previously administered products included for Subclinical hypothyroidism: levothyroxine. Past adverse reactions to the above products included No adverse event with levothyroxine. On an unknown date, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On an unknown date, after starting mRNA-1273 (Moderna COVID-19 Vaccine), the patient experienced THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-Induced Thrombotic Thrombocytopenia) (seriousness criteria hospitalization and medically significant). The patient was treated with DEXAMETHASONE for Thrombosis with thrombocytopenia syndrome, at a dose of 1 dosage form. At the time of the report, THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-Induced Thrombotic Thrombocytopenia) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Activated partial thromboplastin time (23.4-36.2): 59.3 seconds (abnormal) 59.3 seconds. On an unknown date, Anti-platelet factor 4 antibody test: positive (Positive) heparin-induced thrombocytopenia (HIT) antibodies (anti-Platelet factor 4; anti-PF4), as measured by enzyme-linked immunosorbent assay, were positive with an optical density of 0.505 (reference range 0.00-0.349), despite her lack of heparinoid exposure.. On an unknown date, Antiphospholipid antibodies: positive (Positive) Positive. On an unknown date, Blood chloride (98-107): 110 mmol/l (abnormal) 110 mmol/L. On an unknown date, Blood cortisol: unremarkable Unremarkable. On an unknown date, Blood folate: unremarkable unremarkable. On an unknown date, Blood potassium (3.4-4.5): 3.9 mmol/l 3.9 mmol/L. On an unknown date, Blood sodium (136-145): 142 mmol/l (normal) 142 mmol/L. On an unknown date, HIV test: uremarkable unremarkable. On an unknown date, Haemodynamic test: stable Stable. On an unknown date, Haemoglobin (11-14.5): 13.5 g/dl (normal) 13.5 g/dL.	No thrombosis reported, also had positive lupus anticoagulant and mildly elevated HIT anti-PF4 antibodies	

Case ID	Narrative	MAH Comment	WW Identifier
	On an unknown date, Hepatitis viral test: unremarkable Unremarkable. On an unknown date, Physical examination: notable for a petechial rash Physical examination was notable for a petechial rash localized to the dorsal surface of the bilateral hands with multiple bruises.. On an unknown date, Platelet count (150000-450000): 184,000 platelets/mcl (normal) 184,000 platelets/mcL, 65,000 platelets/mcl (abnormal) 65,000 platelets/mcL Platelets after first vaccine dose, 45,000 platelets/mcl (abnormal) 45,000 platelets/mcL 5 days after the second dose of the vaccine, 29,000 platelets/mcl (abnormal) decline in the platelet count to 29,000 platelets/mcL without evidence of clumping, with a preserved white blood cell count and hemoglobin., 35,000/mcl (abnormal) Patient was discharged in stable condition with stable thrombocytopenia (35,000/mcL). and 118,000/mcl (normal) Patients platelet count recovered to 118,000/mcL, 6 weeks after discharge.. On an unknown date, Prothrombin time (11.8-14.6): 13.2 sec (normal) 13.2 sec. On an unknown date, Russell's viper venom time (36.1-50.8): 57.7 seconds (abnormal) 57.7 seconds. On an unknown date, SARS-CoV-2 test: unremarkable unremarkable. On an unknown date, Vitamin B12: unremarkable Unremarkable. On an unknown date, White blood cell count (4000-10,800): 4800/uL White Blood Cell Count 4800/uL 4000–10,800/uL. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-Induced Thrombotic Thrombocytopenia) to be related. Concomitant medication information was not reported. This literature non-study case concerns a 34-year-old, female patient with no reported relevant medical history, who experienced the unexpected, serious (hospitalized, medically significant) AESI Thrombosis with thrombocytopenia syndrome. The event initially presented as petechiae and easy bruising 3 days after the second dose of mRNA-1273 vaccine. She consulted a primary care provider wherein initial tests showed significant decrease in platelet count from 184,000 platelets/mcL (baseline) to 65,000/mcL. The patient was then referred to a hospital for further investigation and appropriate treatment. Upon admission, the patient was noted to have petechial rash localized to the dorsal surface of the bilateral hands with multiple bruises but otherwise, hemodynamically stable. She denied new medications, occupational exposures, illicit substance use, or recent infection. Laboratory tests showed further thrombocytopenia (29,000/mcL) without evidence of clumping, while other cell lines were within normal limits. Additional diagnostic tests were essentially normal with the exception of a mildly elevated aPTT, positive lupus anticoagulant and a mildly prolonged Dilute Russell's Viper Venom screen. Serology screening (hepatitis panel, Human Immunodeficiency Virus, COVID-19 PCR, vitamin B12, folic acid, morning cortisol) were also unremarkable. Heparin-induced thrombocytopenia PF4 antibody		

Case ID	Narrative	MAH Comment	WW Identifier
	was then ordered which revealed low positive optical density of 0.505, despite no prior heparin exposure. At this time, the working diagnosis was Vaccine-Induced Thrombotic Thrombocytopenia and the patient was started on Dexamethasone. She was eventually discharged in stable condition and with recovering levels of thrombocytopenia. On follow-up 6 weeks post-recovery, her platelet count has increased to 118,000/mcL without further episodes of petechiae or bruising. The benefit-risk relationship of mRNA-1273 is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 21-Mar-2022: Follow up received by safety on 22-Mar-2022 has Email with FTA received from SARA team and contains significant information. Reporter details, author details, laboratory details, treatment details, event seriousness criteria and event outcome were updated.		
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 17-Mar-2022 and was forwarded to Moderna on 17-Mar-2022. This regulatory authority case was reported by a consumer and describes the occurrence of PETECHIAE (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies), ANTIPHOSPHOLIPID SYNDROME (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies) and IMMUNE THROMBOCYTOPENIA (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies) in a 38-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. No Information on risk factors or previous illnesses. Medical history 2013, Lupus Erythematosus, 2 months PSL, 12 months Quensyl, clin. remission 09/16 serological sjogren's syndrome asymptomatic / inpatient stay, IVIG and systemic PSL therapy. On 24-Jun-2021, the patient received second dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 01-Jul-2021, the patient experienced PETECHIAE (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies) (seriousness criterion hospitalization), ANTIPHOSPHOLIPID SYNDROME (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies) (seriousness criterion hospitalization) and IMMUNE THROMBOCYTOPENIA (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies) (seriousness criterion hospitalization). At the time of the report, PETECHIAE (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies), ANTIPHOSPHOLIPID SYNDROME (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12	consumer report: immune thrombocytopenia (but no thrombosis) with triple-positivity antiphospholipid autoantibodies and past history of lupus and serologic Sjogren's syndrome,	

Case ID	Narrative	MAH Comment	WW Identifier
	post vaccination new: triple-positivity antiphospholipid autoantibodies) and IMMUNE THROMBOCYTOPENIA (Petechia US from d7 post vaccination Autoimmune thrombocytopenia 3 gpt/l d 12 post vaccination new: triple-positivity antiphospholipid autoantibodies) had resolved. No concomitant drug details were reported. No treatment details were reported. COMPANY COMMENT: This is a Regulatory case concerning an 38-years-old female patient with no clinical history who experienced the unexpected events of PETECHIAE (AESI), ANTIPHOSPHOLIPID SYNDROME (AESI) and IMMUNE THROMBOCYTOPENIA (AESI) 8 days after 2nd dose of RNA-1273 vaccine. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Terms and onset were captured as provided. The case was assessed as serious by the Regulatory Authority's report due to hospitalization		
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 15-Mar-2022 and was forwarded to Moderna on 18-Mar-2022. This case, reported to Takeda by a pharmacist, was received via Moderna's adverse reaction reporting site ([REDACTED]), and reported to the [REDACTED] by a pharmacist, was received via the [REDACTED] (Ref, [REDACTED]). On 06-Jun-2021, the patient received the 1st dose of Coronavirus Modified Uridine RNA Vaccine (SARS-CoV-2) (the vaccine made by Pfizer). On 04-Jul-2021, the patient received the 2nd dose of Coronavirus Modified Uridine RNA Vaccine (SARS-CoV-2) (the vaccine made by Pfizer). On an unknown date, body temperature before the vaccination: 36.1 degrees Celsius. On 03-Mar-2022, at 14:30, the patient received the 3rd vaccination with this vaccine. On 06-Mar-2022, thrombosis with thrombocytopenia developed. Syncope and cold sweat were observed after the patient went to bathroom. On an unknown date, shortness of breath developed. On 09-Mar-2022, the patient visited the reporting hospital. Blood count and coagulation tests were performed. SARS-CoV-2 test by nucleic acid amplification methods (PCR/LAMP) was performed, and the patient tested negative. Chest CT showed thrombi in both lungs. Ultrasonography of the lower extremities showed a thrombus. The patient was diagnosed with pulmonary thromboembolism and deep vein thrombosis. The patient was hospitalized for treatment. On an unknown date, the patient was discharged from the hospital. The outcome of thrombosis with thrombocytopenia, syncope, pulmonary thromboembolism, and deep vein thrombosis was unknown. Follow-up investigation will be made. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.	80 year old man with DVT and pulmonary embolism (common sites), no anti-PF4 antibody studies	

Case ID	Narrative	MAH Comment	WW Identifier
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 18-Mar-2022 and was forwarded to Moderna on 18-Mar-2022. This regulatory authority case was reported by a consumer and describes the occurrence of THROMBOCYTOPENIA (thrombocytopenia (35G/L), thrombosis of lower leg veins) in a 74-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included e.g. anastomosis cancer in e.g. billroth got resection (for ulcer in 1975), curative OP 10/21 (explorative laparotomy, adhesiolysis, total residual gastrectomy, end-to-since esophagojejunostomy, end-to-since oesophagojejunostomy, end-to-since jejunum jejunostomy as roux-y-anastomosis), regression level 3 after Becker adjuvant chemotherapy planned. On 02-Dec-2021, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 12-Jan-2022, the patient experienced THROMBOCYTOPENIA (thrombocytopenia (35G/L), thrombosis of lower leg veins) (seriousness criterion medically significant) and VENOUS THROMBOSIS LIMB (thrombocytopenia (35G/L), thrombosis of lower leg veins). At the time of the report, THROMBOCYTOPENIA (thrombocytopenia (35G/L), thrombosis of lower leg veins) and VENOUS THROMBOSIS LIMB (thrombocytopenia (35G/L), thrombosis of lower leg veins) outcome was unknown. No concomitant medications were reported. Patient reported hematoma after minor trauma on the forearm, otherwise none bleeding signs. Swelling pain and redness of the lower legs on both sides around Christmas. No treatment information was provided. Sonographic detection von superficial thrombosis in the lower leg, especially vaccine-induced thrombocytopenia (case reports described after Moderna vaccination, booster occurs on 02-Dec-2021) DD ITP, (classic HIT2 very unlikely, last heparin administration mid-November), D- dimers continued to increase. Thrombopenia (40 g/L), consultation with clinical chemistry at the [REDACTED] diagnosis for VITT (vaccine-induced thrombocytopenia with thrombosis) was not reliably mapped via internal HIT-2 diagnostics, hence external dispatch to [REDACTED] Pending results.	74 year old man being treated for GI cancer (confounders) and developed DVT in lower leg with thrombocytopenia, TTO 41 days, no anti-PF4 antibody studies reported.	

Case ID	Narrative	MAH Comment	WW Identifier
	Company Comment: This is a regulatory case concerning a 74-year-old male patient with no relevant medical history, who experienced the unexpected serious (medically significant) adverse event of special interest, Thrombocytopenia, and unexpected non-serious adverse event of special interest Venous Thrombosis Leg. The events occurred approximately 1 month after receiving the third dose of mRNA-1273 Vaccine. As reported, the patient presented with hematoma on the forearm due to minor trauma with swelling pain and redness of the lower legs. Sonographic studies revealed superficial thrombosis in the lower leg with increasing D-dimer levels and was diagnosed with vaccine-induced thrombocytopenia with thrombosis. No treatment details were given. It was reported that the outcome of the event was unknown. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report.		
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 23-Mar-2022 and was forwarded to Moderna on 23-Mar-2022. This regulatory authority case was reported by a consumer and describes the occurrence of PETECHIAE (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.), INJECTION SITE SWELLING (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.), EYE HAEMORRHAGE (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.) and THROMBOPHLEBITIS (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.) in a 55-year-old female patient who received mRNA-1273 (Spikevax) (batch no. G26761A) for COVID-19 vaccination. It was reported that No Information on risk factors or pre-existing diseases factor VII deficiency, control, diagnosis of coagulation disorders practice. On 25-Mar-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 07-Apr-2021, the patient experienced PETECHIAE (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.), INJECTION SITE SWELLING (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.), EYE HAEMORRHAGE (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.) and THROMBOPHLEBITIS (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.). At the time of the report, PETECHIAE (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.), INJECTION SITE SWELLING (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.), EYE HAEMORRHAGE (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.) and THROMBOPHLEBITIS (petechiae skin, varicose thrombophlebitis, hematoma in the eye, mutation factor II.) had resolved with sequelae. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown.	Platelets <150 or thrombocytopenia not reported. Mutation factor 2 and factor VII deficiency are confounders.	

Case ID	Narrative	MAH Comment	WW Identifier
	Concomitant medications details were not reported by the reporter. Treatment details was not reported by the reporter. factor VII deficiency/control/diagnosis of coagulation disorders practice. Company comment: This case concerns a 55-year-old female patient with medical history of factor VII deficiency, who experienced the adverse events of special events of petechiae and thrombophlebitis 13 days after a dose of mRNA-1273. The medical history of factor VII deficiency is a confounder. The patient also reports being diagnosed with factor II mutation, although it is unclear whether this is part of medical history or diagnosed after vaccine administration. The benefit-risk relationship of mRNA-1273 is not affected by this report.		
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 30-Mar-2022 and was forwarded to Moderna on 30-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of THROMBOTIC MICROANGIOPATHY (thrombotic microangiopathy), THROMBOCYTOPENIA (Thrombocytopenie), HAEMOLYTIC URAEMIC SYNDROME (atypical HUS) and RENAL DISORDER (kidney problems) in a 38-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 214064) for COVID-19 vaccination. Patient had a rivets relevant. On 04-Jan-2022, the patient received first dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 10-Jan-2022, the patient experienced THROMBOTIC MICROANGIOPATHY (thrombotic microangiopathy) (seriousness criterion hospitalization), THROMBOCYTOPENIA (Thrombocytopenie) (seriousness criterion hospitalization), HAEMOLYTIC URAEMIC SYNDROME (atypical HUS) (seriousness criterion hospitalization) and RENAL DISORDER (kidney problems) (seriousness criterion hospitalization). At the time of the report, THROMBOTIC MICROANGIOPATHY (thrombotic microangiopathy), THROMBOCYTOPENIA (Thrombocytopenie), HAEMOLYTIC URAEMIC SYNDROME (atypical HUS) and RENAL DISORDER (kidney problems) was resolving. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. Patient took treatment plasmaferesis, soliris.	Not a case of TTS. This patient was diagnosed with hemolytic uremic syndrome and was clinically resolving after treatment with plasmapheresis and eculizumab (Soliris) which is not a first-line TTS therapy.	

Case ID	Narrative	MAH Comment	WW Identifier
	Evolution of the ADR Making examinations kidney biopsy, thrombotic microangiopathy, clinical en biochemical beeld van thrombotic microangiopathy ADR description - atypical HUS No concomitant medications were provided by the reporter. Company Comment: This is a regulatory case concerning a 38-year-old female patient with no relevant medical history, who experienced the unexpected serious events of Hemolytic Uremic Syndrome, Renal Disorder, and adverse event of special interest, Thrombotic Microangiopathy, and Thrombocytopenia. The events led to the hospitalization of the patient as reported by the regulatory authority and occurred 6 days after receiving the first dose of mRNA-1273 Vaccine. No clinical or treatment details were given. It was reported that the outcome of the events was resolving. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report.		
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 31-Mar-2022 and was forwarded to Moderna on 06-Apr-2022. This case, initially reported to the [REDACTED] by a physician, was received via the [REDACTED]. On an unknown date, the patient received the first dose of a COVID-19 vaccine (product name unknown). On an unknown date, the patient received the second dose of a COVID-19 vaccine (product name unknown). On 16-Feb-2022, the patient received the third dose of this vaccine. On 19-Feb-2022, the patient experienced vaccination site pain. On 21-Feb-2022, the patient experienced pancytopenia. The patient experienced malaise. In the evening, the patient experienced loss of appetite. On 22-Feb-2022, at 07:00, body temperature was 37.9 degrees Celsius, and the patient made an outpatient visit to the reporting hospital. COVID-19 quantitative antigen test was negative. The patient was hospitalized for detailed examination. The patient had symptoms of pyrexia, malaise, and decreases in white blood cell count and platelet count. At 17:22, the patient was awake and alert with vital signs of body temperature 38.6 degrees Celsius, blood pressure 148/78 mmHg, heart rate 87 bpm, and SpO2 97% (RA). On 23-Feb-2022, at 20:00, the patient was awake and alert with vital signs of body temperature 40 degrees Celsius, blood pressure 132/71 mmHg, heart rate 89 bpm, and SpO2 96% (RA). On 24-Feb-2022, CT with contrast was performed and showed no thrombus. Thrombotic thrombocytopenic purpura was negative with no diffuse vasculitis, pyrexia, nor disturbed consciousness. Because pyrexia does not occur in patients with thrombotic thrombocytopenic purpura, thrombosis with decreased platelets was suspected, and anti-RF4 antibodies was examined. The result was, however, negative. On 25-Feb-2022, the patient received freeze-dried sulfonated human normal immunoglobulin 10 bottles/day for 2 days. On 28-Feb-2022, blood pressure 164/61 mmHg, heart rate 61 bpm, body temperature 36.5 degrees Celsius, and SpO2 96% (RA). The patient was discharged from the hospital. On 07-Mar-2022, the symptoms resolved. The outcome of the events of vaccination site pain, pancytopenia, and suspected thrombosis with decreased platelets was reported as recovered. Follow-up investigation will be made. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.	Pancytopenia. No thrombosis found. Anti-RF4 [sic] antibodies negative.	

Case ID	Narrative	MAH Comment	WW Identifier
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 08-Apr-2022 and was forwarded to Moderna on 12-Apr-2022. This case was reported by a physician via the Drug Information Center. This case was reported without any patient identifiers. On 24-Feb-2022, the patient received this vaccine (the number of doses was unknown). On an unknown date, around 36 days after the vaccination, the patient experienced platelets decreased. Thrombosis with thrombocytopenia was suspected. The patient was in a severe condition. The outcome of suspected thrombosis with thrombocytopenia was reported as ongoing and unchanged. No follow-up investigation will be made.	Very limited information. Thrombosis suspected but not confirmed.	
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 13-Apr-2022 and was forwarded to Moderna on 13-Apr-2022. This regulatory authority case was reported by a pharmacist and describes the occurrence of THROMBOTIC THROMBOCYTOPENIC PURPURA (thrombocytopenic purpura) and ADAMTS13 ACTIVITY DECREASED (ADAMTS13 activity decreased) in a 28-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3006321) for COVID-19 vaccination. No Medical History information was reported. On 27-Dec-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 01-Mar-2022, the patient experienced THROMBOTIC THROMBOCYTOPENIC PURPURA (thrombocytopenic purpura) (seriousness criterion life threatening) and ADAMTS13 ACTIVITY DECREASED (ADAMTS13 activity decreased) (seriousness criterion life threatening). At the time of the report, THROMBOTIC THROMBOCYTOPENIC PURPURA (thrombocytopenic purpura) and ADAMTS13 ACTIVITY DECREASED (ADAMTS13 activity decreased) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 01-Mar-2022, ADAMTS13 inhibitor screen assay: inhibitor detected (abnormal) Inhibitor is detected against ADAMTS 13 at high title.. mRNA-1273 (Spikevax) (Intramuscular) was withdrawn on 27-Dec-2021. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medications were reported. No treatment medications were reported. Company Comment: This regulatory case concerns a 28-year-old, female patient with no reported medical history, who experienced the unexpected, life-threatening AESI	Not TTS because ADAMTS13 ACTIVITY DECREASED--ADAMTS13 activity decreased due to ADAMTS13 inhibitor detected at high "title" [sic]	

Case ID	Narrative	MAH Comment	WW Identifier
	Thrombotic thrombocytopenic purpura with reported ADAMTS13 activity decreased and positive inhibition in ADAMTS13 inhibitor screen assay (unspecified value). The event occurred 65 days after receiving the first dose of mRNA-1273 vaccine. Clinical course and treatment details were not provided in the case. The patient's gender and age (young, adult female) are considered as risk factors for the thrombotic thrombocytopenic purpura. The benefit-risk relationship of mRNA-1273 is not affected by this report. Events' seriousness was assessed as per Regulatory Authority's report.		
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 18-Apr-2022 and was forwarded to Moderna on 21-Apr-2022. This case, initially reported to the [REDACTED] by a pharmacist, was received via the [REDACTED]. On an unknown date, the patient received the 1st dose of a novel coronavirus vaccine (product name unknown). On an unknown date, the patient received the 2nd dose of a novel coronavirus vaccine (product name unknown). On an unknown date, body temperature before the vaccination: 36.5 degrees Celsius. On 12-Feb-2022, the patient received the 3rd vaccination with this vaccine. On 13-Feb-2022, around 14:00, thrombosis with thrombocytopenia developed. The patient noticed that he/she had difficulty moving the left limbs and speaking clearly. On 14-Feb-2022, the symptoms improved slightly, and the patient became able to walk. In the afternoon, the patient was in much the same condition as the previous day. On 15-Feb-2022, the patient had difficulty moving the left leg and walking and was transported to hospital by ambulance. The SARS-CoV-2 test was performed with antigen qualitative testing and was negative. Complete blood count and coagulation system tests were performed. MRI scan of the head showed a high intensity area (HIA) on the right ventral side of lower pons on diffusion-weighted image (DWI), ischemic changes in the cerebral white matter and bilateral corona radiata. MRA showed stenotic changes in the left cervical internal carotid artery. Electrocardiogram showed HR 63, sinus rhythm, and flattening of T wave in V4-6 leads. Chest X-ray showed no evidence of thrombus or embolism. Brain stem infarction and stroke were diagnosed, and the patient was hospitalized. There were no risk factors for thrombus. On 15-Mar-2022, the symptoms were resolving, and the patient was discharged from the hospital. The outcome of thrombosis with thrombocytopenia, brain stem infarction, and stroke was reported as resolving. Follow-up investigation will be made. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.	No information available on platelet count to determine if this is a case of thrombocytopenia. Important information missing from the report	
	This literature-non-study case was reported in a literature article and describes the occurrence of THROMBOTIC THROMBOCYTOPENIC PURPURA (Acute congenital thrombotic thrombocytopenic purpura flare) in a 50-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. LITERATURE REFERENCE:	This is a literature case of a patient experiencing a flare of TTP with a prolonged TTO of two weeks after her second dose of Spikevax. According to the WHO causality assessment this case is unlikely related to the vaccine.	

Case ID	Narrative	MAH Comment	WW Identifier
	Dykes KC, Kessler CM. First report of COVID-19 vaccine included flare of compensated congenital thrombotic thrombocytopenic purpura. Blood Coagul Fibrinolysis. 2022;33(1):71-3 The patient's past medical history included Cerebrovascular accident, Thrombocytopenia, Hemolytic anemia, Schistocytosis, Plasma exchange (The patient was treated with daily plasma exchanges and apheresis with fresh frozen plasma until laboratory testing indicated that her ADAMTS13 activity level was less than 5% with negative ADAMTS13 inhibitor titers.) and Apheresis. Concurrent medical conditions included Thrombotic thrombocytopenic purpura (The patient's initial Congenital thrombotic thrombocytopenic purpura diagnosis was established at the age of 30.). Concomitant products included PLASMA PROTEIN FRACTION (HUMAN) (OCTAPLAS) for an unknown indication. On an unknown date, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On an unknown date, the patient experienced THROMBOTIC THROMBOCYTOPENIC PURPURA (Acute congenital thrombotic thrombocytopenic purpura flare) (seriousness criteria hospitalization and medically significant) and CONDITION AGGRAVATED (Condition aggravated). The patient was treated with LEVETIRACETAM for Adverse event, at an unspecified dose and frequency; ASPIRIN [ACETYLSALICYLIC ACID] for Adverse event, at a dose of 81 milligram; FONDAPARINUX for Adverse event, at an unspecified dose and frequency and ENOXAPARIN for Adverse event, at an unspecified dose and frequency. At the time of the report, THROMBOTIC THROMBOCYTOPENIC PURPURA (Acute congenital thrombotic thrombocytopenic purpura flare) had resolved and CONDITION AGGRAVATED (Condition aggravated) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, ADAMTS13 activity assay: negative (Negative) ADAMTS13 activity level was found to be less than 5% with negative ADAMTS13 inhibitor titres., cttp Genetic testing of ADAMTS13 protein subsequently revealed double heterozygous gene mutations (2293C>T, 571C>T), consistent with cTTP and less than 5% At admission, her ADAMTS13 activity was less than 5% and no inhibitor was identified. On an unknown date, Angiogram: acute infarcts in the left parietal lobe New small acute infarcts in the left parietal lobe without associated hemorrhage. On an unknown date, Blood bilirubin: normal (normal) Normal. On an unknown date, Blood creatinine: 0.96 mg/dl Creatinine was reported as baseline of 0.96 mg/dl.. On an unknown date, Blood fibrinogen: normal (normal) Normal.		

Case ID	Narrative	MAH Comment	WW Identifier
	On an unknown date, Blood lactate dehydrogenase: 440 units/l (High) LDH was mildly elevated at 440 units/l. On an unknown date, Computerised tomogram head: acute infarcts in the left parietal lobe New small acute infarcts in the left parietal lobe without associated hemorrhage.. On an unknown date, Coombs direct test: normal (normal) Normal. On an unknown date, Haemoglobin: normal (normal) Normal. On an unknown date, Haptoglobin: normal (normal) Normal. On an unknown date, Heparin-induced thrombocytopenia test: negative (Negative) Negative. On an unknown date, Immunology test: negative (Negative) Negative. On an unknown date, International normalised ratio: normal (normal) Normal. On an unknown date, Magnetic resonance imaging head: acute infarcts in the left parietal lobe New small acute infarcts in the left parietal lobe without associated hemorrhage. On an unknown date, Platelet count: 98 000/ mcl Platelets were 98 000/ mcL, which was unusually decreased from her baseline normal counts, which were typically in the 200 000/ml range while on her prophylaxis regimen with frozen pooled human plasma infusions. On an unknown date, Prothrombin time: normal (normal) Normal. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered THROMBOTIC THROMBOCYTOPENIC PURPURA (Acute congenial thrombotic thrombocytopenic purpura flare) and CONDITION AGGRAVATED (Condition aggravated) to be related. The patient was presented with 3 days of malaise and neurologic deficits. Three days before acute presentation, the patient experienced malaise and impaired coordination. On the day of presentation, the patient reported difficult motor coordination with small tasks, such as fastening buttons. She also noticed paresthesias in her hands and face. Finally, her arms and hands began contracting involuntarily, at which point emergency response was activated. She subsequently experienced a witnessed, generalized seizure. Before presentation, the patient had been delayed 2 weeks for a scheduled OctaPlas infusion while sequestering during the COVID-19 pandemic. She then received two doses of the Moderna mRNA-1273 COVID-19 vaccine over a 3-week period. This placed her second dose of the COVID-19 vaccine approximately 6 weeks after her last OctaPlas infusion and approximately 1 week before the onset of symptoms that led to her hospitalization. While hospitalized, she received two infusions of OctaPlas. She remained stable throughout the remainder of the hospitalization and after discharge resumed her prophylactic regimen of OctaPlas infusions every 4 weeks. Company Comment:		

Case ID	Narrative	MAH Comment	WW Identifier
	This is a Literature-non-study case, concerning a 50-year-old female patient, with a relevant history of congenital thrombotic thrombocytopenic purpura established at the age of 30 after experiencing cerebrovascular accident, experienced the unexpected, serious (hospitalization, medically significant), event of ACUTE CONGENITAL THROMBOTIC THROMBOCYTOPENIC PURPURA FLARE. The event occurred approximately within two weeks after the second dose of mRNA-1273 vaccine administration. Three days before acute presentation, the patient experienced malaise and impaired coordination. On the day of presentation, the patient reported difficult motor coordination with small tasks, paresthesias on the hands and face, and involuntary contraction of arms and hands, for which emergency response was activated. She subsequently experienced a witnessed, generalized seizure. Computerized tomography (CT) head without contrast, CT angiography and MRI brain revealed new small acute infarcts in the left parietal lobe without associated haemorrhage. LDH was mildly elevated at 440 units/l. peripheral smear had 2-4 schistocytes/hpf with thrombocytopenia. Her platelets were 98 000/ml, which was unusually decreased from her baseline normal counts, which were typically in the 200 000/ml range while on her prophylaxis regimen with frozen pooled human plasma infusions. At admission, her ADAMTS13 activity was less than 5% and no inhibitor was identified. While hospitalized, she received two infusions of Octa-Plas and She was prescribed levetiracetam, aspirin 81mg and fondaparinux transitioned to enoxaparin after her PF4 ELISA and platelet SRA were negative. Patient remained stable during the rest of the hospital stay until discharge. Patient had received two doses of the Moderna mRNA-1273 COVID-19 vaccine over a 3-week period and no adverse reaction reported after the first dose. The patient experienced recurrent flares of cTTP thrice in the previous years (2009, 2011 and 2016) with neurologic events and CVAs, and was placed on prophylaxis regimen with infusions of RBC type-specific viral attenuated frozen pooled human. Patient was doing well without additional Cttp flares until the current presentation with vaccination, however, she had been delayed 2 weeks for a scheduled profilaxis infusion prior to vaccination, and this could be considered a contributor for the event. The benefit-risk relationship of mRNA-1273 is not affected b		
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 19-Apr-2022 and was forwarded to Moderna on 26-Apr-2022. This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 19-Apr-2022 and was forwarded to Moderna on 26-Apr-2022. This case, reported by a physician, was received by Takeda via Moderna's adverse reaction reporting site [REDACTED], and reported to the [REDACTED] by a physician, was received via the [REDACTED]. On 17-Aug-2021, the patient received the 1st dose of this vaccine. On 14-Sep-2021, the patient received the 2nd dose of this vaccine. On 05-Apr-2022, the patient received the 3rd dose of this vaccine. On an unspecified date in Apr-2022, swelling in lower limbs developed. On 10-Apr-2022, at the time of awakening, left hemiplegia developed, and the patient was raced to a hospital. Head MRI showed acute-stage cerebral infarction in the right cerebrum. D-dimer was high at 12.38	No information available on platelet count to determine if this is a case of thrombocytopenia. Important information missing from the report	

Case ID	Narrative	MAH Comment	WW Identifier
	mcg/mL. Chest X-ray showed no findings of thrombosis or embolism. Blood count and coagulation tests were performed. The patient was admitted to the hospital. On 11-Apr-2022, cardiac ultrasonography showed suspected left-to-right shunt. Ultrasonography of lower limbs showed findings of dilated veins in lower limbs. Therefore, it is considered that venous thrombosis resulted in cerebral infarction as paradoxical embolism. On 12-Apr-2022, contrast-enhanced CT of chest and lower limbs revealed deep vein thrombosis of lower limbs and pulmonary embolism. On 13-Apr-2022, lung perfusion scintigraphy was performed. Findings of thrombosis and embolism were noted. Ventilation-perfusion mismatch was observed, although the site was difficult to determine. On an unspecified date in Apr-2022, the patient was diagnosed with stroke. As of 19-Apr-2022, the patient was in the hospital. The outcome of acute-stage cerebral infarction, deep vein thrombosis, stroke, pulmonary thromboembolism, and thrombosis with thrombocytopenia was unknown. Follow-up investigation will be made. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 28-Apr-2022. The most recent information was received on 25-May-2022 and was forwarded to Moderna on 25-May-2022. This regulatory authority case was reported by a physician and describes the occurrence of MESENTERIC VEIN THROMBOSIS (venous mesenteric thrombosis) and PORTAL VEIN THROMBOSIS (portal vein thrombosis) in a 62-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included Diverticulitis (Family history reported as false.), Incision site bleeding (A: Since last week hemorrhoids, thrombosed hemorrhoid was found to be what was incited by the GP. However, after a number of rectal blood loss suffered several times.) on 02-Apr-2021, Thrombosed hemorrhoids (NOS) (A: Since last week hemorrhoids, thrombosed hemorrhoid was found to be what was incited by the GP. However, after a number of rectal blood loss suffered several times.) on 02-Apr-2021 and Rectal blood loss (after incision by general practitioner, several days) on 04-Apr-2021. Previously administered products included for Product used for unknown indication: COVID-19 VACCIN ASTRAZENECA INJVLST in 2021 and COVID-19 VACCIN ASTRAZENECA INJVLST in 2021. Past adverse reactions to the above products included No adverse event with COVID-19 VACCIN ASTRAZENECA INJVLST and COVID-19 VACCIN ASTRAZENECA INJVLST. Concurrent medical conditions included Type 2 diabetes mellitus (Family history reported as false.) and Hypertension (Family history reported as false.). Concomitant products included METFORMIN (METFORMINE [METFORMIN]) and AMLODIPINE for an unknown indication.	As per the reporter laboratory results showed this is not a VTTS case. Patient died two days after receiving a dose of Spikevax. Reported cause of death was multiorgan failure in abdominal sepsis, catastrophic antiphospholipid syndrome (primary) and multiorgan failure in abdominal sepsis.	

Case ID	Narrative	MAH Comment	WW Identifier
	On 09-Apr-2022, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 10-Apr-2022, the patient experienced MESENTERIC VEIN THROMBOSIS (venous mesenteric thrombosis) (seriousness criterion death) and PORTAL VEIN THROMBOSIS (portal vein thrombosis) (seriousness criterion death). 10-Apr-2022, the patient experienced THROMBOCYTOPENIA (Thrombocytopenia). The patient died on 11-Apr-2022. The reported cause of death was multiorgan failure in abdominal sepsis, catastrophic antiphospholipid syndrome (primary) and multiorgan failure in abdominal sepsis. An autopsy was not performed. At the time of death, THROMBOCYTOPENIA (Thrombocytopenia) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 10-Apr-2022, Blood alkaline phosphatase: 87 87. On 10-Apr-2022, Blood bilirubin: 80 80. On 10-Apr-2022, Blood fibrinogen: post operative: unmeasurable low post operative: unmeasurable low. On 10-Apr-2022, Blood test: ph 6.8, lactate 12.7, haptoglobin <0.1, d-dimer pH 6.8, lactate 12.7, haptoglobin <0.1, D-dimer >35, Fibrinogen <1.0. Significant number of values ??could no longer be determined due to hemolytic sample. Has not been redetermined because patient died in a short time.. On 10-Apr-2022, C-reactive protein: 196 196. On 10-Apr-2022, Chest X-ray: abnormal X-thorax: poorly inspired, tube, central venous line and gastric probe lie well. No consolidations. High level right aperture.. On 10-Apr-2022, Computerised tomogram abdomen: abnormal CT abdomen: diffuse venous mesenteric thrombosis with thrombosis vena porta and VMS and branches. On 10-Apr-2022, Culture: per operative ascites moisture: grow negative. per operative ascites moisture: grow negative. No blood cultures have taken place. On 10-Apr-2022, Fibrin D dimer: post operative: unmeasurably high post operative: unmeasurably high. On 10-Apr-2022, Haemoglobin: pre-ok: 9.4 post ok: 7.0 pre-OK: 9.4 Post OK: 7.0. On 10-Apr-2022, Liver function test: af87, ggt 97, asat and alat normal, ldh 300. AF87, GGT 97, ASAT and ALAT normal, LDH 300. pre- OK. On 10-Apr-2022, Platelet count: pre-ok:54 , post ok: 21 Pre-Ok:54 , Post OK: 21. On 10-Apr-2022, Platelet factor 4: pf 4 antibodies negative PF 4 antibodies negative. On 10-Apr-2022, SARS-CoV-2 test: negative (Negative) negative. On 10-Apr-2022, White blood cell count: pre ok : 5.9, post ok: 3 Pre OK : 5.9, post OK: 3. In April 2022, Antinuclear antibody: ana was positive. breakdown was negative. ANA was positive. Breakdown was negative.. In April 2022, Antiphospholipid antibodies: antiphospholipid antibodies are detected. (lac pos Antiphospholipid antibodies are detected. (LAC pos, aCL neg, aB2GPI dub).. In April 2022, Platelet factor 4: negative, making vitt unlikely negative, making VITT unlikely.		

Case ID	Narrative	MAH Comment	WW Identifier
	For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. Treatment details was not reported by the reporter. Most recent FOLLOW-UP information incorporated above includes: On 25-May-2022: Significant Follow up includes patient death cause added, Lab test details added and narrative was updated accordingly. On 25-May-2022: Translated document received on 31-May-2022 contains non significant information as the event verbatim and lab data term got updated from native to English. On 01-Jun-2022: Follow up received contains non significant information (event verbatim changed from thrombopenia to thrombocytopenia).		
	This literature-non-study case was reported in a literature article and describes the occurrence of THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-induced thrombosis with thrombocytopenia) and PULMONARY EMBOLISM (Chest computed tomography angiography revealed large pulmonary emboli, almost completely occluding the right pulmonary artery branches) in an 83-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. LITERATURE REFERENCE: Langerak T, Bakker GJ, Porcelijn L, Eefting M, Lauw MN, van de Laar RJ, et al. Vaccine-induced immune thrombocytopenia and thrombosis after mRNA-1273 booster vaccination. <i>Thromb Res.</i> 2022;214:21-2 The patient's past medical history included Transient ischemic attack. Previously administered products included for Transient ischemic attack: CLOPIDOGREL; for COVID-19 vaccination: PFIZER BIONTECH COVID-19 VACCINE (patient had been vaccinated twice with a BNT162b2 SARS-CoV-2 vaccine (Pfizer/BioNTech) without complications.). Past adverse reactions to the above products included No adverse event with CLOPIDOGREL and PFIZER BIONTECH COVID-19 VACCINE. Concurrent medical conditions included Hypertension. On an unknown date, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On an unknown date, the patient experienced THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-induced thrombosis with thrombocytopenia) (seriousness criteria hospitalization and medically significant), PULMONARY EMBOLISM (Chest computed tomography angiography revealed large pulmonary emboli, almost completely occluding the right pulmonary artery branches) (seriousness criteria hospitalization and medically significant) and INTERCHANGE OF VACCINE PRODUCTS (patient had been vaccinated twice with a BNT162b2 SARS-CoV-2 vaccine). The patient was hospitalized for 20 days due to	Literature article on an 83 year old female with concurrent medical history of hypertension and TIA attack for which she used a platelet aggregation inhibitor clopidogrel (Clopidogrel is labelled for bleeding, TTP, intracranial bleeding, thrombocytopenia, and has a Major bleeding warning) and previous administration of Cominarty who 20 days after receiving a booster dose with Spikevax presented to hospital with dyspnea and retrosternal pain for one day. Pseudo thrombocytopenia was ruled out and the patient was admitted to the Intensive Care department for hemodynamic and respiratory monitoring. Chest computed tomography angiography revealed large pulmonary emboli, almost completely occluding the right pulmonary artery branches. At hospital admission, D-dimer was >6.8 mg/L. Decline in platelet count ($20 \times 10^9/L$) was observed three days after admission and was normalized three days after IVIg initiation. An anti-platelet factor-4 ELISA performed in the presence of PF4 antibodies was measured and was positive. The patient was discharged from the hospital 20 days after admission. No longitudinal follow-up of PF4 levels was performed. The medical history of hypertension, TIA, in addition to the use of concomitant medication clopidogrel known to cause bleeding and cause thrombocytopenia provide a more plausible explanation for the reported events. According to the WHO causality assessment this report is unlikely associated to the vaccine.	

Case ID	Narrative	MAH Comment	WW Identifier
	PULMONARY EMBOLISM and THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME. The patient was treated with DALTEPARIN SODIUM (HEPARIN LMW) (subcutaneous) for Adverse event, at a dose of 7500 international unit twice a day; IMMUNOGLOBULINS NOS (IMMUNOGLOBULIN I.V) for Adverse event, at a dose of 1 gram per kilogram; DANAPAROID (subcutaneous) for Adverse event, at an unspecified dose and frequency; APIXABAN for Adverse event, at a dose of 10 milligram twice a day and APIXABAN ongoing since an unknown date for Adverse event, at a dose of 5 milligram twice a day. At the time of the report, THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-induced thrombosis with thrombocytopenia) and PULMONARY EMBOLISM (Chest computed tomography angiography revealed large pulmonary emboli, almost completely occluding the right pulmonary artery branches) was resolving and INTERCHANGE OF VACCINE PRODUCTS (patient had been vaccinated twice with a BNT162b2 SARS-CoV-2 vaccine) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Activated partial thromboplastin time (20-30): 37 seconds (High) Result was 37 seconds. On an unknown date, Angiogram: revealed large pulmonary emboli, almost completely revealed large pulmonary emboli, almost completely occluding the right pulmonary artery branches.. On an unknown date, Anti-platelet factor 4 antibody test: positive (Positive) An anti-platelet factor-4 ELISA performed in the presence of PF4 antibodies was measured using microtiter plate wells coated with 100 µl of 3 µg/ml PF4 (Chromatec) and was positive.. On an unknown date, Antiphospholipid antibodies: absent Lupus anticoagulant was absent. On an unknown date, Blood fibrinogen (2.0-4.0): 2.8 g/l (normal) Result at admission was 2.8 g/L. On an unknown date, Blood test: showed a thrombocytopenia showed a thrombocytopenia (48*109/mL, 339*109/mL five months earlier) and platelets (20*109/l) was observed Three days after admission, a further decline in platelets (20*109/L) was observed. On an unknown date, Cardiolipin antibody (Unknown-<20): <3 (normal) Result was <3 and 5.0 (normal) Result was 5.0. On an unknown date, Chest X-ray: possible infiltrate right lower pulmonarylobe Chest X-ray reported possible infiltrate right lower pulmonary lobe. On an unknown date, Echocardiogram: dilation of the right atrium and ventricle Dilation of right atrium and ventricle with non-dilated left ventricle was observed. On an unknown date, Fibrin D dimer (Unknown-<0.5): >6.8 mg/l (High) At hospital admission,D-dimer was >6.8 mg/L. On an unknown date, Haemoglobin (7.5-10): 7.0 mmol/l (Low) At hospital admission, hemoglobin was 7.0 mmol/L.		

Case ID	Narrative	MAH Comment	WW Identifier
	On an unknown date, Heparin-induced thrombocytopenia test (>45-Unknown): 20 minutes (Low) Platelet activation assay and time of Serum +0.2 IU heparin was 20 minutes and 45 minutes Platelet activation assay and time of Serum +100 IU heparin was 45 minutes. On an unknown date, Immunology test (Unknown-<1.0): 2.2 (High) PF4 IgG ELISA, optical density was 2.2. On an unknown date, Laboratory test (>45-Unknown): 45 minutes Platelet activation assay and time of Serum + FcγRIIa blocking was 45 minutes. On an unknown date, Platelet count (150-350): 20 x10⁹/l (Low) Decline in platelet count (20 x10⁹/L) was observed three days after admission, increase (High) Modest increase of platelet count was observed and normalized (normal) Platelet count was normalized three days after IVIg initiation. On an unknown date, Platelet factor 4: 5 minutes (normal) Platelet activation assay and time of Serum + PF4 was 5 minutes normal range reported as less than 45. On an unknown date, Prothrombin time (8-11): 13 seconds (High) Prothrombin time peak was 13 seconds. On an unknown date, SARS-CoV-2 test: negative (Negative) SARS-CoV-2 PCR was negative. On an unknown date, White blood cell count (4.3-10): 11.0 x10⁹/l (High) At hospital admission, leukocyte count was 11.0 x10⁹/L. For mRNA-1273 (Spikevax) (Unknown), the reporter considered THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (Vaccine-induced thrombosis with thrombocytopenia), PULMONARY EMBOLISM (Chest computed tomography angiography revealed large pulmonary emboli, almost completely occluding the right pulmonary artery branches) and INTERCHANGE OF VACCINE PRODUCTS (patient had been vaccinated twice with a BNT162b2 SARS-CoV-2 vaccine) to be related. Company comment This literature-non-study case concerns an 83-year-old female patient, with medical history of Transient ischemic attack in treatment with Clopidogrel, who experienced the unexpected serious (hospitalization and medically significant) AESIs of THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME and PULMONARY EMBOLISM, which occurred approximately 20 days after receiving a dose of mRNA-1273 vaccine, considered as the third dose for COVID19 Vaccination (received PFIZER BIONTECH as doses 1 and 2). Patient had presented to hospital with dyspnea and retrosternal pain for one day. Pseudo thrombocytopenia was ruled out and the patient was admitted to the Intensive Care department for hemodynamic and respiratory monitoring. Chest computed tomography angiography revealed large pulmonary emboli, almost completely occluding the right pulmonary artery branches. At hospital admission, D-dimer was >6.8 mg/L. Decline in platelet count (20 x10⁹/L) was observed three days after admission and was normalized three days after IVIg		

Case ID	Narrative	MAH Comment	WW Identifier
	initiation. Platelet transfusion was given to safely continue therapeutic anticoagulation. Danaparoid was also switched to apixaban to achieve more stable therapeutic anticoagulant therapy. Patient's condition improved. Diagnosis of Vaccine-induced thrombosis with thrombocytopenia (VITT) was made and intravenous immunoglobulins (IVIg, Nanogam, 1 g/kg for two days) were given. An anti-platelet factor-4 ELISA performed in the presence of PF4 antibodies was measured and was positive. The patient was discharged from the hospital 20 days after admission. No longitudinal follow-up of PF4 levels was performed. The mentioned medical history could be a contributing factor to the events. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. She received an mRNA-1273 SARS-CoV-2 boost		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 29-Apr-2022. The most recent information was received on 24-May-2022 and was forwarded to Moderna on 24-May-2022. This regulatory authority case was reported by a consumer and describes the occurrence of PLATELET COUNT DECREASED (Platelet 187 on 22-3-2022 and 115 on 23-3-2022) and ISCHAEMIC CEREBRAL INFARCTION (cerebral infarction) in a 71-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 000060ABS) for COVID-19 vaccination. Previously administered products included for Product used for unknown indication: COMIRNATY on 24-Jan-2021, COMIRNATY on 14-Feb-2021 and COMIRNATY on 13-Dec-2021. Past adverse reactions to the above products included No adverse event with COMIRNATY, COMIRNATY and COMIRNATY. On 17-Mar-2022, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 22-Mar-2022, after starting mRNA-1273 (Spikevax), the patient experienced ISCHAEMIC CEREBRAL INFARCTION (cerebral infarction) (seriousness criteria hospitalization and life threatening). On 23-Mar-2022, the patient experienced PLATELET COUNT DECREASED (Platelet 187 on 22-3-2022 and 115 on 23-3-2022) (seriousness criteria hospitalization and life threatening). At the time of the report, PLATELET COUNT DECREASED (Platelet 187 on 22-3-2022 and 115 on 23-3-2022) and ISCHAEMIC CEREBRAL INFARCTION (cerebral infarction) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 22-Mar-2022, Platelet count: 187 187 /nL. On 23-Mar-2022, Platelet count: 115 115 /nL. On an unknown date, Angiogram: normal - CTA from aortic arch to scalp: normal apical lungs, normal aortic branch, normal flow of vertebral arteries, normal aspects os carotid arteries, no stenosis, normal carotis sifon, normal circle of Willis, no acute	Information provided in this report is not clear and contradictory. This is a consumer report with unknown TTO for the occurrence of the reported event of cerebral infarction in a 71 year old male. Important information is missing in this report	

Case ID	Narrative	MAH Comment	WW Identifier
	arterial stop of central cerebral arteries, no colouring of mass in parenchym, normal filling of venous systems. and normal CTA brain: normal pattern of brain, normal grey and white matter, no signs of intracranial haemorrhage, diffuse hypodense spots that occur with vascular white matter abnormalities.. On an unknown date, Perfusion brain scan: abnormal - Perfusion: right CBF parieto-occipital lobe with localised increased TTP.. Concomitant medications were not reported. Treatment information was not provided. Company comment: This regulatory authority case concerns a 71-year-old male patient, with no medical history reported, who experienced the serious (life threatening/hospitalization) unexpected AESI of Ischaemic cerebral infarction, platelet count decreased. Event ischemic cerebral infarction occurred 5 days and platelet count decreased occurred 6 days after mRNA-1273 vaccine. This was the fourth dose of the patient's COVID-19 vaccination schedule that previously included 3 doses of tozinameran (third dose administered approximately 1 month prior to mRNA-1273 vaccination) (Interchange of vaccine products).It is reported that Platelet count was 187 /nL on 22-Mar-2022, Platelet count was 115 /nL on 23-Mar-2022, On an unknown date, Angiogram: normal - CTA from aortic arch to scalp: normal apical lungs, normal aortic branch, normal flow of vertebral arteries, normal aspects os carotid arteries, no stenosis, normal carotis sifon, normal circle of Willis, no acute arterial stop of central cerebral arteries, no colouring of mass in parenchym, normal filling of venous systems. and normal CTA brain: normal pattern of brain, normal grey and white matter, no signs of intracranial haemorrhage, diffuse hypodense spots that occur with vascular white matter abnormalities. On an unknown date, Perfusion brain scan: abnormal - Perfusion: right CBF parieto-occipital lobe with localised increased TTP.Patient's age and gender could be considered underlying risk factors for the reported event. The benefit-risk relationship of mRNA-1273 is not affected by this report. The event were assessed as serious as per Regulatory Authority's report. Most recent FOLLOW-UP information incorporated above includes: On 24-May-2022: Follow up received wherein new event Platelet count decreased and lab tests were added to the case.		
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 01-May-2022 and was forwarded to Moderna on 01-May-2022. This regulatory authority case was reported by a physician and describes the occurrence of SENSORY DISTURBANCE (sensory symptoms), VISUAL IMPAIRMENT (visual disturbance), HEADACHE (headache), NAUSEA (nausea), VOMITING (vomiting), ISCHAEMIC STROKE (Ischaemic stroke) and THROMBOCYTOPENIA (platelet count <150 A-109/L) in a 51-year-old female patient who received mRNA-1273 (Moderna CoviD-19 Vaccine) for COVID-19 vaccination.	Pateint was reported to had a stroke immediately after receiving the 3rd dose of Spikevax. A month later CAT scan showed abnormal results No other information was provided. This report is considered unliukley related to the vaccine given the very short TTO after vaccination and the lack of any indication .	

Case ID	Narrative	MAH Comment	WW Identifier
	The patient's past medical history included Non-smoker and Amblyopia (longstanding right amblyopia). Concurrent medical conditions included Haemochromatosis. On 24-Mar-2022, the patient received third dose of mRNA-1273 (Moderna CoviD-19 Vaccine) (unknown route) 1 dosage form. On 24-Mar-2022, the patient experienced ISCHAEMIC STROKE (Ischaemic stroke) (seriousness criteria disability and medically significant). On an unknown date, the patient experienced SENSORY DISTURBANCE (sensory symptoms) (seriousness criteria disability and medically significant), VISUAL IMPAIRMENT (visual disturbance) (seriousness criteria disability and medically significant), HEADACHE (headache) (seriousness criteria disability and medically significant), NAUSEA (nausea) (seriousness criteria disability and medically significant), VOMITING (vomiting) (seriousness criteria disability and medically significant) and THROMBOCYTOPENIA (platelet count <150 A-109/L) (seriousness criteria disability and medically significant). At the time of the report, SENSORY DISTURBANCE (sensory symptoms), VISUAL IMPAIRMENT (visual disturbance), HEADACHE (headache), NAUSEA (nausea) and VOMITING (vomiting) had resolved, ISCHAEMIC STROKE (Ischaemic stroke) had not resolved and THROMBOCYTOPENIA (platelet count <150 A-109/L) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 05-Apr-2022, Platelet count: normal counts (normal) normal counts. On 27-Apr-2022, Computerised tomogram head: 1 month after small right subacute occipital infar (abnormal) Test Result: 1 month after small right subacute occipital infarct. On 27-Apr-2022, Computerised tomogram venography head: no cvst (normal) Test Result: no CVST. On an unknown date, Anti-platelet factor 4 antibody test: unknown Test Result: Unknown. On an unknown date, Fibrin D dimer (>4000-Unknown): unknown Test Result: Unknown. On an unknown date, Serum ferritin increased: haemochromatosis; no hx of vasculitis (abnormal) Test Result: haemochromatosis; no hx of vasculitis. The action taken with mRNA-1273 (Moderna CoviD-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna CoviD-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. No concomitant medication was reported.		

Case ID	Narrative	MAH Comment	WW Identifier
	Patient has not tested positive for COVID-19 since having the vaccine. Patient was not enrolled in clinical trial. This report did not related to possible myocarditis or pericarditis. This report related to possible blood clots or low platelet counts. There is no any additional medical history, not already provided, that relates to previous venous or arterial thromboses. The patient had no any previous reactions to medications, especially heparin or anticoagulants. Patient has no history of, or concurrent, malignancy. The patient was not reviewed by a haematologist. Patient has no hemorrhage identified. No treatment information was reported. Company Comment- This regulatory case concerns a 51-year-old, female patient with no relevant medical history reported, who experienced the unexpected, serious (disability and medically significant) AESI of ischaemic stroke and thrombocytopenia, and the unexpected, serious (disability and medically significant) events of sensory disturbance, visual impairment, headache, nausea and vomiting. The event ischaemic stroke occurred on the same day after receiving the third dose of the mRNA-1273 vaccine. The start dates of the other events were not provided. The patient experienced headache and visual disturbance (fortification, palinopsia) in the left visual field hours after vaccination. These were accompanied by nausea, vomiting and episodes of left-sided sensory symptoms. The platelet count measured 12 days after vaccination showed normal results. Of note, it was reported that the last platelet count measured before vaccination also showed normal results. The Computerized Tomogram scan of the Head done approximately 1 month after vaccination showed 'small right subacute occipital infarct'. The Computerized Tomogram Venogram showed 'no cerebral venous sinus thrombosis'. Treatment information was not provided. The event ischaemic stroke had not resolved at the time of the report while the outcome of the event thrombocytopenia was unknown. The other events had resolved. The benefit-risk relationship of the mRNA-1273 vaccine is not affected by this report.		
	This regulatory authority case was reported by an other health care professional and describes the occurrence of PULMONARY EMBOLISM (Pulmonary embolism) and THROMBOCYTOPENIA (thrombocytopenia) in a 29-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 1110408) for COVID-19 vaccination. Patient's atypical infection and autoimmune hepatitis profile showed negative. The patient's past medical history included Fatty liver (suspect fatty liver related).	29 – year – old, male patient with medical history of alcohol consumption, overweight, fatty liver, chronic hepatitis, with elevated liver enzymes, splenomegaly, and smoking, who 8 days the 3rd dose of Spikevax experienced fatigue, anorexia, insomnia, fever and dyspnea, therefore he visited the emergency department were lab data revealed leukocytopenia, thrombocytopenia, giant platelet,	

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	Previously administered products included for Drug use for unknown indication: BNT vaccine on 28-Oct-2021 and BNT vaccine on 01-Dec-2021. Past adverse reactions to the above products included Muscle soreness with BNT vaccine and BNT vaccine. Concurrent medical conditions included Chronic hepatitis (with elevated liver enzyme), Splenomegaly since January 2022, Smoker, Alcohol use and Allergy. On 08-Apr-2022, the patient received third dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 16-Apr-2022, the patient experienced PULMONARY EMBOLISM (Pulmonary embolism) (seriousness criterion hospitalization) and THROMBOCYTOPENIA (thrombocytopenia) (seriousness criterion hospitalization). The patient was hospitalized on 16-Apr-2022 due to PULMONARY EMBOLISM and THROMBOCYTOPENIA. At the time of the report, PULMONARY EMBOLISM (Pulmonary embolism) and THROMBOCYTOPENIA (thrombocytopenia) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Alanine aminotransferase: 167 (High) 167. On an unknown date, Aspartate aminotransferase: 136 (High) 136. On an unknown date, Chest X-ray: increased infiltration and enlargement of pulmonar (abnormal) increased infiltration and enlargement of pulmonary vessels. On an unknown date, Computerised tomogram abdomen: peripheral pulmonary embolism may be considered (abnormal) peripheral pulmonary embolism may be considered, nodular lesions noted in bilateral lungs, enlarged lymph nodes (mediastinum, bilateral axillary regions, pancreatic region, retroperitoneal paraaortic region), splenomegaly and gallbladder wall thickening. On an unknown date, Electrocardiogram: sinus tachycardia (abnormal) sinus tachycardia. On an unknown date, Fibrin D dimer: elevated (8150) (High) elevated (8150). On an unknown date, Haemoglobin: mild anemia (13.2) (Low) mild anemia (13.2). On an unknown date, Lymphocyte morphology abnormal: 40.4 % 40.4 %. On an unknown date, Neutrophil count: 31.3 % 31.3 %. On an unknown date, Physical examination: clear consciousness and clear breathing sound (normal) clear consciousness and clear breathing sound. On an unknown date, Platelet count: thrombocytopenia (45000) (Low) thrombocytopenia (45000). On an unknown date, Urine analysis: elevated protein level (High) elevated protein level. On an unknown date, White blood cell count: leukocytopenia (2800) (Low) leukocytopenia (2800).	elevated liver enzyme, elevated d-dimer level, and elevated protein level in the urine. Chest x-ray showed infiltration and enlarged of pulmonary vessels, CAT report informed that peripheral pulmonary embolism could be considerate but did not provided a final report, with nodular lesions bilateral, enlarged lymph nodes, and splenomegaly. Admission differential diagnosis included ITP and atypical infection. The medical history of this patient is an important confounder for the events reported in this case and provide a more plausible explanation for them. According to the WHO causality assessment this report is unlikely.	

Case ID	Narrative	MAH Comment	WW Identifier
	For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Patient BMI reported as 28.1. No concomitant medications were reported. Since receiving moderna vaccine patient had fatigue, anorexia, insomnia. Besides, rapidly increased body weight was noted (from 88 to 97 kg). On the admission day (16-Apr-2022), Patient developed fever and dyspnea, therefore he visited infectious disease out-patient department. The patient was transferred to emergency department for admission survey. Throughout the course, he denied sore throat, lymphadenopathy, cough, dyspnea, vomiting, abdominal pain, diarrhea, tarry stool, bloody stool, dysuria. There was no travel history, no animal contact recently. In emergency department, lab data revealed giant platelet was noted and elevated liver enzyme. Under the impression of vaccine-induced immune thrombotic thrombocytopenia or atypical infection, he was admitted for further survey and treatment. 2nd day: Gasping for breath and chest pain. By 21-Apr-2022, patient was being hospitalized and treated. The Worldwide UID was reported as [REDACTED] Company comment: This regulatory case concerns a 29 – year – old, male patient with relevant medical history of alcohol consumption, overweight, chronic hepatitis, splenomegaly, and smoking, who experienced the unexpected, serious (due to hospitalization) AESI of pulmonary embolism and thrombocytopenia. The events occurred approximately one week after the administration of a dose of mRNA-1273 vaccine, reported as third dose of his COVID – 19 immunization schedules; the patient previously had two doses of “BNT” COVID – 19 vaccines (revaccination with different COVID – 19 vaccine could be considered). The report stated that since receiving mRNA – 1273 vaccine, the patient experienced fatigue, anorexia, insomnia, and body weight gain of 9 Kg. Eight days after vaccination with mRNA – 1273, he developed fever and dyspnea, therefore he visited the emergency department where lab data revealed leukocytopenia, thrombocytopenia, giant platelet, elevated liver enzyme, elevated d-dimer level, and elevated protein level in the urine routine. The computed tomography report informed that peripheral pulmonary embolism could be considered, with nodular lesions bilateral, enlarged lymph nodes, and splenomegaly. Under the impression of vaccine-induced immune thrombotic thrombocytopenia or atypical infection, he was admitted for further survey and unspecified treatment. Patient’s medical history of overweight and smoking could be confounder for pulmonary embolism. Patient’s medical history of splenomegaly and alcohol consumption could be confounder for thrombocytopenia. Patient’s medical history of		

Case ID	Narrative	MAH Comment	WW Identifier
	chronic hepatitis could be confounder for elevated liver enzyme. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.		
	This case was initially received via [REDACTED] (Reference number: [REDACTED]) on 11-May-2022. The most recent information was received on 27-May-2022 and was forwarded to Moderna on 27-May-2022. This regulatory authority case was reported by a physician and describes the occurrence of PULMONARY EMBOLISM (Pulmonary embolism), THROMBOCYTOPENIA (platelet count less than 150 A-109/L), DYSPNOEA (Shortness of breath) and PERIPHERAL SWELLING (Swelling of legs) in a 95-year-old female patient who received mRNA-1273 (Moderna CoviD-19 Vaccine) (batch no. 000081A) for COVID-19 vaccination. The patient's past medical history included Non-smoker and COVID-19 (Covid in Feb 2021 - main symptoms cough, short illness) in February 2021. Concurrent medical conditions included Pulmonary embolism. Concomitant products included TOZINAMERAN (COMIRNATY) from 16-Oct-2021 to an unknown date and COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (VAXZEVRIA) from 18-Apr-2021 to an unknown date for an unknown indication. On 29-Apr-2022, the patient received fourth dose of mRNA-1273 (Moderna CoviD-19 Vaccine) (unknown route) 1 dosage form. On 05-May-2022, after starting mRNA-1273 (Moderna CoviD-19 Vaccine), the patient experienced PULMONARY EMBOLISM (Pulmonary embolism) (seriousness criteria hospitalization, medically significant and life threatening). On an unknown date, the patient experienced THROMBOCYTOPENIA (platelet count less than 150 A-109/L) (seriousness criteria hospitalization, medically significant and life threatening), DYSPNOEA (Shortness of breath) (seriousness criteria hospitalization, medically significant and life threatening) and PERIPHERAL SWELLING (Swelling of legs) (seriousness criteria hospitalization, medically significant and life threatening). The patient was treated with APIXABAN at a dose of 5 milligram twice a day and DALTEPARIN SODIUM (FRAGMIN) at a dose of Unknown. At the time of the report, PULMONARY EMBOLISM (Pulmonary embolism) had resolved with sequelae and THROMBOCYTOPENIA (platelet count less than 150 A-109/L), DYSPNOEA (Shortness of breath) and PERIPHERAL SWELLING (Swelling of legs) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 22-Aug-2021, Platelet count (150-450): 196 (normal) 196. On 05-May-2022, Computerised tomogram thorax: pulmonary embolism Pulmonary Embolism. On 05-May-2022, Fibrin D dimer: d-dimer was greater than 4000 D-dimer was greater than 4000. On 05-May-2022, Platelet count (150-450): 131 (Low) 131.	95 year old female with medical history of pulmonary embolism who 6 days after the 4th dose of Spikevax developed dyspnoea, swelling of legs and was found to have low platelet count, elevated D-dimer, and a recurrence of pulmonary embolism. It is unknown if patient was taking any medication given her history of pulmonary embolism that may involved exposure to heparin. The medical history of pulmonary embolism, and advance age provide a more plausible explanation for the reported symptoms. According to the WHO causality assessment this report is unlikely.	

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	On 08-May-2022, SARS-CoV-2 test: no- negative covid-19 test (Negative) No-Negative COVID-19 test. On an unknown date, Activated partial thromboplastin time: 19.7 19.7. On an unknown date, Blood fibrinogen: 3.5 3.5. On an unknown date, Eosinophil count: 0.0 0.0. On an unknown date, Lymphocyte count: 0.6 0.6. On an unknown date, Platelet count (150-450): 131 (Low) 131. On an unknown date, Prothrombin time: 13.0 13.0. For mRNA-1273 (Moderna Covid-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Patient developed worsening SOB since vaccine and was acutely SOB and distressed when assessed on 5/5/22, noted to have a swollen leg, sent in to hospital acutely and diagnosed with Pulmonary Embolism. Patient had not tested positive for COVID-19 since having the vaccine. Patient was not enrolled in clinical trial. The report relate to possible blood clots or low platelet counts The report did not relate to possible myocarditis or pericarditis. The details of the event: Pulmonary Embolism. Diagnosed: Symptoms, hospitalisation, CT scan. The date of diagnosis was 5/5/22. The platelet count was measured on 5/5/22. The D-dimer was measured on 5/5/22. It was unknown if anti-PF4 antibodies identified. No additional medical history, not already provided, that relates to previous venous or arterial thromboses. The patient did not had any previous reactions to medications, especially heparin or anticoagulants. The patient did not have confirmed or suspected autoimmune or inflammatory disease, including vasculitis. The patient did not have history of, or current, malignancy The lowest platelet count after vaccine (usual normal range 150-450) and what date was this measured: 131 on 5/5/22. The last platelet count before vaccine if known, and what date was this measured (usual normal range 150-450): 196 on 22/8/21. The patient was not reviewed by a haematologist. No haemorrhage was identified. The patient did not have a history of, or concurrent, intracranial malignancy. The patient did not have concurrent or recent intracranial infections. The patient did not had recent surgical or medical interventions to the central nervous system (including lumbar puncture). The patient did not had a recent trauma/head injury.		

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	Follow up information received on 25-May-2022: Now patient was on bloodthinners apixaban 5mg BD. There was no prior risk factors for VTE not any surgery/trauma. Patient returned to nursing home and was quite lethargic its not recovered / not back to baseline and was not on prothombotic meds. Apixaban 5mg BD started upon diagnosis of PE, and patient was not sure what else might have been given in hospital (eg. Fragmin etc), no other info was known or available. Other vaccines were not administered in past 6 weeks.No smear/film reports were available. Lowest platelets on this hospitalization is equal to 131 and lowest platelets ever was equal to196 on Aug 2021,no other tests were performed, no previous adverse events with vaccination and no blood transfusion was done. No other tests done. No previous adverse events with vaccination. No blood transfusion. Most recent FOLLOW-UP information incorporated above includes: On 27-May-2022: Significant follow-up received. Relevant medical history information, laboratory tests, suspect product information (action taken), additional events (shortness of breath, swelling of legs) and case narrative were updated. Company Comment: This regulatory case concerns a 95-year-old female patient with a relevant medical history of pulmonary embolism, who experienced the unexpected serious adverse events of special interest Pulmonary embolism, Thrombocytopenia and Dyspnoea, Peripheral swelling that were life-threatening, medically significant, and led to hospitalization. The event Pulmonary embolism occurred approximately 6 days after receiving a dose of mRNA-1273 vaccine in her fourth COVID-19 vaccination series while Thrombocytopenia, Dyspnoea, Peripheral swelling occurred on an unknown date after administration of the same dose of the vaccine. Patient presented with shortness of breath and a swollen leg. Fibrin D dimer was increased, Platelet count was low, computerized tomogram showed pulmonary embolism, and SARS-CoV-2 test was negative. Patient was treated with Apixaban 5mg, twice daily and Dalteparin of unknown dosage and frequency. The event Pulmonary embolism resolved with sequelae and Thrombocytopenia, Dyspnoea, Peripheral swelling outcome was unknown. The relevant medical history of pulmonary embolism remains a confounder. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.		
	This literature-non-study case was reported in a literature article and describes the occurrence of THROMBOTIC THROMBOCYTOPENIC PURPURA (Thrombotic thrombocytopenic purpura) in an elderly female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. LITERATURE REFERENCE: Herrman E, Ghimire B, Chisti MM. Thrombotic thrombocytopenic purpura following administration of the Moderna booster vaccine. BMJ Case Rep. 2022;15(3):e247576 Concurrent medical conditions included Chronic myeloid leukaemia (Patient has a history of chronic myeloid leukaemia (CML), diagnosed 5 years prior. CML is being	This literature-case concerns an elderly female patient with concurrent medical conditions of Chronic myeloid leukaemia (since 5 years) and being treated with dasatinib, who 2 days after the 3rd dose of Spikevax experienced started to expereinced fatigue, generalised weakness, headache, abdominal pain and haematuria. Eight days later she went to urgent care. On admission, all vitals were within normal limits. There were no gross ecchymoses or petechiae. COVID-19 testing was negative. laboratory findings suggesting TTP	

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	treated with dasatinib, and patient is currently in molecular remission.) since 2017, Hyperlipidemia and Tobacco user. Concomitant products included DASATINIB for Chronic myeloid leukaemia. On an unknown date, the patient received third dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form and first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On an unknown date, after starting mRNA-1273 (Moderna COVID-19 Vaccine), the patient experienced THROMBOTIC THROMBOCYTOPENIC PURPURA (Thrombotic thrombocytopenic purpura) (seriousness criteria hospitalization and medically significant). The patient was treated with METHYLPREDNISOLONE for Thrombotic thrombocytopenic purpura, at a dose of 250 milligram every six hours. At the time of the report, THROMBOTIC THROMBOCYTOPENIC PURPURA (Thrombotic thrombocytopenic purpura) had resolved. Related DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In 2018, Biopsy bone marrow: negative for clonal plasma Bone marrow biopsy was negative for clonal plasma cells. In 2018, Haemoglobin (121-150): 15.3 g/dl The most recent blood count 4 years prior showed a haemoglobin of 15.3 g/dL. In 2018, Platelet count (150-400): 312 bil/l (normal) The most recent blood count 4 years prior showed a platelet count of 312 bil/L. On an unknown date, ADAMTS13 activity assay (Unknown->/=70%): 7% (Low) ADAMTS13 level returned at 7%. On an unknown date, ADAMTS13 inhibitor screen assay: negative (Negative) testing was negative for an ADAMTS13 inhibitor.. On an unknown date, Biopsy bone marrow: adequate trilineage haematopoiesi Bone marrow examination of the left iliac crest showed normocellular bone marrow with adequate trilineage haematopoiesis. No overt evidence of marrow involvement by chronic myeloid leukaemia, lymphoma or metastatic malignancy was identified. Severe normocytic anaemia with schistocytes and severe thrombocytopenia were seen, which was consistent with microangiopathic haemolytic anaemia. These findings were consistent with TTP. On an unknown date, Blood creatinine (0.50-1.10): 0.98 mg/dl (normal) 0.98 mg/dL. On an unknown date, Blood fibrinogen (200-400): 444 mg/dl (High) 444 mg/dL. On an unknown date, Blood immunoglobulin A (70-365): 69 mg/dll (Low) IgA was 69 mg/dL. On an unknown date, Blood immunoglobulin G: normal limits (normal) IgG was within normal limits. On an unknown date, Blood immunoglobulin M: normal limits (normal) IgM was within normal limits.	including severe thrombocytopenia, microangiopathic anemia with elevated hemolytic markers, the presence of schistocytes in peripheral blood, and low ADAMTS13 activity, along with typical clinical symptoms. Her PLASMIC score was 7 indicating severe disease, and she also had a negative PF4 antibody arguing against VITT. The medical history of the patient provide a more plausible explanation for her diagnosis of TTP. According to the WHO causality assessment this report is unlikely associated to the vaccine.	

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	On an unknown date, Blood lactate dehydrogenase (100-240): 1381 u/l (High) 1381 U/L. On an unknown date, C-reactive protein (Unknown-<8.0): 28.2 mg/l (High) 28.2 mg/L. On an unknown date, Capillary nail refill test: 2–3 s prolonged capillary refill at 2–3 s. On an unknown date, Computerised tomogram head: negative (Negative) CT head was ordered to rule out intracranial bleed, which was negative.. On an unknown date, Coombs test: negative (Negative) negative. On an unknown date, Fibrin D dimer (Unknown-0/499 ng/ml): 5838 ng/ml feu (High) 5838 ng/mL FEU. On an unknown date, Flow cytometry: no evidence of a paroxysmal nocturnal haemoglobin Flow cytometric analysis showed no evidence of a paroxysmal nocturnal haemoglobinuria clone based on analysis of glycosylphosphatidylinositol-linked antibodies.. On an unknown date, Glomerular filtration rate (Unknown->60 ml/min/1.73 m²): 58 ml/min/1.73 m² (Low) 58 mL/min/1.73 m². On an unknown date, HIV antigen: non-reactive HIV-1 p24 antigen/HIV-½ antibody screen was non-reactive.. On an unknown date, Haemoglobin (121-150): 78g/l (Low) 78g/L. On an unknown date, Haptoglobin (40-250): less than 8mg/dl (Low) less than 8mg/dL. On an unknown date, Heparin-induced thrombocytopenia test positive (Unknown-<0.400 od): 0.050 od 0.050 OD. On an unknown date, Light chain analysis (0.33-1.94): 5.02 mg/dl (High) Free kappa was slightly elevated at 5.02 mg/dL, 3.44 (High) Free kappa/lambda ratio was elevated at 3.44 and 1.46 mg/dl (normal) free lambda was normal at 1.46 mg/dL. On an unknown date, Physical examination: pertinent only for wheezing Physical exam was pertinent only for wheezing bilaterally on lung exam. There were no gross ecchymoses or petechiae and platelets recovered With initiation of the above treatments, the platelets recovered quickly, increasing to 23 bil/L, followed by 135 bil/L.. On an unknown date, Platelet count (150-400): 10 bil/l (Low) 10 bil/L, platelets recovered With initiation of the above treatments, the platelets recovered quickly, increasing to 23 bil/L, followed by 135 bil/L., 150 bil/l On treatment, the platelet count had recovered to greater than 150 bil/L. and normal range (normal) Platelet count was back to the normal range by the fourth day of treatment.. On an unknown date, Protein total (6.2-8.1): 5.8 g/dl (Low) Monoclonal gammopathy evaluation was only significant for a slightly low total protein level of 5.8 g/dL. No monoclonal proteins were detected. On an unknown date, Red blood cell schistocytes (Unknown-<1, absent): about 3–5/hpf schistocytes about 3–5/HPF (normal <1, absent). On an unknown date, Red blood cell sedimentation rate (0-18): 46 mm/hour (High) 46 mm/hour. On an unknown date, Renal function test: normal Renal function was normal.		

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	On an unknown date, SARS-CoV-2 test: negative (Negative) COVID-19 testing was negative. On an unknown date, Urine analysis: significant for 3+blood (abnormal) Urinalysis was significant for 3+blood (normal=absent).. On an unknown date, Vital signs measurement: normal limits (normal) On admission, all vitals were within normal limits. On an unknown date, White blood cell count (3.3-10.7): 7.7 bil/l (normal) 7.7 bil/L. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered THROMBOTIC THROMBOCYTOPENIC PURPURA (Thrombotic thrombocytopenic purpura) to be related. Patient began to develop symptoms 2 days after receiving her Moderna booster vaccine and presented to urgent care with an 8 day history of fatigue, generalised weakness, headache, abdominal pain and haematuria. Patient was asymptomatic following her first 2 Moderna vaccines. There were no recent medication changes. Pathologist review of the blood sample showed marked thrombocytopenia, worrisome for thrombotic microangiopathy. Therefore, further workup was ordered stat. Genetic testing for congenital TTP was not completed on the patient. Treatment also included therapeutic plasma exchange which was ordered and initiated within 24 hours of admission after a central line was placed by interventional radiology. She underwent daily therapeutic plasma exchange with 100% plasma volume replacement with 4000 mL of fresh frozen plasma. She completed daily exchanges for 4 days, and then these were stopped. Three days after treatment was initiated with steroids and plasmapheresis, the diagnosis of TTP was confirmed The patient recovered well and continues to follow with her haematologist. Patient had laboratory findings suggesting TTP including: severe thrombocytopenia, microangiopathic anaemia with elevated haemolytic markers, the presence of schistocytes in peripheral blood, and low ADAMTS13 activity, along with typical clinical symptoms. Her PLASMIC score was 7 indicating severe disease, and she also had a negative PF4 antibody arguing against VITT. As completed in our patient, urgent plasmapheresis is the cornerstone of TT		

Case ID	Narrative	MAH Comment	WW Identifier
	This case was initially received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 09-May-2022. The most recent information was received on 23-May-2022 and was forwarded to Moderna on 30-May-2022. This case was presented at "The 49th [REDACTED]" "The 47th Annual Meeting of the [REDACTED]" "The 51st [REDACTED]", and "The 38th [REDACTED] Symposium" and published in [REDACTED] 2022. Since the proprietary name of the suspect drug was not specified, the drug is handled as a Takeda product in this case report. Deep vein thrombosis in the leg and thrombocytopenia and pulmonary thromboembolism were assessed as serious by the MAH. This case concerned a 38-year-old female patient who was indicated of anaemia in a medical examination. She had the treatment with ointment for stasis dermatitis involving lower legs by a local doctor. Two days after the first vaccination of SARS-CoV-2 vaccine (mRNA vaccine, the proprietary name was unknown), the patient developed oedema in the leg. The patient visited our hospital on the 10th day and the deep vein thrombosis in the leg and thrombocytopenia ($3 \times 10^4/\text{mcL}$) was noted. Although an ambulatory examination was requested, on the 13th day, the patient was transferred to the hospital by an emergency transfer for disturbed consciousness and left hemiplegia. The patient was hospitalized due to the diagnosis with the subcortical haemorrhage in the right frontal lobe and she received a conservative treatment. The considerable platelets decreased ($0.8 \times 10^4/\text{mcL}$) was noted, and this was considered the cause for cerebral haemorrhage. During follow-up, venous thrombosis in both upper extremities complicated with pulmonary thromboembolism. Although idiopathic thrombocytopenic purpura, antiphospholipid syndrome and thrombotic microangiopathy were considered the cause of the pathophysiology of the tendency of the formation of the thrombus and thrombocytopenia, since the results for each autoantibody and the results for the examination of bone marrow myelogram was abnormal, the possibility of Vaccine-induced Immune Thrombocytopenia and Thrombosis (VITT) was considered from the clinical course, the patient was treated with immunoglobulin intravenous-injection method (1 g/kg/day for 2 days). Consequently, the value of blood platelet increased and the value returned to normal on the 28th day. The patient's general condition was stable and the rehabilitation was continued. Follow-up investigation will be made. Follow-up received on 23-May-2022 Updated: Reporter Information, Literature Information, Narrative Company Comment: The events developed after the administration of elasomeran and there is temporal relationship.	Important information is missing in this report including the vaccine administered as well as laboratory and any other diagnostic test results.	
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 01-Jun-2022. The most recent information was received on 14-Jun-2022 and was forwarded to Moderna on 14-Jun-2022. This regulatory authority case was reported by a consumer and describes the occurrence of PRURITUS (Bruising, thrombosis, swelling of the eye area itchy skin eczema), ECCHYMOSIS (Bruising, thrombosis, swelling of the eye area itchy skin eczema), ECZEMA (Bruising, thrombosis, swelling of the eye area itchy skin eczema), EYE OEDEMA (Bruising, thrombosis, swelling of the eye area itchy skin eczema) and THROMBOSIS (Bruising, thrombosis, swelling of the eye area itchy skin eczema) in a	This is not a case of TTS	

Case ID	Narrative	MAH Comment	WW Identifier
	50-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. No Medical History information was reported. On 16-Nov-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) .25 milliliter. On 16-Nov-2021, the patient experienced PRURITUS (Bruising, thrombosis, swelling of the eye area itchy skin eczema) (seriousness criterion hospitalization), ECCHYMOSIS (Bruising, thrombosis, swelling of the eye area itchy skin eczema) (seriousness criterion hospitalization), ECZEMA (Bruising, thrombosis, swelling of the eye area itchy skin eczema) (seriousness criterion hospitalization), EYE OEDEMA (Bruising, thrombosis, swelling of the eye area itchy skin eczema) (seriousness criterion hospitalization) and THROMBOSIS (Bruising, thrombosis, swelling of the eye area itchy skin eczema) (seriousness criterion hospitalization). At the time of the report, PRURITUS (Bruising, thrombosis, swelling of the eye area itchy skin eczema), ECCHYMOSIS (Bruising, thrombosis, swelling of the eye area itchy skin eczema), ECZEMA (Bruising, thrombosis, swelling of the eye area itchy skin eczema), EYE OEDEMA (Bruising, thrombosis, swelling of the eye area itchy skin eczema) and THROMBOSIS (Bruising, thrombosis, swelling of the eye area itchy skin eczema) had resolved with sequelae. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. Patient had no illness. No concomitant medication were reported. No treatment information was provided by the reporter. It was reported that it was not possible to trace the batch and date of administration of the vaccine. Company comment-This regulatory authority case concerns a 50-year-old female patient with no reported medical history who experienced the unexpected serious (caused hospitalization) events of Pruritus, Eczema, Eye oedema, and AESIs of Ecchymosis and Thrombosis (Bruising, thrombosis, swelling of the eye area itchy skin eczema) which occurred on same day after administration of an unspecified dose of mRNA-1273 vaccine. The benefit-risk relationship of mRNA-1273 is not affected by this report. Events' seriousness assessed as per regulatory authority report Most recent FOLLOW-UP information incorporated above includes:		

Case ID	Narrative	MAH Comment	WW Identifier
	On 06-Jun-2022: Follow-up received contains no new information (NNI). On 14-Jun-2022: Follow-up received include : Suspect (Spikevax) start date of vaccine added.		
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 02-Jun-2022 and was forwarded to Moderna on 08-Jun-2022. This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 02-Jun-2022 and was forwarded to Moderna on 08-Jun-2022. This case, initially reported to the [REDACTED] by a physician, was received via the [REDACTED]. On an unknown date, the patient received the 1st dose of a COVID-19 vaccine (product name unknown). On an unknown date, the patient received the 2nd dose of a COVID-19 vaccine (product name unknown). On 28-Mar-2022, at 16:30, the patient received the 3rd vaccination with this vaccine. On 29-Mar-2022, at 12:00, thrombosis with thrombocytopenia developed. The patient experienced shortness of breath, malaise, chills, and queasy around noon, and had difficulty of meal intake. On 31-Mar-2022, the patient was unable to walk from the morning and was transported to the reporting hospital because of dyspnea, general weakness, and vomiting. After coming to the hospital, the patient tested negative for SARS-CoV-2 test by TRC method. Tests for blood counts and coagulation system were performed. Metabolic acidosis and hypotension were observed, and contrast-enhanced CT of the chest and pelvis revealed findings of embolism in the left main pulmonary artery and the peripheral portions of both pulmonary arteries. In addition, bilateral thrombosis was confirmed, and the patient was diagnosed with extensive pulmonary embolism. The patient was hospitalized. There was no risk factor for thrombosis. Anticoagulation therapy with heparin sodium was started. On 01-Apr-2022, hemodynamic stability was confirmed, and heparin sodium was discontinued, followed by the initiation of oral apixaban. Echocardiography and echography of leg veins revealed a mobile thrombus in the left below-knee vein and a thrombus in the bilateral flounder veins. The patient was diagnosed as deep vein thrombosis. Blood tests showed elevated SCC. Disorders such as heparin-induced thrombocytopenia and antiphospholipid antibody syndrome were excluded. On 07-Apr-2022, contrast-enhanced CT was performed again, and reduction of the thrombus was confirmed. On 08-Apr-2022, echography of leg veins was performed again, and disappearance of the mobile thrombus was confirmed. On 09-Apr-2022, the patient was able to walk. On 13-Apr-2022, disappearance of the symptom and stabilization of walking were confirmed. The patient recovered and was discharged from the hospital. The outcome of thrombosis with thrombocytopenia, difficulty of meal intake, inability to walk, metabolic acidosis, extensive pulmonary embolism, and deep vein thrombosis was reported as resolved. Follow-up investigation will be made. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.	There is no information related to platelet values that could confirmed whether or not this is a case of TTS. Other important information is also missing from this report including patient medical history and concomitant medications	
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 14-Jun-2022 and was forwarded to Moderna on 14-Jun-2022.	63-year-old male patient with medical history of Chronic lymphocytic leukaemia, who the same day after the 1st dose of Spikevax experienced Petechiae, Telangiectasia, Pruritus, Hypoaesthesia,	

Case ID	Narrative	MAH Comment	WW Identifier
	This regulatory authority case was reported by a consumer and describes the occurrence of TELANGIECTASIA (separated blood vessels), PRURITUS (burning in the leg), HYPOAESTHESIA (numbness in the leg, swelling from ankle until over knee, burning in the leg, bleeding in the skin and protruding blood vessels, tiredness), PERIPHERAL SWELLING (swelling from ankle until over knee), FATIGUE (tiredness), PETECHIAE (hemorrhage in the skin) and THROMBOSIS (thrombosis fears) in a 63-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 3003602) for COVID-19 vaccination. The patient's past medical history included CLL. On 13-Jul-2021, the patient received first dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 13-Jul-2021, the patient experienced TELANGIECTASIA (separated blood vessels) (seriousness criterion medically significant), PRURITUS (burning in the leg) (seriousness criterion medically significant), HYPOAESTHESIA (numbness in the leg, swelling from ankle until over knee, burning in the leg, bleeding in the skin and protruding blood vessels, tiredness) (seriousness criterion medically significant), PERIPHERAL SWELLING (swelling from ankle until over knee) (seriousness criterion medically significant), FATIGUE (tiredness) (seriousness criterion medically significant), PETECHIAE (hemorrhage in the skin) (seriousness criterion medically significant) and THROMBOSIS (thrombosis fears) (seriousness criterion medically significant). At the time of the report, TELANGIECTASIA (separated blood vessels), PRURITUS (burning in the leg), HYPOAESTHESIA (numbness in the leg, swelling from ankle until over knee, burning in the leg, bleeding in the skin and protruding blood vessels, tiredness), PERIPHERAL SWELLING (swelling from ankle until over knee), FATIGUE (tiredness), PETECHIAE (hemorrhage in the skin) and THROMBOSIS (thrombosis fears) had resolved. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. No concomitant medications were provided. Company Comment: This is a regulatory case concerning a 63-year-old male patient with medical history of Chronic lymphocytic leukaemia, who experienced the unexpected serious (medically significant) adverse events of special interest of Petechiae and Thrombosis and the unexpected serious (medically significant) events of Telangiectasia, Pruritus, Hypoaesthesia, Peripheral swelling and Fatigue, on the same day after receiving the first dose of mRNA-1273 vaccine. Clinical course, diagnostic tests and treatment details were not provided in the case. The events had resolved at the time of the report. Medical history of Chronic lymphocytic leukaemia remains a risk factor for the events of Petechiae, Thrombosis, Telangiectasia and Fatigue. The benefit-risk relationship of mRNA-1273 is not affected by this report. Events retained as serious as per Regulatory Authority.	Peripheral swelling and Fatigue, and thrombosis. Clinical course, diagnostic tests and treatment details were not provided in the case. The events had resolved at the time of the report. The medical history of Chronic lymphocytic leukaemia remains a risk factor for the events of Petechiae, Thrombosis, Telangiectasia and Fatigue and provide a more plausible explanation for the reported events. According to the WHO causality assessment this report is unlikely.	

Case ID	Narrative	MAH Comment	WW Identifier
	Treatment of side effect 1: medical use, condition over 8 weeks, thrombosis feared treatment of side effect 2: lasting about 10 weeks, no feeling of safety when walking, could only rise sideways steps. As a result of the two vaccinations, it took months for motor skills until be restored. fear of the next vaccination. Consider whether I should dare to get vaccinated. What impact does this... This case was linked to [REDACTED] (E2B Linked Report).		
	This literature-non-study case was reported in a literature article and describes the occurrence of THROMBOTIC THROMBOCYTOPENIC PURPURA (Relapsed Refractory Acquired Thrombotic Thrombocytopenic Purpura (aTTP)) in a 57-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. LITERATURE REFERENCE: Francisco MT, Northfelt D, Kaufman AE, Padrnos L, Rosenthal AC, Andres J et al.. Relapsed refractory acquired thrombotic thrombocytopenic purpura (aTTP) following COVID-19 vaccination. Blood. 2021;138:4218-19 The patient's past medical history included Thrombotic thrombocytopenic purpura in 2016. Previously administered products included for Thrombotic thrombocytopenic purpura: Rituximab, BORTEZOMIB (3 months of weekly bortezomib 1 mg/m²), MYCOPHENOLATE MOFETIL (up-titrated to 1,750 mg twice daily, and then slowly tapered off over a 2-year.) and ECULIZUMAB. Past adverse reactions to the above products included No adverse event with BORTEZOMIB, ECULIZUMAB, MYCOPHENOLATE MOFETIL and Rituximab. On an unknown date, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, after starting mRNA-1273 (Moderna COVID-19 Vaccine), the patient experienced THROMBOTIC THROMBOCYTOPENIC PURPURA (Relapsed Refractory Acquired Thrombotic Thrombocytopenic Purpura (aTTP)) (seriousness criteria hospitalization and medically significant). The patient was treated with DIPHENHYDRAMINE for Thrombotic thrombocytopenic purpura, at an unspecified dose and frequency; RITUXIMAB for Thrombotic thrombocytopenic purpura, at a dose of qwk for 4 weeks; CAPLACIZUMAB for Thrombotic thrombocytopenic purpura, at a dose of 11 milligram once a day; MYCOPHENOLATE MOFETIL for Thrombotic thrombocytopenic purpura, at a dose of 500 milligram twice a day; PREDNISONE for Thrombotic thrombocytopenic purpura, at an unspecified dose and frequency and CYCLOPHOSPHAMIDE (intravenous) for Thrombotic thrombocytopenic purpura, at a dose of 750 mg/m² every three weeks. At the time of	This patient had a pre-existing diagnosis of acquired thrombotic thrombocytopenic purpura associated with ADAMTS13 deficiency that was in remission. He relapsed 7 weeks after the second dose of the Moderna vaccine. His illness differs in pathophysiological mechanism from the TTS that has been reported after adenoviral vaccines against COVID-19 that involves antibodies against platelet factor 4. In addition, he did not have reported thrombosis. The TTO of seven weeks after dose 2 is long for a vaccine adverse reaction.	

Case ID	Narrative	MAH Comment	WW Identifier
	the report, THROMBOTIC THROMBOCYTOPENIC PURPURA (Relapsed Refractory Acquired Thrombotic Thrombocytopenic Purpura (aTTP)) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, ADAMTS13 activity assay: t less than 5 percent ADAMTS13 activity level was t <5% (normal >= 70%), less than 5 percent less than 5 percent and 52-59 percent ADAMTS13 activity level has reached 52-59%. On an unknown date, ADAMTS13 inhibitor screen assay: 1.5 positive ADAMTS13 inhibitor screen and titer of 1.5 (normal <0.4 and 11.4 inhibitor level was the highest that it had ever been at 11.4.. On an unknown date, Blood creatinine: baseline Baseline. On an unknown date, Blood lactate dehydrogenase (122-222): 508 u/l (Low) 508 U/L. On an unknown date, Blood smear test: 1-3 schistocytes per high-powered field 1-3 schistocytes per high-powered field. On an unknown date, Haemoglobin (13.2-16.6): 12.4 g/dl (Low) 12.4 g/dL. On an unknown date, Platelet count ($135 \times 10^9/L$-$317 \times 10^9/L$): $38 \times 10^9/L$ (Low) $38 \times 10^9/L$, 200-300 $\times 10^9/L$ baseline of 200-300 $\times 10^9/L$, normal platelets remained stable within the upper limit of normal during his 30 day course of caplacizumab, $23 \times 10^9/L$ 3 weeks after completion of caplacizumab, he had an acute drop in his platelets to $23 \times 10^9/L$. and normal platelet count normalized and remain stable. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered THROMBOTIC THROMBOCYTOPENIC PURPURA (Relapsed Refractory Acquired Thrombotic Thrombocytopenic Purpura (aTTP)) to be related. Concomitant medications were not reported. The patient was initially diagnosed with aTTP, after presenting with symptoms of dark urine, mild headaches and transient episodes of aphasia and paresthesia. and was required prolonged and extensive treatment including over 5 weeks of daily therapeutic plasma exchange (TPE), followed by gradual reduction in frequency of TPE sessions. The patient was doing well for 3 years without manifestations of aTTP Patient developed a petechial rash 7 week after Moderna COVID-19 vaccine and was referred to the emergency department and was admitted to the hospital, and initiated on daily TPE, with steroids and diphenhydramine prior to each TPE session. He quickly improved with TPE alone and was again hospitalized and underwent 8 sessions of daily TPE. Most recent FOLLOW-UP information incorporated above includes: On 06-Jan-2022: Follow up received by safety 06-JAN-2022 has Email with FTA received from SARA team and does not contain any new information.		

Case ID	Narrative	MAH Comment	WW Identifier
	Company comment: This case concerns a 57-year-old African-American, male patient with relevant medical history refractory acquired thrombotic thrombocytopenic purpura, who experienced the unexpected serious event of Relapsed Refractory Acquired Thrombotic Thrombocytopenic Purpura . The event occurred approximately 7 weeks after the second dose of mRNA-1273 (Moderna covid-19 vaccine). The patient was initially diagnosed with aTTP, after presenting with symptoms of dark urine, mild headaches and transient episodes of aphasia and paresthesia. and was required prolonged and extensive treatment including over 5 weeks of daily therapeutic plasma exchange (TPE), followed by gradual reduction in frequency of TPE sessions. Patient developed a petechial rash 7 week after Moderna COVID-19 vaccine and was referred to the emergency department and was admitted to the hospital, and initiated on daily TPE, with steroids and diphenhydramine prior to each TPE session. He quickly improved with TPE alone and was again hospitalized and underwent 8 sessions of daily TPE.. Laboratory reports showed platelets of 38 x 109/L, mildly elevated LDH (508 u/L), hemoglobin of 12.4 g/dL, creatinine at baseline, and peripheral blood smear showing 1-3 schistocytes per high-powered field, ADAMTS13 activity level was t <5% with positive ADAMTS13 inhibitor screen and titer of 1.5, consistent with diagnosis of relapsed aTTP. The rechallenge was not applicable as event occurred after second dose. This patient's underlying medical condition remains a confounder. The benefit-risk relationship of mRNA-1273 (Moderna covid-19 vaccine) is not affected by this report.		
	This spontaneous case was reported by a consumer and describes the occurrence of CEREBROVASCULAR ACCIDENT (Had a CAT scan because the neurologist saw something and though it was a stroke) in a 69-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch nos. 019B21A and 012AZ1A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concomitant products included AMLODIPINE for Blood pressure, MOMETASONE FUROATE (NASONEX) for an unknown indication. On 03-Mar-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 31-Mar-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On 31-Mar-2021, the patient experienced CEREBROVASCULAR ACCIDENT (Had a CAT scan because the neurologist saw something and though it was a stroke) (seriousness criterion medically significant), VACCINATION COMPLICATION (I've experienced side effects after getting the vaccine), PERIPHERAL SWELLING (Swelling of the arm), INFLUENZA LIKE ILLNESS (Flu like symptoms), VISION BLURRED (didn't go to the doctor until I had blurry vision), CONTUSION (unexplained black and blue bruising/Had the bruising problem for 4 months until it got less and less), HYPOKINESIA (I couldn't move my head for 4 weeks), PLATELET COUNT DECREASED (Low Platelet count), RASH (A rash), PYREXIA (Fever of 102 F) and	This report from a consumer did not document a low platelet count or thrombosis. The platelet issue was reported to have occurred many months after vaccination.	

Case ID	Narrative	MAH Comment	WW Identifier
	HEADACHE (Terribly headache/Took aspirin for headache but didn't go away). On 06-Jan-2022, the patient experienced PLATELET DISORDER (Not sure if the platelet count has to do with the vaccine). The patient was treated with ACETYLSALICYLIC ACID (ASPIRINE) for Headache, at an unspecified dose and frequency. At the time of the report, CEREBROVASCULAR ACCIDENT (Had a CAT scan because the neurologist saw something and thought it was a stroke), VACCINATION COMPLICATION (I've experienced side effects after getting the vaccine), PERIPHERAL SWELLING (Swelling of the arm), INFLUENZA LIKE ILLNESS (Flu like symptoms), VISION BLURRED (didn't go to the doctor until I had blurry vision), CONTUSION (unexplained black and blue bruising/Had the bruising problem for 4 months until it got less and less), HYPOKINESIA (I couldn't move my head for 4 weeks), PLATELET COUNT DECREASED (Low Platelet count), PLATELET DISORDER (Not sure if the platelet count has to do with the vaccine), RASH (A rash), PYREXIA (Fever of 102 F) and HEADACHE (Terribly headache/Took aspirin for headache but didn't go away) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Computerised tomogram: abnormal (abnormal) it was a stroke. On an unknown date, Platelet count: low (Low) Low Platelet count. On an unknown date, Pyrexia: 102 (High) fever of 102 F. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Patient reported that she experienced side effects after receiving the first 2 doses of the Moderna COVID-19 vaccine. Her doctor told that her immune system was too reactive and prescribed her steroids for 5 days and antibiotics but she doesn't know the name. Also, she is confused as one doctor told her to get the booster and another doctor told her that it could be dangerous for her getting the vaccine. Vaccine was given in left arm(IM).		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 13-Jan-2022. The most recent information was received on 09-Feb-2022 and was forwarded to Moderna on 09-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of ISCHAEMIC STROKE (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke), the first episode of ASTHENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke), the second episode of ASTHENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke), THROMBOCYTOPENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke), HEMIPARESIS (hemisphenia left hemiparesis left hemiparesis platelet openia	This 78 year old woman developed an ischemic cerebrovascular accident, a commonly occurring event in the absence of vaccination, 21 days after vaccination. The platelet count was reported as low without quantification. Fibrin D-dimer was not quantified. There was not an anti-PF 4 ELISA result. An identified thrombus was not reported.	

Case ID	Narrative	MAH Comment	WW Identifier
	fragment D-dimer strength deficiency increased ischaemic stroke) and FIBRIN D DIMER INCREASED (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) in a 69-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 immunisation. Concomitant products included CAFFEINE CITRATE, CODEINE PHOSPHATE, PARACETAMOL (TRIAEC-8) and PANTOPRAZOLE SODIUM SESQUIHYDRATE () for an unknown indication. On 07-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) .25 milliliter. On 28-Dec-2021, the patient experienced ISCHAEMIC STROKE (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) (seriousness criterion hospitalization), the first episode of ASTHENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) (seriousness criterion hospitalization), the second episode of ASTHENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) (seriousness criterion hospitalization), THROMBOCYTOPENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) (seriousness criterion hospitalization), HEMIPARESIS (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) (seriousness criterion hospitalization) and FIBRIN D DIMER INCREASED (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) (seriousness criterion hospitalization). At the time of the report, ISCHAEMIC STROKE (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke), the last episode of ASTHENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke), THROMBOCYTOPENIA (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke), HEMIPARESIS (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) and FIBRIN D DIMER INCREASED (hemisphenia left hemiparesis left hemiparesis platelet openia fragment D-dimer strength deficiency increased ischaemic stroke) had resolved with sequelae. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 28-Dec-2021, Computerised tomogram head: borderline (Borderline) Borderline. On 28-Dec-2021, Fibrin D dimer: borderline (Borderline) Borderline. On 28-Dec-2021, Platelet count decreased: borderline (Borderline) Borderline.		

Case ID	Narrative	MAH Comment	WW Identifier
	The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Treatment medications were not reported. It was reported that it was not possible to find the lot number of the vaccine. Company Comment: This regulatory authority case concerns a 69-year-old male patient with no medical history reported, who experienced the serious (hospitalization) unexpected AESI of Ischaemic stroke and Thrombocytopenia, among other related events, approximately 21 days after receiving a dose of mRNA- 1273 vaccine (dosage 0.25 ml). Clinical manifestations included left hemiparesis. Laboratory results showed platelet count decreased (result not reported) and increased Fibrin D dimer. Details regarding brain imaging were not disclosed. At the time of the report, the events had resolved with sequelae. The benefit-risk relationship of mRNA- 1273 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 09-Feb-2022: Follow-up received contains significant information. Updated lab data results and updated event outcome of all events		
	This case was initially received via [REDACTED] Reference number [REDACTED] on 13-Jan-2022. The most recent information was received on 28-Jan-2022 and was forwarded to Moderna on 28-Jan-2022. This regulatory authority case was reported by a physician and describes the occurrence of MESENTERIC VEIN THROMBOSIS (Mesenteric vein thrombosis), SPLENIC VEIN THROMBOSIS (Splenic vein thrombosis), PORTAL VEIN THROMBOSIS (Portal vein thrombosis), INTESTINAL ISCHAEMIA (Ischaemia bowel), PULMONARY EMBOLISM (Pulmonary embolism), VENA CAVA THROMBOSIS (Inferior venacaval thrombosis), THROMBOCYTOPENIA (platelet count <150 A— 109/L), ABDOMINAL PAIN (Abdominal pain) and VOMITING (Vomiting) in a 53-year-old male patient who received mRNA-1273 (Moderna CoviD-19 Vaccine) (batch no. 3005688) for COVID-19 vaccination. Co-suspect products included non-company products COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (COVID-19 VACCINE ASTRAZENECA) for COVID-19 vaccination and COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (COVID-19 VACCINE ASTRAZENECA) for COVID-19 vaccination. The patient's past medical history included Non-smoker. Concomitant products included LEVOTHYROXINE and SIMVASTATIN for an unknown indication.	This 53 year old man developed thrombosis in multiple unusual locations, with thrombocytopenia, 2 weeks after the third dose of Spikevax. He had two prior doses of the Astra Zeneca adenoviral vectored COVID-19 vaccine. However, it was reported, with regard to laboratory results: "Platelet factor 4: anti-pf4 antibodies were not identified". TTS after the Astra Zeneca vaccine usually occurs after the first dose and involves anti-pf4 antibodies, which this patient did not have.	

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	On 24-Mar-2021, the patient received first dose of COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (COVID-19 VACCINE ASTRAZENECA) (unknown route) 1 dosage form. On 12-Jun-2021, the patient received second dose of COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (COVID-19 VACCINE ASTRAZENECA) (unknown route) 1 dosage form. On 17-Dec-2021, the patient received third dose of mRNA-1273 (Moderna CoviD-19 Vaccine) (unknown route) 1 dosage form. On 31-Dec-2021, the patient experienced MESENTERIC VEIN THROMBOSIS (Mesenteric vein thrombosis) (seriousness criteria hospitalization, medically significant and life threatening), SPLENIC VEIN THROMBOSIS (Splenic vein thrombosis) (seriousness criteria hospitalization, medically significant and life threatening) and INTESTINAL ISCHAEMIA (Ischaemia bowel) (seriousness criteria hospitalization, medically significant and life threatening). On 03-Jan-2022, the patient experienced PORTAL VEIN THROMBOSIS (Portal vein thrombosis) (seriousness criteria hospitalization, medically significant and life threatening). On 05-Jan-2022, the patient experienced PULMONARY EMBOLISM (Pulmonary embolism) (seriousness criteria hospitalization, medically significant and life threatening) and VENA CAVA THROMBOSIS (Inferior venacaval thrombosis) (seriousness criteria hospitalization, medically significant and life threatening). On an unknown date, the patient experienced THROMBOCYTOPENIA (platelet count <150 A— 109/L) (seriousness criteria hospitalization, medically significant and life threatening), ABDOMINAL PAIN (Abdominal pain) (seriousness criteria hospitalization, medically significant and life threatening) and VOMITING (Vomiting) (seriousness criteria hospitalization, medically significant and life threatening). On 12-Jan-2022, PULMONARY EMBOLISM (Pulmonary embolism) had resolved. At the time of the report, MESENTERIC VEIN THROMBOSIS (Mesenteric vein thrombosis), SPLENIC VEIN THROMBOSIS (Splenic vein thrombosis), PORTAL VEIN THROMBOSIS (Portal vein thrombosis), INTESTINAL ISCHAEMIA (Ischaemia bowel), VENA CAVA THROMBOSIS (Inferior venacaval thrombosis), THROMBOCYTOPENIA (platelet count <150 A— 109/L) and ABDOMINAL PAIN (Abdominal pain) had resolved and VOMITING (Vomiting) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 25-May-2017, Platelet count: 128 128 More information available-NO. On 03-Jan-2022, Computerised tomogram: small bowel venous ischaemia small bowel venous ischaemia More information available-NO and significant smv/portal/splenic vein thrombus significant SMV/portal/splenic vein thrombus More information available-NO. On 03-Jan-2022, Platelet count: 127 127. More information available-NO and 128 128. More information available-NO. On 03-Jan-2022, Venogram: small bowel venous ischaemia small bowel venous ischemia. More information available-NO and significant smv/portal/splenic vein		

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	thrombus significant SMV/portal/splenic vein thrombus. More information available-NO. On 04-Jan-2022, Fibrin D dimer: 8.53 8.53 ug/ml. On 05-Jan-2022, Computerised tomogram: inferior vena cava thrombus inferior vena cava thrombus More information available-NO and segmental pulmonary arterial thromboembolism segmental pulmonary arterial thromboembolism More information available-NO. On 12-Jan-2022, Computerised tomogram thorax: resolved Resolved More information available-NO. On an unknown date, Activated partial thromboplastin time: 52.6 52.6 More information available-NO. On an unknown date, Blood fibrinogen: 5.69 5.69. More information available-NO. On an unknown date, Investigation: thrombophilia screen: no evidence of malignancy Thrombophilia screen: no evidence of malignancy. More information available-NO and hepatic screen: no pancreatic abnormalities Hepatic screen: no pancreatic abnormalities More information available-NO.. On an unknown date, Platelet factor 4: anti-pf4 antibodies were not identified Anti-PF4 antibodies were not identified. On an unknown date, Prothrombin time: 14.5 14.5. More information available-NO. On an unknown date, SARS-CoV-2 test: negative (Negative) No - Negative COVID-19 test. For mRNA-1273 (Moderna CoviD-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Full thrombophilia and hepatic screens done. No evidence of malignancy, no pancreatic abnormalities. Documented as unexplained/unprovoked. Note it occurred within 14 days of moderna spikevaxbooster. company comment: This regulatory authority case concerns a 53-year-old male patient with no relevant medical history reported, who experienced the unexpected serious (life-threatening, hospitalization and medically significant) AESI events of Mesenteric vein thrombosis, Splenic vein thrombosis, Portal vein thrombosis, Pulmonary embolism , Vena cava thrombosis and Thrombocytopenia, and serious unexpected events of Intestinal ischemia, abdominal pain, and vomiting after third dose of mRNA-1273 vaccine. The onset of the events Intestinal ischemia, Mesenteric vein thrombosis, Splenic vein thrombosis and Portal vein thrombosis occurred approximately 14 days after the booster dose of mRNA- 1273 vaccine. The patient presented with 4 days of abdominal pain and vomiting. Significant findings of small bowel venous ischemia (dilated edematous congested bowel loops) with significant superior mesenteric vein (SMV)/portal/splenic vein thrombus were shown on CT and subsequent CT venogram. Pulmonary embolism and inferior vena cava thrombosis were diagnosed 2 days later, on follow-up imaging. Laboratory results showed thrombocytopenia (lowest		

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	platelet count 127) and negative Anti-PF4 antibodies. Anticoagulant therapy was prescribed. At the time of the report, the patient had been discharged with enoxaparin. Diagnostic work-up did not reveal underlying thrombotic risk factors. Full thrombophilia and hepatic screens done showed no evidence of malignancy, no pancreatic abnormalities. The patient had received initial schedule of vaccination with co-suspect drug COVID-19 Vaccine AstraZeneca 6 months prior the mRNA 1273 vaccine. The co-suspect drug AstraZeneca vaccine remain as confounder to the events. The benefit-risk relationship of mRNA- 1273 vaccine is not affected by this. Most recent FOLLOW-UP information incorporated above includes: On 28-Jan-2022: Follow up included indication for the suspect was updated, lab data updated, Event outcome for initially existing events was updated, additional events were added, action taken and rechallenge was updated and the case narrative was updated.		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 19-Jan-2022. The most recent information was received on 01-Feb-2022 and was forwarded to Moderna on 01-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of TRANSIENT ISCHAEMIC ATTACK (passenger phatic disorders and impairment of motor skills), MYALGIA (Muscle pain) and THROMBOCYTOPENIA (Thrombocytes 78x10 E9/L) in a 78-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 094F21ABS) for COVID-19 vaccination. The patient's past medical history included Chronotropic incompetence (Family history false), Mobitz (type) II atrioventricular block (Family history false) in March 2007, Temporal lobe epilepsy (Family history false), Pacemaker insertion (cardiac) (Family history false), Cardiac pacemaker replacement (Family history false) in January 2013, Laparoscopically assisted hysterectomy (Family history false) in June 2019 and Neurolysis (Family history false) in March 2009. Previously administered products included for Drug use for unknown indication: PFIZER BIONTECH COVID-19 VACCINE on 25-Mar-2021, BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0 and3MLCOVID-19 VACCIN PFIZER INJVLST on 26-Apr-2021. Past adverse reactions to the above products included Minor ischaemic stroke with PFIZER BIONTECH COVID-19 VACCINE; and No adverse reaction with BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0 and3MLCOVID-19 VACCIN PFIZER INJVLST. Concurrent medical conditions included Endometrial carcinoma (Family history false) in June 2019 and Hypertension (Family history false). Concomitant products included LEVETIRACETAM for COVID-19 vaccination, CLOPIDOGREL, AMLODIPINE, FENOTEROL HYDROBROMIDE, IPRATROPIUM BROMIDE (FENOTEROL HYDROBROMIDE;IPRATROPIUM BROMIDE), BECLOMETASONE, FORMOTEROL (BECLOMETASONE;FORMOTEROL), OMEPRAZOLE SODIUM	78 year old woman with endometrial cancer, multiple other cardiovascular disease risk factors and history of mild ischemic stroke was diagnosed with thrombocytopenia and transient ischemic attack two days after Spikevax. She had two prior doses of Pfizer COVID vaccine. She was not diagnosed with a thrombus so did not have TTS.	

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	(OMEPRAZOLE [OMEPRAZOLE SODIUM]), CARBAMAZEPINE, ROSUVASTATIN CALCIUM (ROSUVASTATINE CF), LOSARTAN and DOXAZOSIN for an unknown indication. On 13-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 15-Dec-2021, the patient experienced THROMBOCYTOPENIA (Thrombocytes 78x10 E9/L). On 16-Dec-2021, the patient experienced MYALGIA (Muscle pain). On an unknown date, the patient experienced TRANSIENT ISCHAEMIC ATTACK (passenger phatic disorders and impairment of motor skills). At the time of the report, TRANSIENT ISCHAEMIC ATTACK (passenger phatic disorders and impairment of motor skills) had resolved, MYALGIA (Muscle pain) had not resolved and THROMBOCYTOPENIA (Thrombocytes 78x10 E9/L) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 15-Dec-2021, Activated partial thromboplastin time: 22s (siemens) (Inconclusive) 22s (Siemens). On 15-Dec-2021, Blood pressure measurement: 168/78 mmhg (High) 168/78 mmHg. On 15-Dec-2021, C-reactive protein: 63mg/l (milligram per liter) (High) 63mg/L (milligram per liter). On 15-Dec-2021, Chest X-ray: no infiltrative abnormalities, no pneumothorax (normal) no infiltrative abnormalities, no pneumothorax. On 15-Dec-2021, Computerised tomogram: spinal cord: degenerative abnormalities, no fractu (abnormal) spinal cord: degenerative abnormalities, no fractures. On 15-Dec-2021, Computerised tomogram head: no bleeding, no new abnormalities (normal) no bleeding, no new abnormalities. On 15-Dec-2021, International normalised ratio: 1(inr) (international normalized ratio) (normal) 1(INR) (international normalized ratio). On 15-Dec-2021, Oxygen saturation: 88 (percent) (Low) 88 (percent). On 15-Dec-2021, Platelet count: 78/nl (per nanolitre) (Low) 78/nL (per nanolitre). On 15-Dec-2021, Ultrasound Doppler: the vertebral artery has a normal physiological fl (normal) The vertebral artery has a normal physiological flow profile. (left and right). For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. No treatment drugs were reported. Company comment: This case concerns a 78-year-old female patient with medical history of a minor ischaemic stroke, who experienced the adverse events of special interest Thrombocytopenia and Transient ischaemic attack. Thrombocytopenia		

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	occurred 2 days after the first dose of mRNA-1273 while the event of Transient ischaemic attack occurred after an unspecified number of days post exposure to the vaccine. The medical history of a previous minor ischaemic stroke associated with a previous COVID-19 vaccine (BioNTech/Pfizer) is a confounder. Information regarding clinical presentation, diagnostic tests and treatment provided has not been disclosed. Seriousness assessment has been retained as per Regulatory Authority reporting. The benefit-risk relationship of mRNA-1273 is not affected by this report. This case was linked to [REDACTED] Linked Report). Most recent FOLLOW-UP information incorporated above includes: On 01-Feb-2022: Follow-up information received contains updated medical history, concomitant medications and indication, event and lab data. On 01-Feb-2022: Translation received on 04-FEB-2022: Event verbatim, lab test name were translated.		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED] on 21-Jan-2022. The most recent information was received on 09-Feb-2022 and was forwarded to Moderna on 09-Feb-2022. This regulatory authority case was reported by an other health care professional and describes the occurrence of PULMONARY EMBOLISM (29-12 uptake due to pulmonary embolism bilateral) in an 83-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 045G21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included Food poisoning NOS on 14-Dec-2021, Hyperventilation (2018 SEH hyperventilation with word finding disorders passenger d hyperventilation, stresses. Without evidence of acute pathology or a TIA 2019 SEH: Dizziness, chest pressure and collapse inclination, no indication of ACS, no indication of rhythm disorder on event recorder. WD hyperventilation) in 2018, Supraventricular tachycardia (2020 Supraventricular tachycardia DD paroxysmal atrial fibrillation) in 2020 and Osteoporosis in 2016. Previously administered products included for Drug use for unknown indication: BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0,3MLCOVID-19 VACCIN PFIZER INJVLST on 03-Apr-2021, BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0 and3MLCOVID-19 VACCIN PFIZER INJVLST on 10-May-2021; for Product used for unknown indication: Comirnaty (COVID-19 VACCIN PFIZER INJVLST 0,3ML COVID-19 VACCIN PFIZER INJVLST) on 03-Apr-2021, COMIRNATY (COVID-19 VACCIN PFIZER INJVLST 0 and3ML COVID-19 VACCIN PFIZER INJVLST) on 10-May-2021. Past adverse reactions to the above products included Adverse reaction with BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN	83 year old woman with hypertension and with history of supraventricular tachycardia and paroxysmal atrial fibrillation, developed pulmonary embolism on day of Spikevax administration. She had two prior doses of Pfizer vaccine. Her platelet level was slightly low. Her thrombosis type, pulmonary embolism, was at a common site; she had multiple risk factors for thromobis. Antibodies against PF4 would be necessary, according to CDC, for diagnosis of TTS -- such results are not available.	

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	PFIZER INJVLST 0,3MLCOVID-19 VACCIN PFIZER INJVLST, BioNTech/Pfizer vaccin (Comirnaty) COVID-19 VACCIN PFIZER INJVLST 0 and3MLCOVID-19 VACCIN PFIZER INJVLST; and No adverse reaction with COMIRNATY and Comirnaty. Concurrent medical conditions included Essential hypertension in 2011. Concomitant products included PERINDOPRIL ERBUMINE (PERINDOPRIL GA), COLECALCIFEROL and VERAPAMIL HYDROCHLORIDE (VERAPAMILA) for an unknown indication. On 22-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 22-Dec-2021, the patient experienced PULMONARY EMBOLISM (29-12 uptake due to pulmonary embolism bilateral) (seriousness criterion hospitalization). On 29-Dec-2021, the patient experienced PYREXIA (This morning T38.5, past days 38 degrees) and COUGH (Cough). On an unknown date, the patient experienced THROMBOCYTOPENIA (Passenger thrombopenia) and ELECTROLYTE IMBALANCE (Passenger mild electrolyte disorders). At the time of the report, PULMONARY EMBOLISM (29-12 uptake due to pulmonary embolism bilateral) was resolving, THROMBOCYTOPENIA (Passenger thrombopenia) and ELECTROLYTE IMBALANCE (Passenger mild electrolyte disorders) had resolved and PYREXIA (This morning T38.5, past days 38 degrees) and COUGH (Cough) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 22-Dec-2021, Heart rate: 154 per minute 154 per minute. On 29-Dec-2021, Angiogram: bilateral pulmonary embolism bilateral pulmonary embolism with wedge-shaped consolidation right middle lobe appropriate for lung infarction. On 29-Dec-2021, Blood test: ferritin (h): 370 ug/l (20 - 150) Ferritin (H): 370 UG/l (20 - 150), Leucocytes (H): 10.3 10e9/L (4.3 - 10), Neutrophils (H): 7.8 10e9/l (1.8 - 7.3), EGFR (CKD-EPI) (L): 71 mL/min (>90), Sodium (L): 132 mmol/L (135 - 145), Potassium (L): 3.4 mmol/L (3.5 - 5.0), Albumin (L): 34 g/L (35 - 50), NT-ProBNP (H): 193 pmol/L (<18). On 29-Dec-2021, C-reactive protein (0-10): 120 milligram per litre 120 milligram per litre. On 29-Dec-2021, Chest X-ray: now one direction Equation 21/11/2019. Now one direction. Increased pleural shading basal especially right based on moisture. Lateral on the right, this probably climbs up a bit. Right lateral center increased little dense compaction. First suspected of infiltrate. Increased enlarged cor. Lung drawing does not look overfilled. Oval compaction left parahilar compliant.. On 29-Dec-2021, Electrocardiogram: sinus rhythm 91 /min, with pvc and pacs sinus rhythm 91 /min, with PVC and PACs, IM heart axis, normal conduction times, more PACs versus earlier ECG.		

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	On 29-Dec-2021, Fibrin D dimer (Unknown-0.5): 5.54 milligram per litre 5.54 milligram per litre. On 29-Dec-2021, Heart rate: 101 per minute 101 per minute. On 29-Dec-2021, Influenza A virus test: negative (Negative) Negative. On 29-Dec-2021, Influenza B virus test: negative (Negative) Negative. On 29-Dec-2021, Oxygen saturation: 98 percent 98 percent. On 29-Dec-2021, Platelet count (150-400): 129 per nanolitre 129 per nanoliter. On 29-Dec-2021, Pyrexia: 38.5 degree celsius 38.5 degree Celsius. On 29-Dec-2021, Respiratory syncytial virus test: negative (Negative) Negative. On 29-Dec-2021, SARS-CoV-2 test: negative (Negative) Negative. On 30-Dec-2021, Blood test: egfr (ckd-epi) (l): 69 ml/min (>90) EGFR (CKD-EPI) (L): 69 mL/min (>90), Sodium: 136 mmol/L (135 - 145), Potassium: 4.0 mmol/L (3.5 - 5.0). On 30-Dec-2021, Platelet count (150-400): 160 per nanolitre 160 per nanoliter. On an unknown date, Heart rate: 154/min 154/min (per minute). The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. No treatment medication were reported Company Comment - This regulatory case concerns a 83-year-old female patient, with medical history of essential hypertension, who experienced the serious unexpected event of pulmonary embolism. The event occurred on the same day of the dose of the mRNA-1273 vaccine. Patient's medical history of essential hypertension remains a confounder. The rechallenge is not applicable as there is no information that states vaccination dose number and there is only one dose reported. Treatment details were not provided. The benefit-risk relationship of the mRNA-1273 is not affected by this report. The seriousness was assessed as per regulatory authority report. Most recent FOLLOW-UP information incorporated above includes: On 09-Feb-2022: Significant follow up received on 09-Feb-2022, updated history, added events, lab test updated, added comments.		
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 01-Feb-2022. The most recent information was received on 03-Feb-2022 and was forwarded to Moderna on 03-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (TTS/VITT case (positive tests HIPA/PF4)), THROMBOCYTOPENIA (thrombopenia) and PULMONARY EMBOLISM (Strong pulmonary embolism) in an	This 83 year old woman was diagnosed with thrombocytopenia and pulmonary embolism 16 days after Spikevax and 6.5 months after the 2nd Pfizer dose and 10.5 months after the 1st Pfizer dose. She tested positive on the Heparin-induced thrombocytopenia test. She had multiple risk factors for cardiovascular disease and a history of TIA; in addition, clopidogrel concomitant	

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	83-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The patient's past medical history included TIA. Previously administered products included for Product used for unknown indication: PFIZER BIONTECH COVID-19 VACCINE on 01-Feb-2021 and Pfizer coronavaccin COVID-19 VACCIN PFIZER INJVLST on 01-Jun-2021. Past adverse reactions to the above products included No adverse event with PFIZER BIONTECH COVID-19 VACCINE and Pfizer coronavaccin COVID-19 VACCIN PFIZER INJVLST. Concurrent medical conditions included Obesity (BMI 30.4). Concomitant products included BUMETANIDE, LEVOTHYROXINE, CLOPIDOGREL and LOSARTAN for an unknown indication. On 16-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 01-Jan-2022, the patient experienced THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (TTS/VITT case (positive tests HIPA/PF4)) (seriousness criteria hospitalization and medically significant). 01-Jan-2022, the patient experienced THROMBOCYTOPENIA (thrombopenia) (seriousness criterion hospitalization) and PULMONARY EMBOLISM (Strong pulmonary embolies) (seriousness criterion hospitalization). At the time of the report, THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (TTS/VITT case (positive tests HIPA/PF4)), THROMBOCYTOPENIA (thrombopenia) and PULMONARY EMBOLISM (Strong pulmonary embolies) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 01-Jan-2022, Platelet count: 48 48 /nL (per nanolitre). On 01-Jan-2022, SARS-CoV-2 test negative: negative (Negative) Negative. On 02-Jan-2022, Platelet count: 33 33 /nL (per nanolitre). On 03-Jan-2022, Platelet count: 20 20 /nL (per nanolitre) and 41 41 /nL (per nanolitre). On 04-Jan-2022, Platelet count: 24 24 /nL (per nanolitre). On 05-Jan-2022, Platelet count: 28 28 /nL (per nanolitre). On 06-Jan-2022, Platelet count: 38 38 /nL (per nanolitre). On 07-Jan-2022, Platelet count: 37 37 /nL (per nanolitre). On 08-Jan-2022, Platelet count: 79 79 /nL (per nanolitre). On 09-Jan-2022, Platelet count: 138 138 /nL (per nanolitre). On 10-Jan-2022, Platelet count: 158 158 /nL (per nanolitre). On 12-Jan-2022, Platelet count: 209 209 /nL (per nanolitre). On an unknown date, Activated partial thromboplastin time: 37 37 s (Siemens). On an unknown date, Anti-platelet factor 4 antibody test: positive (Positive) Positive. On an unknown date, Antiphospholipid antibodies negative: negative (Negative) Negative.	medication specifically suggests increased risk for clotting. The date of her TIA was not reported. She might possibly have been treated with heparin for her TIA, but the date of the TIA and its treatment were not reported.	

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	On an unknown date, Blood fibrinogen: 4.1 4.1 (later on) and 2.8 2.8 (admission). On an unknown date, C-reactive protein: 91 91 mg/L (milligram per litre). On an unknown date, Cardiolipin antibody negative: negative (Negative) Negative. On an unknown date, Fibrin D dimer: >6.8 >6.8 ng/ml. On an unknown date, Heparin-induced thrombocytopenia test: positive (Positive) Positive. On an unknown date, Prothrombin time: 13 13 s (Siemens). For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. No treatment medication information was reported Company Comment: This is a regulatory authority case concerns a 83-year-old female patient with relevant medical condition obesity and TIA, who experienced the Serious (Hospitalization) , unexpected AESI events of Pulmonary embolism, Thrombosis With Thrombocytopenia Syndrome, and Thrombocytopenia. The events occurred approximately 17 days after vaccination with an unknown dose number of mRNA-1273 (Moderna covid-19 vaccine) . This patient tested positive for Anti-platelet factor 4 antibody test. Concurrent medical conditions of obesity and TIA are risk factors for thrombosis and Pulmonary embolism remains as a confounder; while the concomitant medication of Clopidrogel (anti-platelet drug) and the age (ageing can lead to bone marrow production problems) of this patient are also confounders for the event thrombocytopenia . The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 02-Feb-2022: Follow-up received and updated drug start date, event, medical history, Lab data and result of lab data. On 02-Feb-2022: Translation received(Follow up) on 04-Feb-2022, dosage text of Losartan, event verbatim and lab test verbatim (lab data) was translated. On 03-Feb-2022: Follow up contains significant information of addition of patient history, new lab data, addition of event and event verbatim updated.		
	This case was received via European Medicines Agency (Reference number [REDACTED] on 03-Feb-2022 and was forwarded to Moderna on 03-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of CARDIO-RESPIRATORY ARREST (Cardiorespiratory arrest), PULMONARY THROMBOSIS (Thrombosis pulmonary) and THROMBOCYTOPENIA (Thrombocytopenia) in a 48-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. Concurrent medical conditions included Obesity, Sleep apnea (treated with forced respiratory pressure CPAP), Thrombosis venous deep (Treated with Lixiana	A 48 year old man experienced Cardiorespiratory arrest, Pulmonary Thrombosis and died 10 days after Spikevax (0.25 ml reported). Autopsy results were not provided. Concurrent medical conditions included Obesity, Sleep apnea (treated with forced respiratory pressure CPAP), Thrombosis venous deep (treated with Lixiana (endoxaban) in the recent past. He also had Factor V Leiden mutation. He had previously received the Pfizer vaccine, without further details. This patient was	

Case ID	Narrative	MAH Comment	WW Identifier
	(endoxaban)27/05/2021 Ecodoppler control for DVT 2020: residual popliteal thrombosis with preserved flow) in 2020, Factor V Leiden mutation and Migraine. Concomitant products included TOZINAMERAN (COMIRNATY) for COVID-19 vaccination, EDOXABAN TOSILATE (LIXIANA) for Thrombosis venous deep. On 29-Dec-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) .25 milliliter. On 07-Jan-2022, the patient experienced CARDIO-RESPIRATORY ARREST (Cardiorespiratory arrest) (seriousness criteria death, hospitalization and life threatening), PULMONARY THROMBOSIS (Thrombosis pulmonary) (seriousness criteria death, hospitalization and life threatening) and THROMBOCYTOPENIA (Thrombocytopenia) (seriousness criteria death, hospitalization and life threatening). The patient died on 08-Jan-2022. An autopsy was performed, but no results were provided. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 07-Jan-2022, Fibrin D dimer: 69000 (High) 69000 microgram per millilitre. On 07-Jan-2022, Platelet count: 134 (Low) 134 thousand per microlitre. On 07-Jan-2022, Prothrombin time: 17.8 (High) 17.8 s. mRNA-1273 (Spikevax) (Intramuscular) was withdrawn on 29-Dec-2021. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No treatment medications provided by the reporter. Company comment: This case concerns a 48-year-old male patient with relevant medical history of Thrombosis venous deep, Obesity and Factor V Leiden mutation who experienced serious unexpected events of Cardio-respiratory arrest, Pulmonary thrombosis and Thrombocytopenia and subsequently died. The events occurred 10 days after the first dose of mRNA-1273. The patient died the following day. Autopsy was performed, however, the results were not provided. Causality is confounded with patient's reported medical history and concomitant use of Tozinameran. The benefit-risk relationship of mRNA-1273 is not affected by this report. Interchange of vaccine products should have been considered in this particular case as the patient also received Tozinameran. It should be noted that it was reported that the patient received first dose of the Company product at the dose of 0.25 ml. This information was retained as such.	at high risk for thrombosis, apart from vaccination; and in the absence of anti-PF4 test positivity, a vaccine link cannot be established.	
	This spontaneous case was reported by a non-health professional and describes the occurrence of THROMBOSIS (thrombosis) and THROMBOCYTOPENIA (thrombocytopenia) in a 37-year-old patient of an unknown gender who received	Not a case of TTS. This patient was diagnosed with Influenza and it seems to also have thrombocytopenia but imaging test done were unremarkable.	

Case ID	Narrative	MAH Comment	WW Identifier
	mRNA-1273 (Spikevax) for COVID-19 prophylaxis. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included SLE, Hashimoto's disease, Asthma, Allergic reaction to antibiotics, Drug allergy, Fruit allergy and Pollen allergy. On 26-Jun-2021, the patient received second dose of mRNA-1273 (Spikevax) (unknown route) dosage was changed to 1 dosage form. On an unknown date, the patient received dose of mRNA-1273 (Spikevax) (unknown route) at an unspecified dose. On 26-Jun-2021, the patient experienced INFLUENZA (flu symptoms), VACCINATION SITE PAIN (pain in the arm and a large red spot at the point of injection) and VACCINATION SITE ERYTHEMA (pain in the arm and a large red spot at the point of injection). On 29-Jun-2021, the patient experienced MUSCLE SPASMS (slight cramps in the legs) and PARAESTHESIA (prickling in the legs started and then in whole body except the left half of the face). On an unknown date, the patient experienced THROMBOSIS (thrombosis) (seriousness criterion medically significant), INAPPROPRIATE SCHEDULE OF PRODUCT ADMINISTRATION (Patient vaccinated on 16 May 2021 and again vaccinated on 26 Jun 2021 with Moderna vaccine), THROMBOCYTOPENIA (thrombocytopenia) (seriousness criterion medically significant) and FIBRIN D DIMER INCREASED (Fibrin D dimer increased). On 27-Jun-2021, INFLUENZA (flu symptoms) had resolved. On 28-Jun-2021, VACCINATION SITE ERYTHEMA (pain in the arm and a large red spot at the point of injection) had resolved. At the time of the report, THROMBOSIS (thrombosis) and MUSCLE SPASMS (slight cramps in the legs) had resolved, PARAESTHESIA (prickling in the legs started and then in whole body except the left half of the face) and VACCINATION SITE PAIN (pain in the arm and a large red spot at the point of injection) had not resolved and INAPPROPRIATE SCHEDULE OF PRODUCT ADMINISTRATION (Patient vaccinated on 16 May 2021 and again vaccinated on 26 Jun 2021 with Moderna vaccine), THROMBOCYTOPENIA (thrombocytopenia) and FIBRIN D DIMER INCREASED (Fibrin D dimer increased) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Blood test: increase in the blood count of d-dimer increase in the blood count of D-Dimer and a thrombocytopenia, thereby thrombosis was verified again and normal After two weeks the values were again normal. On an unknown date, Electrocardiogram: unremarkable unremarkable. On an unknown date, Lumbar puncture: unremarkable unremarkable. On an unknown date, Magnetic resonance imaging: unremarkable unremarkable. On an unknown date, Neurological examination: unremarkable unremarkable. Concomitant product use was not provided by the reporter. An MRI, ECG, neurological test, lumbar puncture was done in the hospital and hourly blood was taken for analysis. Everything was unremarkable, except the increase in the		

Case ID	Narrative	MAH Comment	WW Identifier
	blood count of D-Dimer and a thrombocytopenia, thereby thrombosis was verified again. But, except the blood values, there was no other indication. Then against medical advice, the patient left the hospital, while the patient had a small child at home. The patient's blood was once again examined for two weeks long by my General Practitioner. After two weeks the values were again normal. One day after the hospital, the cramps were gone, but the prickling in the legs is till today present. No treatment information was provided. Company comment: This spontaneous case concerns a 37-year-old patient of unknown gender with relevant medical history of systemic lupus erythematosus (SLE) who experienced the unexpected serious (medically significant) AESIs of Thrombosis and Thrombocytopenia which occurred unknown days after the second dose of mRNA-1273 vaccine. Blood D-dimer was also found to be raised. MRI, ECG and lumbar puncture were also performed and were unremarkable. The interval between the 2 doses was approximately 41 days (Inappropriate Schedule of Vaccine Administration noted). Mentioned history of SLE remains a risk factor for the events. The benefit-risk relationship of mRNA-1273 is not affected by this report. Seriousness of the events assessed as per medical judgement. This case was linked to [REDACTED] (Patient Link).		

Appendix 11.16a Guillain-Barre Syndrome (GBS) Reporting Period Case Listings

Case ID	ALL PTs	Age	Gender	Medical History	Concomitant Medications	Dose Number	Cumulative Brighton Collaboration Case Definition	WHO Causality Assessment	WW Identifier
	Acute motor-sensory axonal neuropathy, Arthralgia, Gait disturbance, Guillain-Barre syndrome, Hypoaesthesia, Inflammatory pain, Musculoskeletal stiffness	46	Female	Lymphadenectomy; Seasonal allergy; Breast cancer(H); Iodine allergy; Food allergy; Mite allergy; Mastectomy		Dose 1	Level 3	Unlikely	
	Aortic stenosis, Atrial fibrillation, Guillain-Barre syndrome, Muscular weakness	67	Female	Plasma cell myeloma(C); Atrial fibrillation(C)	AMIODARONE; HUMAN IMMUNOGLOBULIN	Dose 3	Level 2	Unlikely	
	Guillain-Barre syndrome	33	Male			Unknown	Level 1	Conditional	
	Guillain-Barre syndrome	49	Female	Hypertension(C); Hyperlipidaemia(C); Hypothyroidism(C); Bipolar disorder(C)	MIDODRINE	Unknown	Level 1	Unassessable	
	Guillain-Barre syndrome	61	Female		INFLUENZA VACCINE	Unknown	Level 1	Unassessable	
	COVID-19 immunisation, Guillain-Barre syndrome	67	Male			Unknown	Level 2	Conditional	
	Dyspnoea, Gait inability, Guillain-Barre syndrome, Hypoaesthesia, Muscular weakness, Paraesthesia, Paralysis	40	Female			Dose 3	Level 1	Conditional	
	Guillain-Barre syndrome, Headache	30	Male			Dose 2	Level 1	Possible	
	Areflexia, Dysarthria, Dysuria, Facial paresis, Guillain-Barre syndrome, Hypertensive crisis, Paraesthesia	39	Female	Myofascial pain syndrome(C); Obstructive nephropathy(C); Essential hypertension(C); Nephrolithiasis(C); Cholelithiasis(C)	PRESTARIUM A	Dose 3	Level 2	Conditional	
	Guillain-Barre syndrome	31	Male	Gastroesophageal reflux disease(H); Anxiety(H); Coronavirus infection(H)		Unknown	Level 1	Unassessable	
	COVID-19 immunisation, Guillain-Barre syndrome	66	Male	COVID-19 pneumonia(H)		Dose 3	Level 3	Conditional	
	Abdominal pain lower, Back pain, Balance disorder, COVID-19 immunisation, CSF protein increased, Discomfort, Gait disturbance, Guillain-Barre syndrome, Pain in extremity, Paralysis	55	Female	COMIRNATY		Unknown	Level 3	Conditional	
	Condition aggravated, Guillain-Barre syndrome	60	Male	COVID-19(H); Chronic lymphocytic leukaemia(C); Hypertension(C); Hyperlipidaemia(C); Transient ischaemic attack(C); Spinal osteoarthritis(C)		Unknown	Level 1	Possible	
	Guillain-Barre syndrome, Hypoaesthesia, Muscular weakness, Paraesthesia	42	Male			Dose 3	Level 1	Conditional	
	COVID-19 immunisation, Guillain-Barre syndrome	19	Female		COMIRNATY	Dose 3	Level 1	Possible	
	Guillain-Barre syndrome	60	Male	Ruptured cerebral aneurysm(H); Blindness unilateral(C); Muscular weakness(H); Gait disturbance(H)		Unknown	Level 1	Possible	
	Guillain-Barre syndrome	76	Female	COMIRNATY; COMIRNATY		Dose 3	Level 1	Possible	
	Asthma, Guillain-Barre syndrome, Muscular weakness	61	Male	Hypertension(C); Cardiac disorder(H); Stent placement		Dose 2	Level 3	Unassessable	
	Guillain-Barre syndrome	69	Female	COMIRNATY; COMIRNATY		Unknown	Level 3	Conditional	

Appendix 11.16b Guillain-Barre Syndrome (GBS) Reporting Period Case Narratives

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		This case was received via European Medicines Agency (Reference number: [REDACTED] on 13-Jan-2022 and was forwarded to Moderna on 13-Jan-2022. This case was received via European Medicines Agency (Reference number: [REDACTED] on 13-Jan-2022 and was forwarded to Moderna on 13-Jan-2022. This regulatory authority case was reported by a physician and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome), ACUTE MOTOR-SENSORY AXONAL NEUROPATHY (Axonal polyneuropathy of the lower extremities), MUSCULOSKELETAL STIFFNESS (Stiffness after rest periods), ARTHRALGIA (Pain on palpation of the head of the left fibula), HYPOAESTHESIA (Hypoesthesia in socks up to the knees), the first episode of GAIT DISTURBANCE (walking on a difficult and staggering imaginary line), INFLAMMATORY PAIN (Inflammatory rhythm pain in the lower extremities) and the second episode of GAIT DISTURBANCE (walking on a difficult and staggering imaginary line) in a 48-year-old female patient who received mRNA-1273 (Spikevax) (batch nos. 3002336 and 3002622A) for COVID-19 vaccination. The patient's past medical history included Breast cancer (In situ breast cancer), Lymph node excision (Right mastectomy with removal of subaxillary lymph nodes for in situ breast cancer) and Mastectomy (Right mastectomy). Concurrent medical conditions included Pollen allergy, Iodine allergy, Food allergy (Allergy to crustaceans and stone fruits) and Acaridae allergy. On 24-May-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) .5 ml. On 21-Jun-2021, received second dose of mRNA-1273 (Spikevax) (Intramuscular) dosage was changed to .5 ml. On 25-May-2021, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) (seriousness criteria disability and medically significant), ACUTE MOTOR-SENSORY AXONAL NEUROPATHY (Axonal polyneuropathy of the lower extremities) (seriousness criteria disability and medically significant), MUSCULOSKELETAL STIFFNESS (Stiffness after rest periods) (seriousness criterion disability), ARTHRALGIA (Pain on palpation of the head of the left fibula) (seriousness criterion disability), HYPOAESTHESIA (Hypoesthesia in socks up to the knees) (seriousness criterion disability), the first episode of GAIT DISTURBANCE (walking on a difficult and staggering imaginary line) (seriousness criterion disability), INFLAMMATORY PAIN (Inflammatory rhythm pain in the lower extremities) (seriousness criterion disability) and the second episode of GAIT DISTURBANCE (walking on a difficult and staggering imaginary line) (seriousness criterion disability). At the time of the report, GUILLAIN-	48F with history of breast cancer s/p lymphadenectomy and mastectomy, multiple allergies who experienced GBS and acute motor sensory axonal neuropathy 1 day after dose 1 of mRNA-1273. The patient had signs/symptoms consistent with GBS, however given the TTO of 1 day, a causal association is implausible with alternate etiologies including breast cancer. Case assessed as BC level 3 and WHO-UMC causality as unlikely.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		BARRE SYNDROME (Guillain Barre syndrome), ACUTE MOTOR-SENSORY AXONAL NEUROPATHY (Axonal polyneuropathy of the lower extremities), MUSCULOSKELETAL STIFFNESS (Stiffness after rest periods), ARTHRALGIA (Pain on palpation of the head of the left fibula), HYPOAESTHESIA (Hypoesthesia in socks up to the knees), INFLAMMATORY PAIN (Inflammatory rhythm pain in the lower extremities) and the last episode of GAIT DISTURBANCE (walking on a difficult and staggering imaginary line) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In May 2021, Reflex test: decreased patellar osteotendinous reflexes (abnormal) decreased patellar osteotendinous reflexes and abolished achilles tendon reflex (abnormal) Abolished achilles tendon reflex. In May 2021, Romberg test: slightly shaky (abnormal) Slightly shaky. In 2021, Neurological examination: not reported (Inconclusive) Neurological examination in process and results not reported.. In 2021, Rheumatological examination: negative (Negative) Negative rheumatological examination. For mRNA-1273 (Spikevax) (Intramuscular), the reporter considered GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome), ACUTE MOTOR-SENSORY AXONAL NEUROPATHY (Axonal polyneuropathy of the lower extremities), MUSCULOSKELETAL STIFFNESS (Stiffness after rest periods), ARTHRALGIA (Pain on palpation of the head of the left fibula), HYPOAESTHESIA (Hypoesthesia in socks up to the knees), GAIT DISTURBANCE (walking on a difficult and staggering imaginary line), INFLAMMATORY PAIN (Inflammatory rhythm pain in the lower extremities) and GAIT DISTURBANCE (walking on a difficult and staggering imaginary line) to be possibly related. No concomitant medications were reported. No treatment details were reported.	
		This spontaneous case was reported by an other health care professional and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), ATRIAL FIBRILLATION (Atrial fibrillation), AORTIC STENOSIS (Aortic stenosis) and MUSCULAR WEAKNESS (loss of strength in lower limbs) in a 67-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. Co-suspect product included non-company product JNJ 64007957 solution for injection for Multiple myeloma.	67F with medical history of a fib and plasma cell myeloma (PCM) taking amiodarone and Ig who experienced GBS 38 days after dose 3 mRNA-1273, 202 days after dose 2 mRNA-1273, 220 days after dose 1 mRNA-1273 and 27 days after JNJ vaccine. LP and MRI were reportedly consistent with GBS however assessment is confounded by history of PCM and prior JNJ

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		Concurrent medical conditions included Multiple myeloma and Atrial fibrillation. Concomitant products included AMIODARONE for Atrial fibrillation, IMMUNOGLOBULIN HUMAN NORMAL (HUMAN IMMUNOGLOBULIN) for an unknown indication. On 02-Mar-2021, the patient started JNJ 64007957 (Subcutaneous) 1500 microgram/kilogram once a week. On 23-Apr-2021, the patient received first dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 11-May-2021, received second dose of mRNA-1273 (Spikevax) (unknown route) dosage was changed to 1 dosage form. On 22-Oct-2021, received third dose of mRNA-1273 (Spikevax) (unknown route) dosage was changed to 1 dosage form. On 28-Nov-2021, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criteria hospitalization, medically significant and life threatening) and MUSCULAR WEAKNESS (loss of strength in lower limbs) (seriousness criterion hospitalization). On 29-Nov-2021, the patient experienced ATRIAL FIBRILLATION (Atrial fibrillation) (seriousness criteria hospitalization and medically significant) and AORTIC STENOSIS (Aortic stenosis) (seriousness criteria hospitalization and medically significant). The patient was hospitalized on 28-Nov-2021 due to AORTIC STENOSIS, ATRIAL FIBRILLATION, GUILLAIN-BARRE SYNDROME and MUSCULAR WEAKNESS. The patient was treated with CEFTRIAXONE for Adverse event, at a dose of 1 milligram and Manual therapy (intubated with mechanical ventilation) for Guillain-Barre syndrome. At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) was resolving and ATRIAL FIBRILLATION (Atrial fibrillation), AORTIC STENOSIS (Aortic stenosis) and MUSCULAR WEAKNESS (loss of strength in lower limbs) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 29-Nov-2021, Lumbar puncture: guillain-barre syndrome (abnormal) Guillain-Barre syndrome. On 29-Nov-2021, Magnetic resonance imaging: guillain-barre syndrome (abnormal) Guillain-Barre syndrome. On an unknown date, Coma scale: 6/15 (abnormal) 6/15. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments.	vaccine. Case assessed as BC level 2 and WHO-UMC causality as unlikely.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		On 29-Nov-2021, the patient was taken to intensive Care Unit (ICU) for stronger supervision. After an MRI scan, lumbar puncture, and evaluation by the neurological team the neurologist determined a diagnosis of Guillain Barre Syndrome without knowing the exact cause. On the same day symptoms worsened and the patient was intubated with mechanical ventilation. The patient also went into atrial fibrillation and was administered amiodarone as a bolus and continuous perfusion achieving sinus rhythm. After a cardiology assessment, severe aortic stenosis was observed. Glasgow coma score was 6/15 with spontaneous eye opening and eyelid and lip cortissure movement. She was hemodynamically stable, respiratory continued with invasive mechanical ventilation, and continued to be fed through enteral nutrition. She received 5 plasmapheresis session since admission to the ICU and a full course of human immunoglobulin. As of 10-JAN-2022 the patient was still in ICU. Company comment: This is a spontaneous case concerning a 67-year-old female patient with medical history of Multiple myeloma, medicated with Amiodarone for Atrial fibrillation, who experienced the serious, unexpected, according CCDS, events of Guillain-Barre syndrome, Atrial fibrillation (AESI), Aortic stenosis and muscular weakness. The events Guillain-Barre syndrome and muscular weakness occurred approximately 21 days after the third dose of mRNA-1273 vaccine. Atrial fibrillation and Aortic stenosis occurred approximately 22 days after the third dose of mRNA-1273 vaccine. The rechallenge is not applicable since the AEs occurred after the third dose. The medical history of atrial fibrillation remains a confounder for atrial fibrillation. The medical history of Multiple myeloma remains a confounder for muscular weakness. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. This case was linked to [REDACTED] (Patient Link).	
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 28-Jan-2022 and was forwarded to Moderna on 28-Jan-2022. This regulatory authority case was reported by a consumer and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) in a 33-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 3003609) for COVID-19 vaccination. No Medical History information was reported. On 13-Jul-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 23-Jul-2021, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) (seriousness	Consumer report of 33M who experienced GBS 10 days after dose 1 mRNA-1273 with diagnostic work-up reportedly showing proximal weakness of extremities symmetrically, proximally emphasized paraparesis M4-/3 symmetrically with reduced reflexes and cytoalbumin dissociation from LP. No medical history or concomitant medications were provided, thus limiting evaluation, however there is a plausible temporal association. Furthermore, there is no medical confirmation of the laboratory findings. Case assessed as BC level 1 and WHO-UMC causality

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		criterion hospitalization). At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) had not resolved. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. No relevant concomitant medications were reported. Treatment included Therapy with iVigs 30g 5 days, monitoring on stroke unit, physiotherapy, occupational therapy. Patient reported Proximal weakness of extremities symmetrically, proximally emphasized paraparesis M4-/3 symmetrically with reduced reflexes. LP: cytoalb. Dissociation from 16-Aug-2021. Company comment: This regulatory authority case concerns a 33-year-old male patient with no medical history reported, who experienced, the unexpected serious AESI event of Guillain-Barre syndrome. The event occurred approximately 10 days after the second dose of the mRNA-1273 and resulted in hospitalization. The patient was treated with IV Ig. At the time of the report the outcome of the events was not resolved. The benefit-risk relationship of mRNA-1273 is not affected by this report.	as conditional pending further information and medical confirmation.
		This literature-non-study case was reported in a literature article and describes the occurrence of GUILLAIN-BARRE SYNDROME (Sub-acute Onset of Guillain-Barre Syndrome) in a 49-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. LITERATURE REFERENCE: Nagalli S, Kikkeri NS. Sub-acute onset of Guillain-Barré Syndrome post-mRNA-1273 vaccination: a case report. SN Compr Clin Med. 2022;4(1):41 Concurrent medical conditions included Hypertension, Hyperlipidemia, Hypothyroidism and Bipolar disorder. Concomitant products included MIDODRINE for Hypotension. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, after starting mRNA-1273 (Moderna COVID-19 Vaccine),	Literature report of a 49F with HTN, hyperlipidemia, bipolar disorder and hypothyroidism who experienced GBS on an unknown date after dose 1 of mRNA-1273. Workup performed on an unknown date revealed high CSF protein, normal glucose/RBC/WBC/lactate, EMG and nerve conduction studies abnormal and suggestive of GBS. The TTO is not known and evaluation is confounded by underlying HTN and hypothyroidism. Case assessed as BC level 1 and WHO-UMC causality as unassessable due to missing information and confounders.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		the patient experienced GUILLAIN-BARRE SYNDROME (Sub-acute Onset of Guillain-Barre Syndrome) (seriousness criteria hospitalization and medically significant). The patient was treated with Surgery (Plasma exchange and Endotracheal intubation) for Guillain-Barre syndrome. At the time of the report, GUILLAIN-BARRE SYNDROME (Sub-acute Onset of Guillain-Barre Syndrome) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, CSF glucose (50-70): 65 mg/dl (normal) 65 mg/dL. On an unknown date, CSF lactate (1.2-2.1): 1.6 mmol/l (normal) 1.6 mmol/L. On an unknown date, CSF protein (20-40): 59 mg/dl (High) 59 mg/dL. On an unknown date, CSF red blood cell count (0-less than 1): 0 cells/cumm (normal) 0 cells/cumm. On an unknown date, CSF white blood cell count (0-5): less than 1 cells/cumm (normal) less than 1 cells/cumm. On an unknown date, Electromyogram: abnormal (abnormal) demonstrated borderline reduced recruitment with borderline high amplitude, long duration motor unit potentials in the triceps, deltoid, vastus medialis, and tensor fascia lata muscles.. On an unknown date, Magnetic resonance imaging: normal (normal) showed no evidence of acute intracranial hemorrhage, ischemia/infarct, or brain edema, normal (normal) Axial section of MRI Brain FLAIR showing normal cerebral structures and normal (normal) Sagittal T2 of cervical, thoracic, and lumbar spines showing normal appearance of spinal cord, conus medullaris, and cauda equina. On an unknown date, Nerve conduction studies: abnormal (abnormal) revealed absent sural response and decreased peroneal motor response and the median and ulnar motor responses were of low amplitude. On an unknown date, Physical examination: abnormal (abnormal) remarkable for decreased power of 2/5 in bilateral lower extremities involving proximal and distal muscles and 4/5 in bilateral upper extremities throughout.. On an unknown date, SARS-CoV-2 test: negative (Negative) Negative. On an unknown date, Serology test: negative (Negative) negative for GQ1B antibodies. On an unknown date, Xanthochromia: absent Absent. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown.	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered GUILLAIN-BARRE SYNDROME (Sub-acute Onset of Guillain-Barre Syndrome) to be related. Patient's symptoms included worsening weakness involving her lower extremities for 8 weeks. Her weakness started in her bilateral feet, gradually ascended up to involve the waist and upper extremities. This was associated with ataxia and falls. Numbness in lower extremities and voice changes were also reported. The patient denied a history of diarrhea, rhinorrhea, cough, or congestion prior to the onset of the above symptoms. Muscle tone and bulk were normal. Sensations were diminished to light touch throughout in lower and upper extremities. Severe dysmetria was noted during the finger-nose-finger test. Deep tendon reflexes were absent in the lower and upper extremities. No involuntary movements were noted during the physical exam. Patient had a gradual onset of lower extremity weakness with a nadir of symptoms reached 10 and 12 weeks after the onset. This protracted course (sub-acute) is atypical for a "classical" GBS. The presence of an antecedent event, autonomic symptoms such as hypotension, and the need for ventilator support favored the diagnosis of GBS. Company comment: This case concerns a 49-year-old female patient with no relevant medical history who experienced serious unexpected event of Guillain-Barre syndrome. The event occurred 10 days after the first dose of mRNA-1273. The patient had a gradual onset of lower extremity weakness with a nadir of symptoms reached 10 and 12 weeks after the onset. Authors speculated that this protracted course (sub-acute) is atypical for a "classical" GBS, however, the presence of an antecedent event, autonomic symptoms such as hypotension, and the need for ventilator support favored the diagnosis of GBS. The event was resolving at the time of the report. The Reporter assessed the event as related to the Company product. The benefit-risk relationship of mRNA-1273 is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 03-Feb-2022: Follow up received by safety on 03-Feb-2022 has Email with FTA received from SARA team and contains significant information. Patient medical history and lab investigations, hospitalization, treatment of autonomic symptoms, second author's middle name received in follow up.	
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 02-Feb-2022 and was forwarded to Moderna on 02-Feb-2022.	Consumer report of a 61F with no provided medical history or concomitant medications other than influenza vaccine, who experienced GBS 1 day following mRNA-1273. Minimal information

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		This regulatory authority case was reported by a consumer and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) in a 61-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. Concomitant products included INFLUENZA VACCINE from 08-Nov-2021 to an unknown date for Prophylactic vaccination. On 11-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 12-Dec-2021, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) (seriousness criterion hospitalization). At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) had not resolved. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. No treatment medications reported. The patient had cytalbuniary dissociation in cerebrospinal fluid, typical electrophysiology, inconspicuous MRI imaging of brain and spinal cord. Inpatient admission with the above diagnostics took place on 20-Dec-2021, therapy with IVIG began on 20-Dec-2021 Company comment: This regulatory case concerns a 61-year-old female patient, with no medical history reported, who experienced the serious (hospitalization) unexpected AESI of GUILLAIN-BARRE SYNDROME, on the following day of an unknown dose of the mRNA-1273 vaccine. Patient received INFLUENZA vaccine in the previous month. The patient was admitted and diagnosed with the cerebrospinal fluid test and Magnetic Resonance Imaging of the brain and spinal cord. She received Intravenous Immunoglobulin Therapy, but at the time of the report, the event had not resolved. The benefit-risk relationship of the mRNA-1273 is not affected by this report. The seriousness was assessed as per regulatory authority report.	is provided with prior flu vaccine being a confounder, however a TTO of 1 day suggests an implausible temporal association. Case assessed as BC level 1 and WHO-UMC causality as unassessable pending further information and medical confirmation.
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 07-Feb-2022 and was forwarded to Moderna on 07-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) and COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) in a 67-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 3006276) for COVID-19 vaccination.	HCP report of a 67M with no provided medical history who experienced GBS (possibly an acute demyelinating polyneuropathy) 11 days after dose 3 mRNA-1273, 5 and 8 months after dose 2 and 1 Vaxzevria. EMG suggestive of an acute demyelinating polyneuropathy but no CSF provided. There is an 11 day time to onset that

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		Co-suspect product included non-company product COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (VAXZEVRIA) for COVID-19 vaccination. No Medical History information was reported. On 22-Apr-2021, the patient received dose of COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (VAXZEVRIA) (unknown route) at an unspecified dose. On 01-Jul-2021, received dose of COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (VAXZEVRIA) (unknown route) dosage was changed to at an unspecified dose. On 15-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 26-Dec-2021, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) (seriousness criterion hospitalization) and COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) (seriousness criterion hospitalization). At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) and COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 19-Jan-2021, Mycoplasma test: igg positive igm negative IgG positive IgM negative. On 19-Jan-2022, Laboratory test: clamydia pneumonia: igg positive, igm inconclusive Chlamydia Pneumonia: IgG positive, IgM inconclusive.. On 20-Jan-2022, Electromyogram: sensitive-motor polyneuropathy of demyelinating ty Sensitive-motor polyneuropathy of demyelinating type with data on involvement in both MM SS and MM II, predominance in MM II, including increase in bilateral phrenic latencies, in EMG findings there is no objective of active denervation. Given the clinical context, it could correspond to demyelinating polyneuropathy with acute course.. On 24-Jan-2022, Laboratory test: negative Ac antigangliosides: Negative. Ac AntiCapyLobacter: Negative.. mRNA-1273 (Spikevax) (Unknown) was withdrawn on 15-Dec-2021. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments.	indicates a reasonable temporal relationship, however assessment is confounded by prior Vaxzevria and limited by lack of medical history and conmeds. No conclusive diagnosis of GBS could be established. Case assessed as BC level 2 and WHO-UMC causality as conditional pending further information.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		No concomitant medication was provided. No treatment medication was provided. Company comment: This is a regulatory case concerning a 67-year-old, male patient with medical history of concomitant product of VAXZEVRIA (non-company product COVID-19 VACCINE), who experienced the unexpected serious (hospitalization) events of Guillain Barre syndrome and COVID-19 immunisation. The events started 11 days after the patient received dose of dose of mRNA-1273. The medical history of concomitant product of VAXZEVRIA (non-company product COVID-19 VACCINE) could be confounders. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report. Events seriousness assessed as per Regulatory Authority reporting. Most recent FOLLOW-UP information incorporated above includes: On 09-Feb-2022: lab data was updated	
		This case was initially received via [REDACTED] (Reference number: [REDACTED] on 13-Feb-2022. The most recent information was received on 05-Mar-2022 and was forwarded to Moderna on 05-Mar-2022. This regulatory authority case was reported by a consumer and describes the occurrence of HYPOAESTHESIA (numbness in hands), GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome), PARALYSIS (Paralysis), GAIT INABILITY (Unable to walk), MUSCULAR WEAKNESS (Weakness of limbs), PARAESTHESIA (Paraesthesia) and DYSPNOEA (Breathlessness) in a 40-year-old female patient who received mRNA-1273 (Moderna CoviD-19 Vaccine) for an unknown indication. No Medical History information was reported. On 08-Jan-2022, the patient received third dose of mRNA-1273 (Moderna CoviD-19 Vaccine) (unknown route) 1 dosage form. On 11-Jan-2022, after starting mRNA-1273 (Moderna CoviD-19 Vaccine), the patient experienced GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) (seriousness criteria hospitalization and medically significant). On 11-Feb-2022, the patient experienced DYSPNOEA (Breathlessness) (seriousness criteria hospitalization and medically significant). On an unknown date, the patient experienced HYPOAESTHESIA (numbness in hands) (seriousness criteria hospitalization and medically significant), PARALYSIS (Paralysis) (seriousness criteria hospitalization and medically significant), GAIT INABILITY (Unable to walk) (seriousness criteria hospitalization and	Consumer report of 40F with no provided medical history or concomitant medications who experienced GBS 19 days after dose 3 of mRNA-1273. SARS-CoV-2 test was negative and reportedly a "Consultant confirmed GBS following lumbar puncture, mri scan and electro tests." however results have not been confirmed. Case assessed as BC level 1 and WHO-UMC causality as conditional pending further information and medical confirmation.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		medically significant), MUSCULAR WEAKNESS (Weakness of limbs) (seriousness criteria hospitalization and medically significant) and PARAESTHESIA (Paraesthesia) (seriousness criteria hospitalization and medically significant). At the time of the report, HYPOAESTHESIA (numbness in hands), GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome), PARALYSIS (Paralysis) and GAIT INABILITY (Unable to walk) was resolving and MUSCULAR WEAKNESS (Weakness of limbs), PARAESTHESIA (Paraesthesia) and DYSPNOEA (Breathlessness) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 02-Feb-2022, Investigation: electro tests confirmed guillain barre syndrome (abnormal) Electro tests confirmed Guillain Barre syndrome. On 02-Feb-2022, Lumbar puncture: confirmed guillain barre syndrome (abnormal) confirmed Guillain Barre syndrome. On 02-Feb-2022, Magnetic resonance imaging: confirmed guillain barre syndrome (abnormal) confirmed Guillain Barre syndrome. On 02-Feb-2022, SARS-CoV-2 test: no - negative covid-19 test (Negative) No - Negative COVID-19 test. Patient had tested positive for COVID-19 since having the vaccine. Patient was not enrolled in clinical trial. This report was not related to possible myocarditis or pericarditis. Concomitant product use was not provided by the reporter. The patient experienced numbness in hands, unable to lift arms, unable to dress/feed herself, was unable to walk unaided. Intravenous immunoglobulin (IVIG) treatment completed, got ability in legs/arms back, however she was still very weak. Consultant confirmed Guillain Barre syndrome (GBS) following lumbar puncture, MRI scan and electro tests. Follow up information on 27 Feb 2022: Symptoms of Guillain-Barre Syndrome started 3 days following jab and then occurred again 1 week 6 days after jab. The patient experienced limb weakness in arms and legs and tingling in hands, balance was affected, falling over and was unable to get herself back up unaided. Symptoms started in shoulders and moved down arms to hands tingling. Then weakness in hips moving down legs. The patient had an MRI and lumbar puncture on 02 Feb 2022 which confirmed that patient had Guillain-Barre Syndrome. Patient was admitted to hospital and received IVIG treatment for 5 days and was discharged from hospital on 08 Feb 2022. On 11 Feb 2022, the weakness returned in arms and legs and the patient was becoming breathless. She was readmitted to hospital on 14	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		Feb 22, as the symptoms worsened, causing patient to fall twice in hospital. On 18 Feb 2022, another electro test was completed, and 2nd set of 5 IVIG treatment was started on 21 Feb 2022. At the time of this report, it was stated that weakness was still ongoing. Patient did not have any similar reactions in the past to other vaccines. Patient did not have any history of long-term medical conditions, nor any medical conditions that affected the nervous system, The patient did not take any regular medication. Company comment: This regulatory authority case concerns a 40-year-old female patient with no medical history reported, who experienced the serious (hospitalization and medically significant) unexpected AESI of Guillain-Barre syndrome and associated serious unexpected events of Hypoaesthesia, Paralysis, Gait inability, Muscular weakness, Paraesthesia, as well as serious unexpected event of Dyspnoea. The event of Guillain-Barre syndrome occurred three days after the patient had received the third dose of the mRNA-1273 vaccine. Reportedly, the patient developed numbness in hands and had balance disorder. The patient was unable to walk unaided, unable to lift arms and unable to dress/feed herself. The symptoms started from shoulders and moved down to the patient's arms and hands. The patient also had weakness in hips that moved down to legs. MRI and lumbar puncture confirmed that Guillain-Barre Syndrome. The patient was admitted to hospital and received intravenous immunoglobulin therapy for 5 days. The patient then was discharged from hospital. However, the as the weakness in arms and legs returned and she was becoming breathless and the patient was readmitted to hospital and the therapy immunoglobulin was restarted. At the time of this report, the events of Guillain-Barre Syndrome, Hypoaesthesia, Paralysis and Gait inability were resolving, while the outcome of the remaining events was reported as unknown as per structured fields of the source document. The benefit-risk relationship of the mRNA-1273 vaccine is not affected by this report. Event seriousness assessed as per Regulatory Authority reporting. Most recent FOLLOW-UP information incorporated above includes: On 05-Mar-2022: Follow-up received included new events of paralysis, unable to walk, weakness in limbs, paraesthesia, breathlessness, laboratory data was added and narrative was updated.	
		This case was initially received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 08-Feb-2022. The most recent information was received on 06-Apr-2022 and was forwarded to Moderna on 14-Apr-2022. This case, initially reported to the [REDACTED] by a vaccinator other than a physician, was received via [REDACTED]	Possible HCP report of 30M with no provided medical history who experienced GBS 11 days after dose 2 of mRNA-1273 with workup revealing CSF cytoalbumin dissociation, axonal damage on nerve conduction study. Progressed to paralysis requiring intubation. While there is a

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		the [REDACTED] On 06-Apr-2022, follow-up information was received from a vaccinator other than a physician. On an unknown date, the patient received the 1st dose of this vaccine. On an unknown date, body temperature before the vaccination: 36.5 degrees Celsius. On 17-Sep-2021, the patient received the 2nd dose of this vaccine. Headache developed after the vaccination. There were no symptoms of infection. On 28-Sep-2021, from the time of awakening, the patient experienced queasy and numbness of limbs. On 30-Sep-2021, the patient had difficulty walking and was urgently hospitalized. Quadriplegia, bulbar palsy, respiratory disorder, and cerebrospinal fluid protein cell dissociation were noted, and nerve conduction test showed axi damage. The patient was diagnosed with Guillain-Barre syndrome. On 02-Oct-2021, due to respiratory muscle paralysis and severe quadriplegia, tracheal intubation and ventilator management were started and performed in the ICU. On 08-Dec-2021, the ventilator was removed. The patient remained with severe quadriplegia and was unable to be discharged. On 04-Feb-2022, the patient was transferred to a rehabilitation hospital. As a sequela, the patient remained with quadriplegia. The outcome of headache was unknown. The outcome of Guillain-Barre syndrome was reported as ongoing and unchanged. No follow-up investigation will be made. Clinical symptoms: Bilateral and loose muscle weakness of the upper and lower limbs(day of onset:28-Sep-2021). Decreased or absent deep tendon reflexes in the upper and lower limbs leading to muscle weakness. Up to the time of the report, Hughes' functional scale classification for the extreme phase of the symptoms was 5 assisted ventilation was required. Disease process: The patient showed a monophasic disease pattern with intervals of 12 hours to 28 days between the onset of muscle weakness and the worst condition, followed by a clinical stable phase. Electrophysiological examination: Decreased motor nerve conduction velocity, abnormal temporal dispersion, conduction block, decreased M-wave amplitude, and decreased frequency of F-wave appearance were consistent with GBS. Cerebrospinal fluid examination (date of exam: 01-Oct-2021): Cell count: 7/3 /mcL, glucose: 56 mg/dL, and protein: 182.7 mg/dL. There was protein-	temporal association, further information such as medical history and concomitant therapy would be beneficial in further assessment. Case assessed as BC level 1 and WHO-UMC causality as possible.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		cell dissociation (elevated CSF protein level above laboratory normal level and total CSF white blood cell count below 50 cells/L). Differential diagnosis: No other diseases were applicable. Imaging test (date of exam: On an unknown date): Cervical MRI: no findings. Autoantibody test (date of exam: 01-Oct-2021): Anti-GM1 antibody: negative, anti-GQ1b antibody: negative. Presence or absence of antecedent infection: None Reporter comments: It is thought to be Guillain-Barre syndrome associated with this vaccination. No other causes were found. The timing of the onset of Guillain-Barre syndrome is consistent, so the occurrence of adverse events is temporally related to the timing of the administration of this vaccine. The occurrence of adverse events is not related to concomitant drugs. Since there is no underlying disease or complication in particular, the occurrence of adverse events is not related to pathological factors of underlying diseases and complications. Guillain-Barre syndrome developed 11 days after administration of this vaccine. Since the clinical course and laboratory results showed no possible course or findings leading to Guillain-Barre syndrome, such as infection consistent with Guillain-Barre syndrome, this vaccine is considered to be related to Guillain-Barre syndrome. Follow-up received on 06-APR-2022 Updated: Patient Information, Lab Data, Event Information, Narrative, Reporter Comments. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.	
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 01-Mar-2022 and was forwarded to Moderna on 01-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of FACIAL PARESIS (Facial paresis), DYSARTHRIA (Dysarthria), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) and AREFLEXIA (Patellar tendon reflex absent on right side, 1+ on left side) in a 39-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3005244) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Myofascial pain syndrome (cervicobrachial myofascial pain syndrome), Obstructive nephropathy (on right side), Primary hypertension (stage 2), Kidney stone (large kidney stone in left kidney) and Gallstones. Concomitant products included PERINDOPRIL ARGININE (PRESTARIUM A) for Primary hypertension.	HCP report from HA of 39F with myofascial pain syndrome, hypertension taking perindopril, arginine who experienced GBS 29 days after dose 3 mRNA-1273. LP shows albuminocytological dissociation, however EMG not provided. Assessment is confounded by myofascial pain syndrome, hypertension and hypertensive crisis preceding reported GBS, which offer alternate etiologies. Further important information including details of clinical course, results diagnostic evaluation including EMG, and treatment is lacking and is crucial in properly assessing causality. Case classified as BC level 2 and WHO-UMC causality category as conditional.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		On 28-Dec-2021, the patient received third dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 21-Jan-2022, the patient experienced HYPERTENSIVE CRISIS (Hypertensive crisis), DYSURIA (Urination impaired) and PARAESTHESIA (Tingling sensation). On 26-Jan-2022, the patient experienced FACIAL PARESIS (Facial paresis) (seriousness criterion hospitalization), DYSARTHRIA (Dysarthria) (seriousness criterion hospitalization), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criterion hospitalization) and AREFLEXIA (Patellar tendon reflex absent on right side, 1+ on left side) (seriousness criterion hospitalization). At the time of the report, FACIAL PARESIS (Facial paresis), HYPERTENSIVE CRISIS (Hypertensive crisis), DYSARTHRIA (Dysarthria), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), PARAESTHESIA (Tingling sensation) and AREFLEXIA (Patellar tendon reflex absent on right side, 1+ on left side) was resolving and DYSURIA (Urination impaired) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 01-Feb-2022, Lumbar puncture: albuminocytological dissociation Albuminocytological dissociation. On 01-Feb-2022, Magnetic resonance imaging head: head mri with contrast medium showed inflammation Head MRI with contrast medium showed inflammation of facial nerve in both sides.. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No treatment information was provided. company comment-This regulatory case concerns a 39-year-old female patient with relevant medical history of Myofascial pain syndrome and primary hypertension, who experienced the unexpected serious (hospitalization) AESI event of Guillain-Barre syndrome, expected(unlisted for Thai SmPC) serious (hospitalization) event of Facial paresis, unexpected serious (hospitalization) events of Dysarthria and Areflexia approximately 30 days after third dose of mRNA-1273 Vaccine administration. She also experienced unexpected non-serious events of Hypertensive crisis, Paresthesia and Dysuria. Lumbar puncture done showed Albumin cytological dissociation suggesting Guillain-Barre syndrome. Magnetic resonance image of Head showed inflammation of facial nerve in both sides. No treatment details were given. The outcome of the events were recovering at the time of the report. The relevant medical history could be possible	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		confounders. Benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report. The case seriousness was assessed as per Regulatory Authority report.	
		This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 02-Mar-2022. The most recent information was received on 14-Mar-2022 and was forwarded to Moderna on 14-Mar-2022. This regulatory authority case was reported by a pharmacist and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain-Barr syndrome suspected: hypoesthesia of the hands and impairment strength deficit, ataxia and mild albumino-cytological dissociation and axonal polyneuropathic suffering in the 4 limbs.) in a 31-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 000030A) for COVID-19 vaccination. The patient's past medical history included Gastroesophageal reflux disease, Anxiety and Coronavirus infection. On 25-Jan-2022, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 26-Jan-2022, after starting mRNA-1273 (Spikevax), the patient experienced GUILLAIN-BARRE SYNDROME (Guillain-Barr syndrome suspected: hypoesthesia of the hands and impairment strength deficit, ataxia and mild albumino-cytological dissociation and axonal polyneuropathic suffering in the 4 limbs.) (seriousness criterion hospitalization). At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain-Barr syndrome suspected: hypoesthesia of the hands and impairment strength deficit, ataxia and mild albumino-cytological dissociation and axonal polyneuropathic suffering in the 4 limbs.) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 02-Feb-2022, Computerised tomogram head: inconclusive (Inconclusive) Inconclusive. On 03-Feb-2022, Chest X-ray: inconclusive (Inconclusive) Inconclusive. On 03-Feb-2022, Spinal X-ray: inconclusive (Inconclusive) Inconclusive. On 04-Feb-2022, Electroneurography: inconclusive (Inconclusive) Inconclusive. On 05-Feb-2022, CSF test abnormal: inconclusive (Inconclusive) Inconclusive. On 09-Feb-2022, Magnetic resonance imaging abnormal: inconclusive (Inconclusive) Inconclusive.	HCP report from HA of 31M with GERD, anxiety, who experienced GBS 1 day after an unknown dose of mRNA-1273. Patient reportedly met clinical criteria for GBS with albuminocytological dissociation and "axonal polyneuropathic suffering", however electroneurography and CSF results also stated as inconclusive. Case assessed conservatively as BC level 1 and WHO-UMC causality category as unassessable given conflicting clinical presentation and lab values.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Patient was received COVID-19 vaccine first dose 02 Jul 2021 and second dose received 07 Aug 2021. Patient was admitted Covid ward on 05 FEB 2022. Patient was positive at the SARS-CoV-2 Covid-19 test. No concomitant medications were provided by the reporter. No treatment information was provided by the reporter. Study information provided was An Emergency Use Authorization (EUA) program to permit the emergency use of the unapproved product Moderna COVID-19 Vaccine for active immunization against coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus in persons 18 years of age and older Company Comment: This is a regulatory case concerning a 30-year-old female patient with relevant medical history of Coronavirus Infection, who experienced the unexpected serious adverse event of special interest, Guillain-Barre Syndrome. The event led to the hospitalization of the patient as reported by the regulatory authority and occurred 2 days after receiving an unspecified dose of mRNA-1273 Vaccine. Diagnostic and Laboratories were done but results were inconclusive, no other clinical or treatment details were given. It was reported that the outcome of the event was resolving. The medical history of Coronavirus Infection remains a confounder. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report. 1st access in PS 02/02 2nd access in PS 04/02 and admitted on 07/02 (in progress) in the Covid ward On 05/02/2022 the patient was positive at the SARS-CoV-2 Covid rapid buffer until 10/01 (not recorded on SSN) 1st and 2nd doses Comirnaty (nnd date) Most recent FOLLOW-UP information incorporated above includes: On 14-Mar-2022: Significant follow up received which includes study name and study information update.	
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 07-Mar-2022 and was forwarded to Moderna on 07-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of GUILLAIN-BARRE SYNDROME (guillain barre syndrome) in a 66-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 216035) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below.	HA report from HCP of 66M with prior COVID-19 pneumonia, no other medical history or comeds reported who experienced GBS 5 days after dose 3 Spikevax, 181 days after dose 2 Spikevax and 244 days after dose 1 Vaxzevria, EMGs post dose 3 consistent demyelinating polyradiculoneuropathy, CT and brain scan

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		Co-suspect product included non-company product COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (VAXZEVRIA) for COVID-19 vaccination. COVID-19 has passed. The patient's past medical history included COVID-19 pneumonia (positive PCR. He required hospital admission, but not the ICU. MODERATE PNEUMONIA (Brixia 7) DUE TO SARS COV-2) on 15-Oct-2020. On 19-May-2021, the patient received dose of COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (VAXZEVRIA) (unknown route) 1 dose. On 21-Jul-2021, received dose of COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19) (VAXZEVRIA) (unknown route) dosage was changed to 2 doses. On 13-Jan-2022, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 18-Jan-2022, the patient experienced COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) and GUILLAIN-BARRE SYNDROME (guillain barre syndrome) (seriousness criterion hospitalization). At the time of the report, COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) and GUILLAIN-BARRE SYNDROME (guillain barre syndrome) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 18-Jan-2022, Chest X-ray: no data on acute cardiopulmonary pathology. No data on acute cardiopulmonary pathology.. On 18-Jan-2022, Scan brain: no data on acute intracranial pathology. No data on acute intracranial pathology.. On 21-Jan-2022, Electromyogram: findings consistent with the existence of sensorim Findings consistent with the existence of sensorimotor polyradiculoneuropathy, in the hyperacute stage of evolution. On 28-Jan-2022, Electromyogram: acute, generalized, sensory-motor polyradiculoneur Acute, generalized, sensory-motor polyradiculoneuropathy, demyelinating type, moderate grade.. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. Concomitant medications were not reported. Treatment medications were not reported.	negative, and no LP reported. No further clinical details provided. Case classified as BC level 3. Evaluation is confounded by prior pneumonia and Vaxzevria, WHO-UMC is assessed as conditional.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		Company comment: This is a case of Revaccination with different COVID-19 vaccine (two-dose primary series of Vaxzevria, last dose received approximately 6 months ago) for this 66-year-old male patient with no relevant medical history who experienced serious, unexpected event of Guillain barre syndrome which occurred 5 days after the administration of a dose of mRNA-1273 vaccine (reported as the third dose of the COVID-19 vaccination schedule) and led to patient hospitalization. Reported diagnostic test results included chest X-ray: no data on acute cardiopulmonary pathology; scan brain: no data on acute intracranial pathology; electromyogram performed on 21-Jan-2022: findings consistent with the existence of sensorimotor polyradiculoneuropathy, in the hyperacute stage of evolution; electromyogram performed on 28-Jan-2022: acute, generalized, sensory-motor polyradiculoneuropathy, demyelinating type, moderate grade. No further details regarding clinical course, diagnostic tests or treatment performed were disclosed. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.	
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 12-Apr-2022 and was forwarded to Moderna on 12-Apr-2022. This regulatory authority case was reported by a consumer and describes the occurrence of ABDOMINAL PAIN LOWER (SEVERE LOWER ABDOMINAL PAIN / MENSTRUAL-LIKE PAIN), PARALYSIS (PARALYSIS OF PARTS OF TOES, FEET, CALVES, THIGHS AND HIP), BACK PAIN (SEVERE LOW BACK PAIN), CSF PROTEIN INCREASED (CSF PROTEIN INCREASED), PAIN IN EXTREMITY (SEVERE PAIN IN THIGHS AND LOWER LEGS) and GUILLAIN-BARRE SYNDROME (ACUTE INFLAMMATORY DEMYELINATING POLYRADICULOPATHY) in a 55-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient has no allergies. Previously administered products included for Vaccination: Comirnaty. Past adverse reactions to the above products included No adverse event with Comirnaty. On 13-Jan-2022 at 9:29 AM, the patient received third dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 13-Jan-2022, the patient experienced COVID-19 IMMUNISATION (REVACCINATION WITH DIFFERENT COVID-19 VACCINE). On 01-Feb-2022, the patient experienced ABDOMINAL PAIN LOWER (SEVERE LOWER ABDOMINAL PAIN / MENSTRUAL-LIKE PAIN) (seriousness criterion	Consumer report from HA of 55F with no medical history or concomitant medications report, no allergies who experienced GBS 19 days after dose 3 mRNA-1273 and previous COMIRNATY. CSF showed increased protein but "nerve analysis" was reportedly normal. Case is lacking important information such as clinical course and verified work-up. Case classified as BC level 3 and WHO-UMC causality category as conditional.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		hospitalization), BACK PAIN (SEVERE LOW BACK PAIN) (seriousness criterion hospitalization) and PAIN IN EXTREMITY (SEVERE PAIN IN THIGHS AND LOWER LEGS) (seriousness criterion hospitalization). On an unknown date, the patient experienced PARALYSIS (PARALYSIS OF PARTS OF TOES, FEET, CALVES, THIGHS AND HIP) (seriousness criteria hospitalization and medically significant), DISCOMFORT (DISCOMFORT LOWER LEGS), CSF PROTEIN INCREASED (CSF PROTEIN INCREASED) (seriousness criterion medically significant), GAIT DISTURBANCE (GAIT DISTURBANCE), BALANCE DISORDER (UNSTEADINESS) and GUILLAIN-BARRE SYNDROME (ACUTE INFLAMMATORY DEMYELINATING POLYRADICULOPATHY) (seriousness criterion medically significant). At the time of the report, ABDOMINAL PAIN LOWER (SEVERE LOWER ABDOMINAL PAIN / MENSTRUAL-LIKE PAIN), PARALYSIS (PARALYSIS OF PARTS OF TOES, FEET, CALVES, THIGHS AND HIP), BACK PAIN (SEVERE LOW BACK PAIN) and PAIN IN EXTREMITY (SEVERE PAIN IN THIGHS AND LOWER LEGS) was resolving and DISCOMFORT (DISCOMFORT LOWER LEGS), CSF PROTEIN INCREASED (CSF PROTEIN INCREASED), GAIT DISTURBANCE (GAIT DISTURBANCE), COVID-19 IMMUNISATION (REVACCINATION WITH DIFFERENT COVID-19 VACCINE), BALANCE DISORDER (UNSTEADINESS) and GUILLAIN-BARRE SYNDROME (ACUTE INFLAMMATORY DEMYELINATING POLYRADICULOPATHY) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In 2022, CSF test: increased protein. Increased protein.. In 2022, Computerised tomogram: no signs of kidney stone. No signs of kidney stone.. In 2022, Gynaecological examination: normal findings. Normal findings.. In 2022, Magnetic resonance imaging: mri of the back with normal findings MRI of the back with normal findings.. In 2022, Neurological examination: of calves/thighs with normal findings. The patient had a "nerve analysis" of of calves/thighs with normal findings.. Company comment: This is a regulatory case concerning a 55-year-old female patient with no relevant medical history, who experienced the serious unexpected AESI Guillain-Barre syndrome, approximately 15 days after dose of mRNA-1273 (third dose of COVID-19 vaccine; previous primary vaccination with Comirnaty). Patient started with discomfort and pain in	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		lowers legs, which increase in severity and spreads to backside of thighs, lower back and lower abdomen, without response to analgesics. Later she experienced that parts of toes, feet, lower legs and hips were paralysed and had gait disturbance. A CT was performed due to suspected kidney calculus that showed no abnormalities. 17 days after the first symptoms occurred she was hospitalized for 3 days: MRI of the back, gynecological examination and a "nerve analysis" of lower legs had normal findings; CSF showed increased protein and was diagnosed with AIDP. Revaccination with different COVID-19 vaccine was also reported as an event. The benefit-risk relationship of mRNA-1273 is not affected by this report. It was reported that patient was reported sick leave due to the events and the patient does not use any medication or dietary supplements (except cranberry if she has urinary infection). Patient experienced that event started as Discomfort / "grumble" in lower legs L during some nights and the symptoms was disappeared during daytime but later turned into severe pain that spread to backside of thighs, lower back and lower abdomen (Menstrual like pain). One of physician prescribed Vimovo which had no effect on the pain and The patient took [REDACTED] and noticed at the same time that parts of toes, feet, lower legs and hips was paralyzed. She initially thought it was due to the [REDACTED] and she was unsteady and had walking problems. She went to the out-of-hours medical care center where they suspected kidney stone. She had a CT with no signs of this, and was still in pain and later on. went back to the ou	
		This literature-non-study case was reported in a literature article and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) in an 80-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. LITERATURE REFERENCE: Anjum Z, Iyer C, Naz S, Jaiswal V, Nepal G, Laguio-vila M, et al. Guillain-Barre syndrome after mRNA-1273 (Moderna) COVID-19 vaccination: a case report. Clin Case Rep. 2022;10:e05733 The patient's past medical history included COVID-19 (COVID-19 infection the previous year, from which patient had an uneventful recovery.). Concurrent medical conditions included Chronic lymphocytic leukemia (Chronic lymphocytic leukemia without the end organ involvement for which patient did not received any treatment.), Hypertension, Hyperlipidemia, Transient ischemic attack (remote history of TIA) and Lumbar spine degeneration (degenerative disease of lumbar spine).	Literature report of 80M with relevant medical history of prior uneventful COVID-19 infection, CLL, HTN, TIA, hyperlipidemia, no "exposure to drugs" who experienced GBS that presented as paraesthesia and bilateral ascending lower extremity weakness after dose 1 mRNA-1273 and severe bilateral lower extremity weakness one day after dose 2 of mRNA-1273, Diagnostic evaluation revealed CSF with cytoalbuminologic dissociation and EMG showed widespread demyelinating polyneuropathy affecting LE > UE, consistent with AIDP. The patient was treated with IVIG 5 days with improvement. This case is classified according to the Brighton collaboration case definition for GBS Level 1, and according to the WHO-UMC causality assessment classified as possible.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		In January 2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. In February 2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On an unknown date, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criterion medically significant) and CONDITION AGGRAVATED (Condition exacerbated). The patient was treated with IMMUNOGLOBULINS NOS (IMMUNOGLOBULIN I.V) (intravenous) for Adverse event, at a dose of 400 milligram/kilogram once a day. At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) was resolving and CONDITION AGGRAVATED (Condition exacerbated) outcome was unknown. Related DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Albumin CSF: ascending bilateral lower limb weakness CSF findings of albumin-cytological dissociation along with his classic presentation of rapidly progressive ascending bilateral lower limb weakness, with diminished deep tendon reflexes and sensory loss were concerning for acute inflammatory demyelinating poly neuropathy (AIDP). On an unknown date, Blood culture: negative (Negative) Negative. On an unknown date, Body temperature: 101.4 f vitals were notable for mild hypertension, Body temperature was observed 101.4 F.. On an unknown date, Cardiovascular examination: normal (normal) Normal. On an unknown date, Computerised tomogram head: head was negative Head was negative for any mass occupying lesion or infarct or hemorrhage was found.. On an unknown date, Electromyogram: consistent with the diagnosis of gbs Consistent with the diagnosis of GBS and widespread demyelinating polyneuropathy Widespread demyelinating polyneuropathy affecting the lower extremities more than the upper extremities, consistent with AIDP was showed.. On an unknown date, Inspiratory capacity: negative (Negative) Daily negative inspiratory force (NIF) test was done and remained negative throughout.. On an unknown date, Laboratory test: normal (normal) General, cardiovascular, respiratory, and abdominal examination were otherwise normal.. On an unknown date, Lumbar puncture: consistent with the diagnosis of gbs Consistent with the diagnosis of GBS and colorless cerebrospinal fluid Colorless cerebrospinal fluid (CSF) with albumin cytological dissociation was showed..	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		On an unknown date, Lymphocyte count: lymphocyte predominant Laboratory findings were notable for lymphocyte predominant leukocytosis (in the setting of CLL). On an unknown date, Magnetic resonance imaging: lumbar spine Lumbar spine without IV contrast showed findings consistent with degenerative disease was observed.. On an unknown date, Nerve conduction studies: consistent with the diagnosis of gbs Consistent with the diagnosis of GBS. On an unknown date, Neurological examination: power and sensations in bilateral upper limbs Neurological examination was notable for intact power and sensations in bilateral upper limbs, normal for bilateral brachioradial, triceps and biceps reflexes.. On an unknown date, Physical examination: consistent with the diagnosis of gbs Consistent with the diagnosis of GBS. On an unknown date, Urine analysis: negative (Negative) Negative. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) and CONDITION AGGRAVATED (Condition exacerbated) to be related. Patient received his first dose of Moderna vaccine in the last week of January 2021, following which he noticed bilateral lower extremity paresthesia (tingling and numbness), which was followed by progressive bilateral lower limb distal weakness, beginning at his feet and then ascending to involve his legs, knees, and hips. He then received the second dose of his vaccine in February 2021. The next morning, he was unable to get out of his bed due to severe bilateral lower extremity weakness, and he therefore presented to the emergency room. Company comment: This literature case concerns an 80-year-old male patient, with relevant medical history of COVID-19 Infection (three months prior to the event) reported, who experienced the unexpected serious (medically significant) AESI of Guillain-Barre Syndrome after the second dose of mRNA-1273. Patient experienced progressive, ascending bilateral lower extremity paresthesia, and weakness after 1st dose of COVID-19 (Moderna) vaccine. He had multiple falls due to gait imbalance and was using walker for ambulation. After the 2nd dose of vaccine, the next day he had severe bilateral lower extremity weakness and was unable to get out of bed and visited emergency for the same. On examination, vitals stable with temperature of 101.4 F. Neurological examination was consistent with the diagnosis of Guillain-Barre Syndrome. Lab findings showed blood culture, urine analysis negative, CT head normal, MRI of lumbar spine showed spinal degenerative disease and Lumbar puncture showed colorless	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		cerebrospinal fluid with albuminocytological dissociation. Lab findings along with his classic presentation of rapidly progressive ascending bilateral lower limb weakness, with diminished deep tendon reflexes and sensory loss were concerning for acute inflammatory demyelinating polyneuropathy (AIDP). Patient was started on intravenous immunoglobulin (IVIg) at 400 mg/kg/day for 5 days. Daily negative inspiratory force test done was negative throughout. After 5 days of treatment, patient noted significant improvement in bilateral lower extremity strength, and began to ambulate with help from physical therapy. patient was discharged to rehabilitation facility. He underwent outpatient nerve conduction study and electromyography which showed widespread demyelinating polyneuropathy affecting the lower extremities more than the upper extremities, consistent with AIDP. There was evidence of reinnervation without ongoing denervation on EMG indicating recovery stage. Elderly age of the patient and relevant medical history remains as confounders to the event. This case report suggest that physician should remain vigilant for GBS following COVID-19 vaccination. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 28-Apr-2022: Follow up received by safety 29-Apr-2022 has Email with FTA received from SARA team and contains significant information. Reporter information, literature information, medical history and lab data were updated.	
		This regulatory authority case was reported by an other health care professional and describes the occurrence of GUILLAIN-BARRE SYNDROME (Acute inflammatory demyelination polyradiculopathy (Guillain Barre syndrome)), PARAESTHESIA (Paresthesia (abnormal sense of touch sense of pain, sense of cold/hot)), HYPOAESTHESIA (Numbness of limbs) and MUSCULAR WEAKNESS (Weakness of limb) in a 42-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. No Medical History information was reported. On 13-Feb-2022, the patient received third dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 26-Feb-2022, the patient experienced GUILLAIN-BARRE SYNDROME (Acute inflammatory demyelination polyradiculopathy (Guillain Barre syndrome)) (seriousness criterion hospitalization), PARAESTHESIA (Paresthesia (abnormal sense of touch sense of pain, sense of cold/hot)) (seriousness criterion hospitalization), HYPOAESTHESIA (Numbness of limbs) (seriousness criterion hospitalization) and MUSCULAR WEAKNESS	HA report from HCP of 42M with no relevant MH, CM reported who experienced GBS 13 days after dose 3 Spikevax. Symptoms included progressive limb weakness and pain. CSF excluded infective cerebritis but showed albuminocytological dissociation and EMG showed prominent motor-sensory polyneuropathy with conduction and temporal dispersion. On an unknown date, the patient was diagnosed with peripheral vertigo and hyperventilation. While the workup points towards GBS, there is no mention of areflexia at initial presentation and furthermore, the mention of peripheral vertigo confounds evaluation. Clarification of diagnoses and provision of actual lab results would assist in further evaluation. This case is classified as BC level 1 and WHO-UMC is classified as condition.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		(Weakness of limb) (seriousness criterion hospitalization). The patient was treated with MECOBALAMIN for Neuropathy, at an unspecified dose and frequency and GABAPENTIN for Neuropathy, at an unspecified dose and frequency. At the time of the report, GUILLAIN-BARRE SYNDROME (Acute inflammatory demyelination polyradiculopathy (Guillain Barre syndrome)), PARAESTHESIA (Paresthesia (abnormal sense of touch sense of pain, sense of cold/hot)), HYPOAESTHESIA (Numbness of limbs) and MUSCULAR WEAKNESS (Weakness of limb) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 03-Mar-2022, CSF test: albuminocytological dissociation albuminocytological dissociation. On 21-Mar-2022, Corneal reflex test: non-pick up in facial nerves r2 response non-pick up in facial nerves R2 response. On 21-Mar-2022, Nerve conduction studies: prominent motor-sensory polyneuropathy prominent motor-sensory polyneuropathy with conduction and temporal dispersion. On an unknown date, Neurological examination: peripheral vertigo, hyperventilation No focal weakness and steady gait. The impression is peripheral vertigo, hyperventilation.. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medications reported. Patient's first onset of neurological signs was dizziness, numbness of limbs, tongue on 26-Feb-2022. He visited our ER. Because of progressive four limbs weakness and numbness since 26-Feb-2022 (present severe back pain, limb numbness and general weakness), he visited Neuro OPD on 03-Mar-2022. Dr impressed ed Guillain Barre syndrome. The CSF study excluded infective cerebritis but revealed albumin cytological dissociation. Then he was admitted to neurology ward for future evaluation. On 04-Mar-2022: He denied respiratory distress, dysarthria. Under consecutive treatment, the motor symptoms slowly improved since 04-Mar-2022. But he still complained persist numbness sensation of the limbs. Mecobalamin and Gabapentin are prescribed for neuropathy. The rehabilitation program was also arranged. On 21-Mar-2022: Performed four limbs NCV again on 21-Mar-2022 and Blink study for assessment of peripheral nerves. The data still reveals prominent motor-sensory polyneuroaty with conduction and temporal dispersion in NCV and non-pick up in facial nerves R2 response in blink reflex study.	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		On 28-Mar-2022: Clinically, his muscle power nearly total recovery with present DTR including biceps and knee jerk. Transferred him to rehabilitation ward for further rehabilitation program. Company comment: This regulatory authority case concerns a 42-year-old male patient, with no medical history reported, who experienced the unexpected serious events of Guillain-Barre syndrome (AESI), Paraesthesia, Hypoesthesia and Muscular weakness. The events occurred approximately 13 days after receiving the third dose of mRNA-1273 Vaccine and resulted in hospitalization. Due to progressive weakness of extremities, neurological consultation was done and subsequent tests led to a diagnosis of Guillain-Barre syndrome. The patient was treated with Mecobalamin and Gabapentin, and underwent rehabilitation. The outcome of the events was reported as resolving. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report.	
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 06-May-2022 and was forwarded to Moderna on 06-May-2022. This regulatory authority case was reported by a physician and describes the occurrence of COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) and GUILLAIN-BARRE SYNDROME (Guillain Barre Syndrome) in a 19-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 018J21A) for COVID-19 vaccination. Concomitant products included TOZINAMERAN (COMIRNATY) from 05-Aug-2021 to 26-Aug-2021 for COVID-19 vaccination. On 03-Mar-2022, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 03-Mar-2022, the patient experienced COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) (seriousness criteria hospitalization and life threatening). On 23-Mar-2022, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain Barre Syndrome) (seriousness criteria hospitalization and life threatening). At the time of the report, COVID-19 IMMUNISATION (Revaccination with different COVID-19 vaccine) and GUILLAIN-BARRE SYNDROME (Guillain Barre Syndrome) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 26-Mar-2022, Alanine aminotransferase: gpt (alt) =547 u/l GPT (ALT) =547 U/L. On 26-Mar-2022, Aspartate aminotransferase: got (ast)=187 u/l GOT (AST)=187 U/L.	HA report from HP of 19F with no medical history or concomitant medications reported who experienced GBS 20 days after Spikevax and 209 and 230 days after Comirnaty vaccinations. No clinical details or treatment for GBS was provided, however investigation revealed increased protein 102 (assuming units mg/dL), WBC apparently < 50 ("Only 38 PMN:5 Neutrophils, 20 Lymphocytes and 13 Monocytes are observed"), and EMG consistent with GBS. No alternate etiology identified and prior vaccine interchange confounds evaluation, however there is a plausible temporal relationship. Case is classified as BC level 1 and WHO-UMC causality is assessed as possible.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		On 26-Mar-2022, CSF oligoclonal band: oligoclonal igg lcr bands; no oligoclonal bands ob Oligoclonal IgG LCR bands; No oligoclonal bands observed (Pattern 1.Normal). On 26-Mar-2022, CSF test: bq: glucose * 78 total proteins ** 102.00 lactate . BQ: Glucose * 78 Total Proteins ** 102.00 Lactate * 20.5 . CYTOBIOCHEMISTRY: Nucleated cells CSF 3 Hematies 18 Macroscopic aspect Transparent Xanthochromia (visual inspection) Negative. Observations: Only 38 PMN:5 Neutrophils, 20 Lymphocytes and 13 Monocytes are observed. Abundant red blood cells.. On 26-Mar-2022, Cytomegalovirus test: igm + cmv; we request quantitative dna (5500 copie IgM + CMV; we request quantitative DNA (5500 copies/mL, next control in decline).. On 26-Mar-2022, SARS-CoV-2 test: pcr (nasopharyngeal exudate): negative PCR (nasopharyngeal exudate): NEGATIVE. On 26-Mar-2022, Scan brain: cranial ct without urgent vsd. - we conducted stud CRANIAL CT WITHOUT URGENT VSD. - We conducted studies from the base of the skull to vertex without contrast administration. We do not have any previous TC to compare. No signs of intra- or extraxial bleeding are observed. Centered midline. Cortical groove pattern preserved. Ventricular system of normal size and morphology. Adequate differentiation between gray and white matter. Free basal cisterns.. On 22-Apr-2022, Electromyogram: emg:: “the neurophysiological study shows suggestiv EMG:: “The neurophysiological study shows suggestive data of acute polyneuropathy with very severe conduction involvement that meets demyelinating criteria, but which has an important associated axonal component, with active denervation throughout the musculature explored and registering only few potentials of motor unit in the upper limb”.. mRNA-1273 (Spikevax) (Unknown) was withdrawn on 03-Mar-2022. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. Treatment medications were not reported. Company Comment: This is a regulatory case of revaccination with different COVID-19 vaccine for this 19-year-old, female patient with history of concomitant administration of two doses of Comirnaty (Pfizer/BioNTech COVID-19 mRNA vaccine), who experienced the unexpected, serious (life-threatening and hospitalization) AESI of Guillain-Barre syndrome. The event occurred 20 days after receiving the third dose of the mRNA-1273 vaccine. Three days after the onset of the event, various diagnostic tests were done. The Cerebrospinal fluid (CSF) test showed elevated Total	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		Proteins (102) and normal Glucose (78). Cytochemistry showed 'Nucleated cells CSF 3 Hematocytes 18 Macroscopic aspect Transparent Xanthochromia (visual inspection) Negative. Observations: Only 38 PMN:5 Neutrophils, 20 Lymphocytes and 13 Monocytes are observed. Abundant red blood cells.' The CSF oligoclonal band test showed 'Oligoclonal IgG LCR bands; No oligoclonal bands observed (Pattern 1.Normal)'. The Cytomegalovirus (CMV) antibody test showed 'IgM + CMV' which indicates a recent infection. The Brain scan was unremarkable and the SARS-CoV-2 PCR test was negative. Approximately 1 month after the onset of the event, the Electromyogram done showed 'suggestive data of acute polyneuropathy with very severe conduction involvement that meets demyelinating criteria, but which has an important associated axonal component, with active denervation throughout the musculature explored and registering only few potentials of motor unit in the upper limb'. No further clinical information (including details about hospitalization) was available for medical review. Treatment information was also not provided. The event had not resolved at the time of the report. The laboratory finding of recent infection with CMV, which is a known risk factor for Guillain-Barre syndrome, remains a confounder. The benefit-risk relationship of the mRNA-1273 vaccine is not affected by this report.	
		This literature-non-study case was reported in a literature article and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain-Barré syndrome after Moderna vaccine) in a 6-decade-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination.	
		LITERATURE REFERENCE: George TB, Kainat A, Pachika PS, Arnold J. Rare occurrence of Guillain-Barré syndrome after Moderna vaccine. BMJ Case Rep. 2022;15(5):e249749 The patient's past medical history included Ruptured cerebral aneurysm (Left Middle Cerebral Artery aneurysm status post clipping 2005), Weakness of limbs (weakness of his legs and fatigue for 3 days) and Gait instability (Presented with complaints of loss of balance for 3 days.). Concurrent medical conditions included Blind right eye (residual right eye blindness). On an unknown date, the patient received first dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On an unknown date, received second dose of mRNA-1273 (Spikevax) (unknown route) dosage was changed to 1 dosage form. On an unknown date, after starting mRNA-1273 (Spikevax), the patient experienced GUILLAIN-BARRE SYNDROME (Guillain-Barré syndrome after Moderna vaccine) (seriousness criteria hospitalization and medically significant). The patient was treated with IMMUNOGLOBULINS NOS	Literature report of 60M with history of ruptured left MCA aneurysm and residual right blindness, right LE weakness with gait instability who experienced GBS 4 weeks after dose 1 Spikevax and the same day as dose 2 Spikevax. The patient was in his usual state of health prior to Spikevax. Symptoms included absent DTRs, generalized weakness with diagnostic evaluation revealing conduction deficits consistent with demyelination on EMG and CSF albuminocytological dissociation. The patient was treated with daily IVIG for 5 days with improved strength continued areflexia except in the right biceps tendon. This report is classified as BC level 1 and WHO-UMC causality is assessed as possible based on temporal association and the absence of alternate etiologies.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		(IMMUNOGLOBULIN I.V) (intravenous) for Guillain-Barre syndrome, at a dose of .4 gram per kilogram once a day and Rehabilitation therapy (1 week in inpatient rehabilitation) for Guillain-Barre syndrome. At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain-Barré syndrome after Moderna vaccine) had resolved. Related DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Angiogram: albumino-cytological dissociation With a high suspicion for stroke, CT head and CT angiogram head and neck were performed and demonstrated no acute intracranial bleeding and no vascular abnormalities other than a 50% stenosis of the proximal left internal carotid artery. Given the generalised weakness and diffusely absent DTRs, we had high suspicion for GBS, and neurology was consulted for further evaluation.. On an unknown date, Babinski reflex test: mute bilaterally Babinski reflex was mute bilaterally. On an unknown date, CSF test: albumino-cytological dissociation To help with the diagnosis, we obtained a lumbar puncture. Cerebrospinal fluid (CSF) analysis was significant for albumino-cytological dissociation with a protein of 90 mg/dL and white cell count (WCC) of 0 cells x 10⁶/L.. On an unknown date, Cardiovascular examination: unremarkable cardiovascular exam was unremarkable. On an unknown date, Electrocardiogram: normal sinus rhythm ECG demonstrated a normal sinus rhythm. On an unknown date, Electromyogram: evidence of demyelination Electromyogram (EMG) with nerve conduction study showed evidence of demyelination with prolonged distal latency of above 130% of the upper limit of normal with slowed conduction velocity below 75% of the lower limit of normal (LLN) of the right fibular motor response. The conduction velocity of the left fibular and right ulnar motor responses was slowed to approximately 80% of the LLN.. On an unknown date, Full blood count: within normal limits (normal) within normal limits. On an unknown date, Inspiratory capacity: without evidence of respiratory compromise without evidence of respiratory compromise. On an unknown date, Metabolic function test: normal (normal) within normal limits. On an unknown date, Neurological examination: notable for bilateral and symmetric 3/5 strength Notable for bilateral and symmetric 3/5 strength in the following muscle groups: biceps, triceps, wrist flexors and extensors, and iliopsoases. He had trace right biceps reflex, but the remainder of his deep tendon reflexes (DTRs) were absent across triceps, brachioradialis, ankle and knee reflex. On coordination testing, dysmetria on finger-to- nose. No dysmetria or ataxia on heel to-shin. Slow rapid alternating hand movements..	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		On an unknown date, Physical examination: unremarkable respiratory exam was unremarkable. On an unknown date, Scan brain: normal (normal) According to the patient, in the hospital, the brain scans were done which looked fine. On an unknown date, Sensory level: light touch and pinprick was intact Sensory examination to light touch and pinprick was intact across bilateral medial and lateral aspects of lower extremities. He was noticed to have a loss of vibration sense below dermatomes T11 on he left, L2 on the right.. On an unknown date, Vital capacity: without evidence of respiratory compromise. vital capacity were serially monitored without evidence of respiratory compromise. On an unknown date, Vital signs measurement: stable patient's vital signs were stable. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. For mRNA-1273 (Spikevax) (Unknown), the reporter considered GUILLAIN-BARRE SYNDROME (Guillain-Barré syndrome after Moderna vaccine) to be related. Patient was in his usual state of health before receiving his second Moderna vaccine injection. In the evening after receiving his second injection, patient was unable to fall asleep and, when he tried to get out of bed, noticed that his balance was off and he had an episode of urinary incontinence. The next day he was fatigued and unable to walk to the bathroom. At baseline, he rarely uses a cane for his gait instability but since his symptoms began, he was weak to the point where he relied on his cane for walking. Later that day he lost his balance and fell in his kitchen, but did not injure himself or lose consciousness. On the third-day post vaccination, as his symptoms failed to improve, he presented to the emergency department (ED) on the advice of his primary care physician (PCP). Tests also included coordination testing, he was noticed to have dysmetria on finger-to- nose. No dysmetria or ataxia on heel-to- shin. Slow rapid alternating hand movements. Patient completed his IVIG treatments without complication. Based on the history, physical examination and testing including CSF analysis and EMG results this patient's clinical presentation is most consistent with the diagnosis of GBS. Patient's strength showed marked improvement, 5/5 throughout except for 4/5 right wrist extension and he continued to have are flexia except in the right bicep's tendon. From his acute hospitalisation, he spent 1 week in	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		inpatient rehabilitation before being discharged home. At PCP follow-up 3 weeks following his initial ED presentation he was back to his functional baseline with no residual weakness. Since patient did not have any history or symptoms suggestive of other known antecedents, his precipitating event is hypothesized to be the first dose of Moderna vaccination which he received 4 weeks before the presentation. The second vaccine dose is unlikely to have been the precipitating event as he developed symptoms on the same day. Company Comment: This is a literature non-study case concerning a 6-decade-old male patient with medical history of ruptured left middle cerebral artery aneurysm, status post clipping 2005 with residual right eye blindness and right leg weakness with gait instability, who experienced the unexpected serious (medically significant) adverse event of special interest GUILLAIN-BARRE SYNDROME, which led to hospitalization, 4 weeks after receiving the first dose of mRNA-1273 vaccine and on the same day after receiving the second dose of mRNA-1273. It was reported that the patient was in his usual state of health before receiving his second Moderna vaccine injection. In the evening after receiving his second injection, patient noticed that his balance was off and he had an episode of urinary incontinence. The next day he was fatigued and unable to walk. He was weak to the point where he relied on his cane for walking. Later that day he lost his balance and fell, but did not injure himself or lose consciousness. On the third-day post-vaccination, as his symptoms failed to improve, he presented to the emergency department (ED) on the advice of his primary care physician. On presentation to the ED, his neurological exam	
		This case was initially received via Takeda Pharmaceuticals (Reference number: [REDACTED] on 18-May-2022. The most recent information was received on 20-Jun-2022 and was forwarded to Moderna on 27-Jun-2022. This case, initially reported to the [REDACTED] by a physician, was received via the [REDACTED] On 20-Jun-2022, follow-up information was received from a physician. On an unspecified date in Jun-2021, the patient received the 1st dose of non-company coronavirus modified uridine RNA vaccine (SARS-CoV-2). On an unspecified date in Jul-2021, the patient received the 2nd dose of non-company coronavirus modified uridine RNA vaccine (SARS-CoV-2). On 04-Mar-2022, the patient received the 3rd vaccination with this vaccine. On 10-Mar-2022, Guillain-Barre syndrome developed. The paresthesia of distal extremities and muscle weakness of both lower extremities appeared from the hospital day 1st. Symptoms progressed slowly. On 11-Mar-2022, one week after the vaccination, sensory disturbance developed in both hands and	HA report from HCP of 76F with no MH or CM reported who experienced GBS 7 days after the third dose of Spikevax with symptoms including sensory disturbance, loss of lower limb DTRs and progressive lower extremity weakness. CSF revealed protein/cell dissociation, electrophysiologic examination suggested demyelinating disorder and MRI showed lesions of cauda equina. Report is classified as BC level 1 and WHO-UMC causality is assessed as possible based on the plausible temporal association.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		extended to the lower limbs. On 18-Mar-2022, two weeks after the vaccination, muscle weakness in the lower limbs developed and worsened, leading to difficulty walking. On 23-Mar-2022, 19 days after the vaccination, the patient visited the reporting hospital. The cranial nerve system was normal. Limb tendon reflexes disappeared, and the patient had difficulty walking due to muscle weakness in both lower limbs. Dysaesthesia was observed in the distal extremities, but there was no bladder or rectal disturbance. The pharyngeal swab fluid was negative for COVID-19 antigen. Protein cell dissociation was observed in the test on spinal fluid. Extension of motor nerve distal latency and F wave shortest latency and sural sparing pattern were observed in the peripheral nerve conduction study. The patient was hospitalized. On 25-Mar-2022, lumbar MRI showed contrast lesions in the cauda equina. The patient was diagnosed with Guillain-Barre syndrome based on progressive motor and sensory disturbance with loss of tendon reflexes, positive albuminocytologic dissociation of cerebrospinal fluid, electrophysiological examination and MRI findings. High-dose immunoglobulin therapy, oral treatment of vitamin B 12, and rehabilitation were performed. On 28-Apr-2022, on hospital day 50, the treatment was successful, and the patient was discharged on foot. There was no side reaction which attributed to high-dose immunoglobulin therapy and oral treatment of vitamin B12. On 30-Apr-2022, the symptom was resolving. The outcome of Guillain-Barre syndrome was reported as resolving. No follow-up investigation will be made. Reporter comments continuation: The patient was diagnosed as Guillain-Barre syndrome from progressive motor and sensory disturbance with loss of tendon reflex, positive albuminocytologic dissociation of cerebrospinal fluid, electrophysiological examination and MRI findings. Based on the absence of antecedent infection symptoms and the clinical course of the disease six days after vaccination, the patient was considered to have developed the disease associated with this vaccine. It was considered that the progress in which the high-dose immunoglobulin therapy was effective did not contradict Guillain-Barre syndrome. Follow-up received on 20-JUN-2022 Updated: Patient Information, Other Relevant History, Lab Data, Event Information, Narrative, Reporter Comments [Clinical symptom] - Bilateral and flaccid muscle weakness of the upper and lower limbs. (day of onset: 16-Mar-2022) - Decreased or absent deep tendon reflexes in the upper and lower limbs resulting in muscle weakness. - Up to the time of the report, Hughes' functional scale classification for the extreme phase of symptoms was 4. Limited to in bed or wheelchair (even with support, unable to walk 5 m). [Course of the disease] - The symptom had a monophasic disease pattern, with an interval of 12 hours to 28 days between the onset of muscle weakness and the worst condition, followed by a period of clinical stability. [Electrophysiological examination] (date of exam: 23-Mar-2022) - Prolonged distal latency, decreased frequency of F-wave appearance, and prolonged F-wave latency, which were consistent with GBS. [Spinal fluid examination] (date of exam: 23-Mar-2022) - Cell count:	

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		1/mcL, glucose: 60 mg/dL, protein: 63 mg/dL. - There was protein-cell dissociation from elevated CSF protein level above the laboratory normal value and CSF total white blood cell count below 50 cells/mcL. [Differential diagnosis] - No other diseases were applicable. [Autoantibody test] (date of exam: 23-Mar-2022) - Anti-GM1 antibody was negative. Anti-GQ1b antibody was negative. [Presence or absence of antecedent infection] - None. Company Comment: The event developed after the administration of ELASOMERAN and there is temporal relationship.	
		This regulatory authority case was reported by an other health care professional and describes the occurrence of GUILLAIN-BARRE SYNDROME (Respiratory asthma, and suspected GBS), ASTHMA (Respiratory asthma, and suspected GBS) and MUSCULAR WEAKNESS (Limb weakness) in a 61-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 prophylaxis. The patient's past medical history included Heart disease, unspecified and Stent insertion NOS (1 stent implanted). Concurrent medical conditions included Hypertension. On 07-Apr-2022, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 30-May-2022, the patient experienced GUILLAIN-BARRE SYNDROME (Respiratory asthma, and suspected GBS) (seriousness criterion hospitalization), ASTHMA (Respiratory asthma, and suspected GBS) (seriousness criterion hospitalization) and MUSCULAR WEAKNESS (Limb weakness) (seriousness criterion hospitalization). The patient was hospitalized on 25-May-2022 due to ASTHMA, GUILLAIN-BARRE SYNDROME and MUSCULAR WEAKNESS. The patient was treated with HYDROCORTISONE on 26-May-2022 at a dose of 100 milligram every eight hours. At the time of the report, GUILLAIN-BARRE SYNDROME (Respiratory asthma, and suspected GBS), ASTHMA (Respiratory asthma, and suspected GBS) and MUSCULAR WEAKNESS (Limb weakness) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 25-May-2022, Chest X-ray: acute interstitial pneumonia Patient had acute interstitial pneumonia, for which he was hospitalized.. On 27-May-2022, Lumbar puncture: guillain-barre syndrome was suspected Guillain-Barre Syndrome was suspected.. On 27-May-2022, Nerve conduction studies: sensory-motor polyneuropathy Sensory-motor polyneuropathy was found, which was most serious on the legs..	HA report from HCP of 61M with hypertension, "heart disease" s/p stent placement, no CM reported who experienced GBS, asthma and muscular weakness 53 days after second dose of Spikevax. A week after vaccination, the patient had progression limb weakness leading to ED treatment for weakness, asthma and fever. Later admitted to ICU for mechanical ventilation for "hydrops". CXR revealed interstitial pneumonia. LP was reported to be suspicious for GBS (findings not provided) and nerve conduction study revealed sensorimotor polyneuropathy, "most serious on the legs." Evaluation is confounded by the clinical picture with superimposed asthma, "hydrops", interstitial pneumonia and provision of incomplete diagnostic evaluation. Report is assessed as BC level 3 and WHO-UMC causality is classified as unassessable.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No relevant concomitant medications were reported. One week after vaccination, the patient felt progressive weakness of the limbs. On 25 May 2022, the patient came to the emergency department for consultations and treatments due to respiratory asthma, limb weakness, asthma and fever. Upon follow up on 31 May 2022, the wife of the patient said that the patient was hospitalized in an intensive care unit at that time and had hydrops, and the patient had to rely on a respirator to maintain the oxygen concentration. Earlier on 31 May 2022, she went to the hospital to sign a consent for spinal cord puncture. This was the second puncture. After the previous puncture, the doctor said that the patient might have acute neuritis caused by vaccination. The WWID was reported as [REDACTED]. Company comment: This regulatory authority case concerns a 61 year old male patient with no relevant medical history, who experienced the unexpected serious (hospitalization) events of Guillain-Barre syndrome(AESI), Asthma and Muscular weakness, about 1 month and 23 days after receiving the second dose of mRNA-1273 vaccine in the COVID-19 vaccination series. One week after the vaccine, patient felt progressive weakness of the limbs. After about 1 month and 11 days, he sought emergency medical consultation for respiratory asthma, limb weakness and fever. Chest X Ray revealed acute interstitial pneumonia for which the patient was hospitalized. Nerve conduction study, 2 days later showed sensory-motor polyneuropathy, which was most serious on the legs. Lumbar puncture was performed and Guillain-Barre Syndrome was suspected. He was treated with Hydrocortisone 100 mg Q8H. Upon follow up, it was reported that he was in an intensive care unit and had hydrops. He was put on a respirator to maintain oxygen concentration. He was scheduled for a second lumbar puncture. Patient's doctor opined that the patient might have had acute neuritis caused by vaccination. The events were resolving. Acute interstitial pneumonia could be a risk factor for the events Guillain-Barre syndrome and Asthma. The benefit-risk relationship of mRNA-1273 is not affected by this report. Events' seriousness retained as per Regulatory Authority reporting.	
		This case was received via European Medicines Agency (Reference number: [REDACTED]) on 16-Jun-2022 and was forwarded to Moderna on 16-Jun-2022. This regulatory authority case was reported by a consumer and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain Barre	HA report from consumer of 89F with no medical history reported who experienced GBS approximately two months after dose 3 Spikevax, and 10 and 8 months after dose 2 and dose 1 Comirnaty. CSF reportedly revealed cytoalbuminologic dissociation. Nerve conduction study was uninformative revealing

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		syndrome) in an 89-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3004235) for COVID-19 vaccination. Previously administered products included for Product used for unknown indication: Comirnaty BNT162b2 on 29-Apr-2021 and Comirnaty BNT162b2 on 10-Jun-2021. Past adverse reactions to the above products included No adverse event with Comirnaty BNT162b2 and Comirnaty BNT162b2. On 06-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 3 dosage form. In February 2022, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) (seriousness criterion hospitalization). At the time of the report, GUILLAIN-BARRE SYNDROME (Guillain Barre syndrome) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Anti-ganglioside antibody: detection of ganglioside gm1-Igm ak from a guillai detection of ganglioside Gm1-IgM AK from a Guillain Barre syndrome. On an unknown date, CSF test: cytoalbumin dissociation cytoalbumin dissociation. On an unknown date, Nerve conduction studies: severe lesion of the examined arm and leg nerves severe lesion of the examined arm and leg nerves. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. No concomitant products were reported. It was reported that rapidly progressive (for 2 weeks) distally and right stressed sensorimotor paresis of extremes, clinical evidence of moderate distal paresis, extinct MER on all extremes, severe acral hypesthesia at all extremes, cerebrospinal fluid detection cytoalbumin dissociation, electrophysiological detection of severe lesion of the examined arm and leg nerves and laboratory chemical detection of ganglioside Gm1-IgM AK from a guillain Barre syndrome. Therapy: multiple IVigs, rehab, GBS-BC level 1.	"severe lesion of the examined arm and leg nerves". The patient was treated with rehab and IVIG. Confirmation of CSF results and clarity on nerve conduction studies would support further evaluation which is confounded by vaccine interchange. Report is classified as BC level 3 and WHO-UMC is assessed as conditional.

Case ID	WW Identifier	Narrative (Complete)	MAH Comment
		Company Comment: This is a regulatory case concerning an 89-year-old female patient with no medical history reported, who experienced the unexpected serious adverse event of special interest Guillain-Barre syndrome, which led to hospitalization, approximately 2 months after receiving a dose of mRNA-1273 as the third dose of COVID-19 vaccine. Patient had received 2-dose primary series of Comirnaty COVID-19 vaccine with no reported adverse event, approximately 6 months prior to mRNA-1273 vaccination (Interchange of vaccine products). It was reported that the patient had rapidly progressive sensorimotor paresis of the right distal extremities with clinical evidence of moderate distal paresis and severe hypoesthesia of all extremities. Patient underwent cerebrospinal fluid analysis which revealed cytoalbumin dissociation, electrophysiological test which showed severe lesion of the examined arm and leg nerves, and detection of ganglioside Gm1-IgM. Patient was treated with multiple Intravenous Immunoglobulin, rehabilitation therapy, and level 1 GBS-BC. It was reported that the event was not resolved. The benefit-risk relationship of mRNA-1273 is not affected by this report. Events' seriousness assessed as per Regulatory Authority reporting.	

Appendix 11.17a Acute Disseminated Encephalomyelitis (ADEM): Detailed Summary of Cumulative Data Concerning ADEM and Brighton’s Collaboration Level of diagnostic certainty 1 to 5: Case Listings

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Spontaneous	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovered/Resolved with Sequelae			Unknown	7	6/15/2022	Initial	NA (IRD in current SSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalitis, Encephalomyelitis	Recovering/Resolving	Hypertension(C)		Dose 3	17	4/11/2022	Initial	NA (IRD in current SSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Muscular weakness, Wheelchair user	Not Recovered/Not Resolved	Nephropathy(H); Cardiac failure(H); Diabetic complication(C); Renal failure(C); Neuropathy peripheral(C); Dialysis(H); Rash(H); Sepsis(H)		Unknown	1	4/18/2022	Initial		
Literature-Non-Study	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovering/Resolving			Dose 2	4	4/25/2022	Prior	NO (IRD in a previous MSSR, but initi Book-in in current MSSR RP)	
Regulatory Authority	Encephalomyelitis	Serious	Demyelination, Encephalitis, Encephalomyelitis, Hypoaesthesia	Recovering/Resolving	Hypoaesthesia(H); Vitamin D deficiency(H); Hypothyroidism(H)		Dose 2	3	5/31/2022	Initial	NA (IRD in current SSR)	
Spontaneous	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Binocular eye movement disorder, Condition aggravated, Diplopia, Myelin oligodendrocyte glycoprotein antibody-associated disease	Recovering/Resolving	Myelin oligodendrocyte glycoprotein antibody-associated disease(C); COMIRNATY; COMIRNATY		Dose 3	3	6/6/2022	Initial	NA (IRD in current SSR)	
Regulatory Authority	Encephalomyelitis	Serious	Asthenia, Constipation, Dizziness, Encephalitis, Encephalomyelitis, Fall, Gait disturbance, Incontinence, Lethargy, Muscular weakness, Pollakiuria	Recovering/Resolving			Dose 3	13	6/6/2022	Initial	NA (IRD in current SSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Not Recovered/Not Resolved			Dose 3	1	2/18/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovered/Resolved with Sequelae	COVID-19(H)		Dose 2	1	2/22/2022	Initial	NA (IRD in current MSSR)	
Spontaneous	Encephalomyelitis	Serious	Encephalomyelitis	Unknown			Dose 3	14	2/21/2022	Initial	NA (IRD in current MSSR)	
Spontaneous	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Vaccination site pain	Not Recovered/Not Resolved	Hepatitis C(H)		Dose 3	1	2/28/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalitis, Encephalomyelitis	Not Recovered/Not Resolved	Diabetes mellitus(C); Hypertension(C); Hyperlipidaemia(C)		Dose 3	1	3/1/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalomyelitis	Not Recovered/Not Resolved	Chronic kidney disease(C); Colitis ulcerative(C); Depression(C); Anxiety(C)	ASACOL	Dose 1	47	3/8/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovering/Resolving			Dose 3	1	3/14/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Confusional state, Crying, Headache, Irritability	Not Recovered/Not Resolved			Dose 3	0	3/15/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalomyelitis	Not Recovered/Not Resolved	Alopecia areata(H)		Unknown	17	3/16/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Chronic inflammatory demyelinating polyradiculoneuropathy, Guillain-Barre syndrome, Overlap syndrome	Recovered/Resolved with Sequelae			Dose 3	9 days prior to Dose 3	3/17/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy	Recovering/Resolving	Tobacco user(H)	XARELTO; NEBILET; ATORVASTATINE PFIZER; LISINAPRIL; PANTOZOLE; DAFALGAN	Dose 3	2	3/29/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Not Recovered/Not Resolved	Pregnancy(H); Gastrectomy; Obesity(C); Ex-tobacco user(C)	LOVENOX HP	Unknown	38	3/31/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Unknown	COVID-19(H)		Unknown	123	4/1/2022	Initial	NA (IRD in current MSSR)	
Spontaneous	Encephalomyelitis	Serious	Encephalomyelitis	Recovering/Resolving	Rectosigmoid cancer stage III(H); Hypertension(H); Hepatic function abnormal(H); Cholelithiasis(H); Iron deficiency anaemia(H); Fibromyalgia(H); Femur fracture(H); Decreased activity(H); Influenza(H)		Dose 3	1	4/7/2022	Initial	NA (IRD in current MSSR)	
Literature-Non-Study	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Fatal			Dose 1	13	4/11/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Cranioencephal injury, Encephalomyelitis, Pupillary reflex impaired, Visual impairment	Fatal	Alcoholism(H)		Unknown		1/5/2022	Initial	NA (IRD in current MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Death, Depressed level of consciousness, Epilepsy	Fatal			Dose 1	1	1/7/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalomyelitis	Recovered/Resolved			Dose 1	8	2/2/2022	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Cerebral infarction	Unknown	Hypertension(C)		Dose 1	4	2/5/2021	Follow-up	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Autoimmune demyelinating disease	Serious	Autoimmune demyelinating disease, Cauda equina syndrome, Gait disturbance, Guillain-Barre syndrome, Paresthesia, Peripheral motor neuropathy, Peripheral sensory neuropathy, Pruritus, Vaccination site erythema, Vaccination site reaction, Vaccination site warmth	Unknown	Immune system disorder(H); Hypothyroidism(H); Anaemia(H); Rubber sensitivity; Drug hypersensitivity		Dose 1	7	3/2/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Arthralgia, Brain oedema, Chills, Diplopia, Fatigue, Immediate post-injection reaction, Noninfective encephalitis, Pyrexia	Not Recovered/Not Resolved	Rubber sensitivity	LISINAPRIL; VITAMIN D 2000; ASPIRIN (E.C.); MULTIVITAMIN & MINERAL	Dose 2	1	3/16/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Spontaneous	Encephalomyelitis	Serious	Aphasia, Encephalitis, Encephalomyelitis, Sinus node dysfunction	Recovering/Resolving	Drug hypersensitivity; Thrombosis prophylaxis(H); Gastrointestinal disorder prophylaxis(H); Skin graft; Milk allergy; Atrioventricular block(C); Hyperlipidaemia(C); Dyslipidaemia(C); Hypertension(C); Wolff-Parkinson-White syndrome(C); Cardiac pacemaker insertion	ALEVE; AMLODIPINE; ATORVASTATIN; PANTOPRAZOLE	Dose 2	18	5/2/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Spontaneous	Demyelinating polyneuropathy	Serious	Acute respiratory failure, Anaemia, Asthenia, Bulbar palsy, Demyelinating polyneuropathy, Gait disturbance, Glaucoma, Ileus paralytic, Loss of personal independence in daily activities, Muscular weakness, Obesity, Pneumonia, Respiratory failure	Not Recovered/Not Resolved	Diabetes mellitus(C); Hypertension(C); Glaucoma(C); Hyperlipidaemia(C)	LISINAPRIL; ATORVASTATIN; METFORMIN	Dose 1	21	4/30/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Haemorrhagic infarction, Headache, Intracranial pressure increased, Mental status changes, Pleocytosis	Not Recovered/Not Resolved	Ventricular drainage; Endotracheal intubation	TYLENOL	Dose 1	0	5/11/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Guillain-Barre syndrome	Recovering/Resolving	Guillain-Barre syndrome(H)		Unknown		5/23/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Brain stem infarction, Cerebrovascular disorder, Dysarthria, General physical health deterioration, Ischaemia, Osmotic demyelination syndrome	Fatal	Drug hypersensitivity; Lactose intolerance; Diabetes mellitus(C); Hypertension(H); Hypertension(H); Obesity(H); Sleep apnoea syndrome(H); Positive airway pressure therapy	ASTELIN [AZELASTINE HYDROCHLORIDE]; PROTONIX [OMEPRAZOLE]; LIPITOR; CALCIUM CARBONATE; CARDURA; FLONASE [MOMETASONE FUROATE]; ROBITUSSIN [DEXTROMETHORPHAN HYDROBROMIDE]; LANTUS; LOPRESSOR; REMERON; ZYPREXA; ZOFRAN [ONDANSETRON]; MIRALAX; FLORASTOR [LACTOBACILLUS ACIDOPHILUS]	Dose 2	8	6/1/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Asthenia, Demyelinating polyneuropathy, Gait disturbance, Guillain-Barre syndrome, Muscular weakness	Not Recovered/Not Resolved	Hypertension(C); Anxiety(C); Lumbar puncture(C); Immunoglobulin therapy(C)	HCTZ	Dose 1	1	6/1/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Hypoaesthesia, Paraesthesia	Not Recovered/Not Resolved			Dose 2	25	6/1/2021	Prior	YES (IRD and init Book-in a previous MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Asthenia, Cranial nerve disorder	Not Recovered/Not Resolved	Sleep apnoea syndrome(C); Cerebrovascular accident(C); Lung disorder(H); Diverticulitis(C); Obesity(C); Milk allergy; Hypersensitivity; Hypertension(C); Diabetes mellitus(C); Chronic kidney disease(C); Hyperlipidaemia(C)	ATORVASTATIN; METOPROLOL; PANTOPRAZOLE; CALCIUM GLUCONATE; PROBIOTICS NOS; CARDURA; INSULIN	Dose 1	28	6/8/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Asthenia, Demyelinating polyneuropathy, Fatigue, Gait inability, Incorrect route of product administration, Muscular weakness, Myalgia, Respiratory failure, Speech disorder	Not Recovered/Not Resolved	Hypertension(C); Diabetes mellitus(C); Hypocholesterolaemia(C); Glaucoma(C)	LISINAPRIL; ATORVASTATIN; METFORMIN; DORZOLAMIDE; LATANOPROST; BRIMONIDINE; PILOCARPINE; TIMOLOL	Unknown		6/15/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Acute polyneuropathy, Asthenia, Bronchitis, Demyelinating polyneuropathy, Paraesthesia	Not Recovered/Not Resolved	Hypertension(C); Food allergy; Allergy to chemicals	CHLORTHALIDONE	Dose 1	17	6/15/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Asthenia, Chills, Disturbance in attention, Encephalomyelitis, Fatigue, Headache, Hypoaesthesia, Pain	Not Recovered/Not Resolved	Drug hypersensitivity; Food allergy; Hypertension(C); Hyperlipidaemia(C); Angioedema; Drug hypersensitivity	LISINAPRIL HCTZ; ATENOLOL	Dose 1	1	6/15/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalomyelitis	Not Recovered/Not Resolved			Dose 1	7	6/15/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Acute polyneuropathy, Demyelinating polyneuropathy, Gait disturbance, Hypoaesthesia, Inflammation, Muscular weakness, Pain, Pruritus, Sensorimotor disorder	Not Recovered/Not Resolved		MULTIVITAMIN [VITAMINS NOS]	Unknown		6/15/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Muscular weakness, Paraesthesia, Sensory loss	Not Recovered/Not Resolved	Hyperlipidaemia(C); Diabetes mellitus(C); Hypertension(C); INFLUENZA VACCINE	AMITRIPTYLINE; ASPIRIN 81; DULOXETINE; GABAPENTIN; GLIMEPIRIDE	Dose 1	2	6/29/2021	Prior	YES (IRD and init Book-in a previous MSSR)	
Regulatory Authority	Immune-mediated neuropathy	Serious	Haematuria, Immune-mediated neuropathy, Proteinuria, Pyrexia	Recovered/Resolved	Anxiety(C); Depression(C); Obesity(C); Nonalcoholic fatty liver disease(C); IgA nephropathy(C)	SERTRALINE; FAMOTIDINE; OMEPRAZOLE; LORATADINE; VITAMIN D [COLECALCIFEROL]	Dose 2	1	6/29/2021	Prior	NO (IRD in a previous MSSR, but init Book-in in current MSSR RP)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Asthenia, Cerebral infarction, Demyelinating polyneuropathy, Endotracheal intubation, Hypoaesthesia, Immunoglobulin therapy, Mobility decreased, Paraesthesia, Plasmapheresis, Respiratory distress	Not Recovered/Not Resolved			Dose 1	11	7/6/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Aphasia, Ascites, Dyspnoea, Pleural effusion, Pulmonary oedema, Status epilepticus, Unresponsive to stimuli, Vaccination complication, White matter lesion	Recovered/Resolved	Drug hypersensitivity; Type 2 diabetes mellitus(C); Chronic obstructive pulmonary disease(C); Hypertension(C); Brain injury(C); Hyperlipidaemia(C)	ALOGLIPTIN; ATORVASTATIN; CLONIDINE; DIPHENHYDRAMINE; FUROSEMIDE; DUONEB; METFORMIN; METOPROLOL TARTRATE; PREDNISONE; SIMVASTATIN; SITAGLIPTIN	Dose 2	48	7/6/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Headache	Not Recovered/Not Resolved			Dose 2	0	7/9/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Back pain, Chest pain	Recovered/Resolved with Sequelae			Dose 1	7	7/7/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Headache, Laboratory test abnormal, Magnetic resonance imaging abnormal, Nausea, Posterior reversible encephalopathy syndrome, Subarachnoid haemorrhage, Vomiting, White matter lesion	Not Recovered/Not Resolved	COVID-19(H); Cerebrovascular accident(H); Pulmonary embolism(H); Obesity(H); Anaemia macrocytic(H); Chronic kidney disease(C)	WARFARIN; FERROUS FUMARATE; PANTOPRAZOLE; ATORVASTATIN [ATORVASTATIN CALCIUM]	Unknown		7/13/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Movement disorder, Pyrexia	Unknown			Dose 1	8	7/15/2021	Initial	NA (IRD in current MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Paraesthesia	Recovering/Resolving			Dose 2	32	7/20/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Amnesia, Arthralgia, Ataxia, Diplopia, Dizziness, Encephalomyelitis, Headache, Nausea, Pyrexia, Radiculopathy	Not Recovered/Not Resolved	Chronic pigmented purpura(C); Viral hepatitis carrier(C); Rheumatoid arthritis(C); Leiomyoma(C); Uveitis(C); Uterine leiomyoma(C); Cryoglobulinaemia(C); Cataract; Hepatic steatosis(C)	CALCIUM CARBONATE; LANSOPRAZOLE; BACTRIM; COLCHICINE; LAMIVUDINE; ALENDRONATE SODIUM; HYDROXYCHLOROQUINE SULFATE	Unknown		7/22/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Autoimmune demyelinating disease	Serious	Asthma, Autoimmune demyelinating disease, Central nervous system lesion, Hypoaesthesia, Multiple sclerosis, Paraesthesia	Not Recovered/Not Resolved	Appendicectomy; Sinus bradycardia(C)	LACTULOSE; COLACE	Unknown		7/27/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Aphasia, Cognitive disorder, Condition aggravated, Demyelination, Feeling abnormal, Impaired work ability, Memory impairment, Paraesthesia, Sjogren's syndrome	Unknown	Drug hypersensitivity; Drug hypersensitivity; Abdominal distension(H); Abdominal distension(H); Weight increased(H); Anxiety disorder(H); Arthritis(H); Benign neoplasm(H); Haematuria(H); Lymphadenopathy(H); Hypertrophy of tongue papillae(H); Demyelination(H); Dental restoration failure(H); Diverticulum(H); Dysphagia(H); Fatty acid deficiency(H); Exposure to fungus(H); Fatigue(H); Stomatitis(H); Stress urinary incontinence(H); Gastroesophageal reflux disease(H); Hyperglycaemia(H); Hyperreflexia(H); Tuberculosis(C); Female orgasmic disorder(H); Insomnia(H); Nephrolithiasis(H); Cognitive disorder(H); Hyperhidrosis(H); Nonalcoholic fatty liver disease(H); Osteopenia(H); Osteitis deformans(H); Paraesthesia(H); Rheumatoid arthritis(H); Sjogren's syndrome(H); Urinary incontinence(H); Vulvovaginal dryness(H); Vitamin D deficiency(H); Dry mouth(H)	FLORASTOR [LACTOBACILLUS ACIDOPHILUS]; COQ10 [UBIDECARENONE]; OHA; OMEGA-3 NOS; KRILL COMPLEX & VITAMIN D	Unknown		8/3/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Balance disorder, Condition aggravated, Face injury, Fall, Feeding disorder, Gait disturbance, Ischaemia, Loss of personal independence in daily activities, Mental status changes, Movement disorder, Myelitis transverse, Skin abrasion, Spinal cord disorder, Spinal cord injury cervical, Urinary incontinence, Vertebral osteophyte, White matter lesion	Unknown	Drug hypersensitivity; Drug hypersensitivity; Schizophrenia(C); Dementia(C); Acute disseminated encephalomyelitis(C); Tachycardia(C)	CLOZAPINE; METOPROLOL; CHOLECALCIFEROL	Dose 2	22	8/3/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Not Recovered/Not Resolved			Unknown		8/4/2021	Initial	NA (IRD in current MSSR)	
Spontaneous	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Dysaesthesia, Guillain-Barre syndrome, Neuropathy peripheral	Not Recovered/Not Resolved			Unknown		7/22/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Unknown			Unknown		8/6/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Arthralgia, Back pain, Gait disturbance, Hypoaesthesia, Myelitis, Pain in extremity, Pyramidal tract syndrome, Pyrexia, Sensory disturbance, Spinal cord infarction	Recovered/Resolved with Sequelae			Dose 1	2	8/16/2021	Initial	NA (IRD in current MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovering/Resolving	No adverse event(H)		Dose 1	0	8/10/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Autoimmune demyelinating disease	Serious	Autoimmune demyelinating disease, Balance disorder, Central nervous system lesion, Congenital central nervous system anomaly, Decreased appetite, Discomfort, Dizziness, Dysaesthesia, Encephalomalacia, Erectile dysfunction, Fatigue, Hypoaesthesia, Pain, Paraesthesia, Pyrexia, Weight decreased, White matter lesion	Unknown	Hypertension(C); Hypercholesterolaemia(C); Obesity(C)		Dose 2	17	8/17/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovering/Resolving			Dose 2	32	8/19/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalomyelitis	Unknown	TETANUS VACCINE		Unknown		8/25/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Peripheral motor neuropathy, Peripheral sensory neuropathy	Recovering/Resolving	Intervertebral disc protrusion(H)		Unknown		8/25/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Decreased appetite, Encephalomyelitis, Herpes zoster, Hypokinesia, Somnolence, Speech disorder	Unknown			Unknown		8/19/2021	Initial	NA (IRD in current MSSR)	
Spontaneous	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Back pain, Headache, Nausea, Neck pain, Pyrexia, Urinary retention, Vomiting	Unknown	Dermatitis atopic(H); Depression(H); Upper respiratory tract infection(H); Diarrhoea(H)		Unknown		9/4/2021	Initial	NA (IRD in current MSSR)	
Literature-Non-Study	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Urinary retention	Recovered/Resolved with Sequelae	Dermatitis atopic(C); Depression(C)		Unknown		9/5/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Immune-mediated neuropathy	Serious	Arthralgia, Brachial plexopathy, Glucose tolerance impaired, Guillain-Barre syndrome, Hypoaesthesia, Immune-mediated neuropathy, Injection site pain, Movement disorder, Neuralgic amyotrophy, Pain, Paraesthesia	Not Recovered/Not Resolved	Drug hypersensitivity; Drug hypersensitivity; Drug hypersensitivity; Drug hypersensitivity; Hypersensitivity; Obesity(H); Asthma(C)	ACETAMINOPHEN; ALVESCO; FLUOXETINE; LEVONORGESTREL; LEVOTHYROXINE; LISINAPRIL; VENTOLIN HFA	Dose 2	14	9/7/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovering/Resolving			Dose 1	13	9/17/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Arthralgia, Asthenia, Cervical spinal stenosis, Chronic inflammatory demyelinating polyradiculoneuropathy, Demyelinating polyneuropathy, Fine motor skill dysfunction, Impaired driving ability, Mobility decreased, Muscular weakness, Musculoskeletal disorder, Musculoskeletal stiffness, Myoclonus, Spinal osteoarthritis, Walking aid user, Wheelchair user, White matter lesion	Not Recovered/Not Resolved	Peripheral venous disease(H); Bipolar disorder(C)	WELLBUTRIN XL; LORAZEPAM; ALBUTEROL [SALBUTAMOL]; ASMANEX	Dose 1	7	9/21/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Not Recovered/Not Resolved	Amblyopia(C)		Dose 1	39	9/23/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Aphasia, Candida infection, Dehydration, Dementia, Disorientation, Dysgeusia, Encephalitis, Encephalomyelitis, Herpes oesophagitis, Meningitis aseptic, Meningoencephalitis herpetic, Pain, Pharyngitis streptococcal, Retching, Speech disorder, Toxic encephalopathy, Type V hyperlipidaemia, Vomiting	Recovered/Resolved	Oropharyngeal pain(C); Toxic encephalopathy(C); Meningitis aseptic(C); Encephalomyelitis(C); Type V hyperlipidaemia(C); Candida infection(C); Pharyngitis streptococcal(C); Aphasia(C); Spinal cord drainage; Gastrostomy; Central venous catheterisation	TYLENOL; MELOXICAM; GABAPENTIN; FINASTERIDE; TAMUSULOSIN; ALPRAZ	Dose 2	2	9/28/2021	Initial	NA (IRD in current MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Demyelinating polyneuropathy	Serious	Back pain, Chest discomfort, Demyelinating polyneuropathy, Groin pain, Impaired driving ability, Intervertebral disc protrusion, Loss of personal independence in daily activities, Muscular weakness, Musculoskeletal stiffness, Neck pain, Pain in extremity, Radiculopathy	Not Recovered/Not Resolved	Drug hypersensitivity; Blood cholesterol increased(C)		Dose 1	17	9/28/2021	Initial	NA (IRD in current MSSR)	
Spontaneous	Encephalomyelitis	Serious	Anaemia folate deficiency, Anamnestic reaction, Arthralgia, Asthenia, Ataxia, Autoimmune disorder, Back pain, Central nervous system lesion, Condition aggravated, Cranial nerve disorder, Depression, Discomfort, Encephalomyelitis, Feeling of body temperature change, Gait disturbance, Headache, Hernia, Hyperhidrosis, Hypoaesthesia, Inflammation, Intervertebral disc protrusion, Multiple sclerosis, Muscle spasms, Muscle tightness, Muscular weakness, Mydriasis transverse, Nausea, Nerve compression, Nervous system disorder, Neuromyelitis optica spectrum disorder, Pain, Pain in extremity, Paraesthesia, Pyrexia, Sciatica, Sleep disorder, Somnolence, Spinal cord injury, Taste disorder, Vision blurred	Unknown	Nerve compression(C); Nicotine dependence(H); Breast cancer(FH); Allergy to animal; Allergy to animal; Seasonal allergy; Seasonal allergy; Helicobacter gastritis(C)		Dose 2	30	9/28/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Bone marrow oedema, Demyelinating polyneuropathy, Guillain-Barre syndrome, Muscular weakness, Vertebral lesion	Recovered/Resolved	Drug hypersensitivity; Drug hypersensitivity; Anxiety(C); Depression(C); Gastroesophageal reflux disease(H); Schizoaffective disorder(C); Hepatic steatosis(H); Guillain-Barre syndrome(C); Immunoglobulin therapy	REXULT; INVEGA [PALIPERIDONE]	Dose 2	4	10/12/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Ear pain, Encephalitis, Fatigue, Headache, Pyrexia	Recovering/Resolving	Gluten sensitivity; Genital herpes(C); Osteopenia(C); Meningitis(H); Deep vein thrombosis(H)	HIPREX [CHLORTALIDONE]; CALCIGRAN FORTE	Dose 1	43	10/14/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalomyelitis	Not Recovered/Not Resolved	Hepatic enzyme increased(H); Transitional cell carcinoma(H); Oesophageal carcinoma(H); Drug hypersensitivity		Dose 2	40	10/20/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Central nervous system lesion, Eye pain, Optic neuritis, Papilloedema, Pyrexia, Scleral haemorrhage, Spinal cord injury thoracic, Visual acuity reduced, Visual impairment	Not Recovered/Not Resolved	Scleritis(H)		Dose 2	14	10/15/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Guillain-Barre syndrome, Hypoaesthesia, Pain in extremity	Unknown			Dose 1	96	10/27/2021	Initial	NA (IRD in current MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Immune-mediated neuropathy	Serious	Abdominal pain upper, Anhidrosis, Arthralgia, Asthenia, Autonomic neuropathy, Burning sensation, Chest pain, Decreased appetite, Electric shock sensation, Fatigue, Frustration tolerance decreased, Gait disturbance, Headache, Hypoaesthesia, Immune-mediated neuropathy, Impaired work ability, Loss of personal independence in daily activities, Muscle contractions involuntary, Muscle spasms, Muscle twitching, Nasal discomfort, Nausea, Nerve injury, Pain, Paraesthesia, Petechiae, Postural orthostatic tachycardia syndrome, Product dose omission issue, Skin burning sensation, Small fibre neuropathy, Tongue discomfort, Tremor, Urinary incontinence	Not Recovered/Not Resolved	Ventricular extrasystoles(H); Vertigo(H); Vitamin D decreased(H); Drug hypersensitivity; Drug hypersensitivity	VITAMIN D 3	Dose 1	0	11/2/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Asthenia, Demyelinating polyneuropathy, Diplopia, Eyelid ptosis, Facial paralysis, Gait inability, Limb discomfort, Paraesthesia	Recovered/Resolved	Benign prostatic hyperplasia(C); Hypertension(C); Hyperlipidaemia(C); Hypersensitivity	AMLODIPINE; BENAZEPRIL; ATORVASTATIN; VITAMIN D [COLECALCIFEROL]	Unknown		11/2/2021	Initial	NA (IRD in current MSSR)	
Spontaneous	Acute disseminated encephalomyelitis	Serious	Abdominal pain upper, Acute disseminated encephalomyelitis, Anxiety, Asthenia, Asthenopia, Balance disorder, Chest discomfort, Chest pain, Chills, Confusional state, Decreased appetite, Dizziness, Dyskinesia, Dysphagia, Dyspnoea, Dyspnoea exertional, Dysstasia, Ear infection, Ear pain, Eye pain, Fatigue, Head discomfort, Headache, Hyperacusis, Hypoaesthesia, Increased upper airway secretion, Limb discomfort, Loss of consciousness, Muscle discomfort, Muscular weakness, Musculoskeletal stiffness, Myalgia, Nausea, Neck pain, Oropharyngeal pain, Palpitations, Paraesthesia, Perfume sensitivity, Photophobia, Presyncope, Skin irritation, Throat tightness, Vaccination site pain, Vertigo, Vision blurred, Vitreous floaters	Unknown	Diabetes mellitusFH; Crohn's diseaseFH; Gastroesophageal reflux disease(C); MENINGOCOCCAL VACCINE; MENINGOCOCCAL VACCINE B; HPV VACCINE; TETANUS TOXOID VACCINE ADSORBED; MENINGOCOCCAL VACCINE B; HPV VACCINE; HEPATITIS A VACCINE; VARICELLA VACCINE; MEASLES MUMPS AND RUBELLA VACCINE LIVE ATTENUATED; POLIOVIRUS VACCINE, INACTIVATED; ACCELLULAR PERTUSSIS VACCINE; POLIOVIRUS VACCINE, INACTIVATED; HEPATITIS B VACCINE; PNEUMOCOCCAL CONJUGATE VACCINE; HAEMOPHILUS INFLUENZAE TYPE B CONJUGATE VACCINE; DIPHTHERIA, TETANUS AND ACCELLULAR PERTUSSIS; VARICELLA VACCINE; MEASLES MUMPS AND RUBELLA VACCINE LIVE ATTENUATED; PNEUMOCOCCAL CONJUGATE VACCINE; HEPATITIS B VACCINE; PNEUMOCOCCAL CONJUGATE VACCINE; HAEMOPHILUS INFLUENZAE TYPE B VACCINE CONJUGATED; HEPATITIS B VACCINE; DIPHTHERIA TETANUS ACCELLULAR PERTUSSIS; PNEUMOCOCCAL CONJUGATE VACCINE- POLIOVIRUS		Dose 2	157	11/2/2021	Initial	NA (IRD in current MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Demyelinating polyneuropathy	Serious	Angiogram pulmonary normal, Areflexia, Arthralgia, Asthenia, Back pain, Blood creatine phosphokinase increased, Blood immunoglobulin G normal, Blood immunoglobulin M normal, Chest X-ray normal, Computerised tomogram head normal, Computerised tomogram spine, CSF glucose normal, CSF protein increased, CSF test, CSF white blood cell count increased, Demyelinating polyneuropathy, Electrocardiogram normal, Fibrin D dimer increased, Guillain-Barre syndrome, Hypoaesthesia, Immunoglobulin therapy, Lumbar puncture, Muscular weakness, Neurological examination, Neuropathy peripheral, Paraesthesia, Pollakiuria, Pruritus, Pyrexia, Traumatic lumbar puncture, West Nile virus test negative	Unknown	Drug hypersensitivity; Hypertension(C); Hyperlipidaemia(C); Gastrooesophageal reflux disease(C); Arthritis(C); Gout(C); Obesity(C)	ALLOPURINOL; CELEBREX; VALSARTAN; SIMVASTATIN; SYMBICORT	Dose 2	0	11/9/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Non Serious	Abdominal pain upper, Acute disseminated encephalomyelitis, Asthenopia, Balance disorder, Chest pain, Chills, Computerised tomogram head normal, Confusional state, Costochondritis, Decreased appetite, Diplopia, Discomfort, Dizziness, Dyspnoea, Dysstasia, Ear discomfort, Ear inflammation, Ear pain, Eye pain, Fatigue, Gait disturbance, Head discomfort, Headache, Hyperacusis, Hypoaesthesia, Hypoaesthesia oral, Hypoaesthesia teeth, Magnetic resonance imaging abnormal, Memory impairment, Muscle disorder, Muscular weakness, Myalgia, Nausea, Neck pain, Oropharyngeal discomfort, Pain of skin, Paraesthesia, Paraesthesia oral, Parosmia, Photophobia, SARS-CoV-2 test negative, Sensory disturbance, Somnolence, Vertigo, Visual impairment, X-ray normal	Unknown			Dose 2	25	11/16/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Asthenia, Demyelinating polyneuropathy, Myalgia	Recovering/Resolving	Respiratory tract infection(H)		Unknown		11/17/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovering/Resolving			Unknown		11/16/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis	Recovered/Resolved			Unknown		11/24/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Herpes zoster reactivation	Recovering/Resolving	Oesophageal carcinoma(C); Deafness(C); Irritable bowel syndrome(C); Drug hypersensitivity; Osteoarthritis(C); Bladder transitional cell carcinoma(H)	HARPAGOMED; HEPA-S; CONDROSULF; MAGNESIUM DIASPORAL [MAGNESIUM CITRATE]; VITAMIN D3	Dose 2	12	11/24/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Non Serious	Acute disseminated encephalomyelitis, Bedridden, Cerebrovascular accident, Demyelination, Gait disturbance, Hypokinesia, Lymphoma, Neurological symptom	Not Recovered/Not Resolved			Dose 2	47	11/30/2021	Initial	NA (IRD in current MSSR)	

Report Type	PT	Case Seriousness	ALL PTs	Event Outcome	Medical History	Concomitant Medications	Dose no prior to onset (simplified)	Time to Onset (TTO) (Days)	Initial Receipt Date	Initial / Follow-up	Initial Case presented in previous MSSR	WW Identifier
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Immunglobulin therapy, Magnetic resonance imaging abnormal, Multiple sclerosis, Visual impairment	Not Recovered/Not Resolved			Dose 2	111	11/30/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Acute disseminated encephalomyelitis	Serious	Acute disseminated encephalomyelitis, Disseminated intravascular coagulation, Pneumonia aspiration, Renal failure, Sepsis	Not Recovered/Not Resolved			Dose 1	17	12/6/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Encephalomyelitis	Serious	Encephalitis, Encephalomyelitis	Not Recovered/Not Resolved	Type 2 diabetes mellitus(C); Dyslipidaemia(C)		Dose 2	14	12/6/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy, Dysaesthesia	Recovering/Resolving			Dose 1	0	12/22/2021	Initial	NA (IRD in current MSSR)	
Regulatory Authority	Demyelinating polyneuropathy	Serious	Demyelinating polyneuropathy	Unknown	Monoclonal gammopathy(H)		Unknown		12/23/2021	Initial	NA (IRD in current MSSR)	

Appendix 11.17b Acute Disseminated Encephalomyelitis (ADEM): Detailed Summary of Cumulative Data Concerning ADEM and Brighton’s Collaboration Level of diagnostic certainty 1 to 5: Case Narratives

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	This case was received via an unknown source (no reference has been entered for a health authority or license partner) on 15-Jun-2022 and was forwarded to Moderoa on 20-Jun-2022. This case, initially reported to the [REDACTED] by a [REDACTED] physician, was received via the [REDACTED]. On an unknown date, the patient received the 1st dose of a COVID-19 vaccine (product name unknown). On an unknown date, the patient received the 2nd dose of a COVID-19 vaccine (product name unknown). On 18-Feb-2022, at 16:15, the patient received the 3rd vaccination with this vaccine. Around 25-Feb-2022, the patient experienced malaise and high body temperature. Subsequently, pyrexia developed and subsided repeatedly. On 04-Mar-2022, the patient experienced headache. On 06-Mar-2022, consciousness disturbance with JCS of double digits was noted, and the patient visited the previous physician. Initially, meningitis was suspected as urinary retention and spinal fluid abnormality were found and head MRI showed no abnormalities. The patient received antimicrobial medication, acyclovir, and antifungal medication for the treatment of meningitis, and consciousness disturbance improved. On 18-Mar-2022, the patient was admitted to the reporting hospital. On 20-Mar-2022, complete paralysis (paraplegia) in both lower limbs was noted. On 22-Mar-2022, MRI of the cervical spine showed swelling throughout the length of the cervical spine and diffuse prolonged signals in T2 of the cervical spine. MRI of the brain showed multiple prolonged signals in T2 and a lesion in the deep gray matter. The patient was diagnosed with acute disseminated encephalomyelitis (ADEM). On an unknown date, after the patient was treated with 6 times of plasma exchange, 3 courses of steroid pulse therapy, and oral administration of steroids, paralysis of both lower limbs improved. On 28-Apr-2022, the patient was transferred to a recovery rehabilitation hospital. Gait disturbance and impaired urination remained as sequelae. The outcome of acute disseminated encephalomyelitis was reported as sequelae. Follow-up investigation will be made. Clinical manifestations Inflammatory demyelination was presumed to be the cause. The patient experienced the event for the first time. Clinically multifocal central nervous system disorder (event). Encephalopathy (alteration of consciousness and behavioral change) which was unable to be explained by pyrexia. As localized or multiple findings that were attributable to the central nervous system, encephalopathy, localized cortical signs, primitive reflexes, motor paralysis, sensory abnormality, and alteration in deep tendon reflexes developed on 06-Mar-2022. Image test (MRI) (Date of test: 22-Mar-2022) Both or either of the following two criteria of MRI for multiple sclerosis were met: Demonstration of spatial multiplicity by MRI: One or more T2 lesions were shown in at least	MRI, cervical spine: swelling throughout the length of the cervical spine and diffuse prolonged signals in T2. MRI brain: multiple prolonged signals in T2 and a lesion in the deep gray matter. No infectious disease panel reported.	Level 2	Level 5	Level 5	Unclassified	This is a spontaneous case concerning a 25 year old female, with no reported past medical condition and concomitant medications, who received heterologous dose 3 Spikevax and 7 days post vaccine, experienced progressive malaise, fever, headache, 'disturbance of consciousness' and urinary retention. Diagnostic results: CSF abnormality (specifics not provided), MRI head: no abnormality. Treated with antimicrobials, antiviral and antifungal, with improvement of level of consciousness. 31 days post vaccine, patient developed paraplegia. Repeat MRI, cervical spine: MRI of the cervical spine showed swelling throughout the length of the cervical spine and diffuse prolonged signals in T2 of the cervical spine. MRI of the brain showed multiple prolonged signals in T2 and a lesion in the deep gray matter. Dx: ADEM. Treated with steroids, and plasma. Patient recovered with sequelae. This case is classified as Brighton's level 2 ADEM based on MRI brain findings consistent with ADEM. According to WHO-UMC causality assessment, the case is assess as Unclassified due to missing relevant information, including medical history and concomitant medications, and information can not be complemented.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	two of the four CNS regions (periventricular, subcutaneous, infratentorial, spinal cord). Demonstration of temporal multiplicity by MRI: Asymptomatic gadolinium-enhanced lesions and asymptomatic non-enhanced lesions coexist. Or there are new symptomatic or asymptomatic T2 lesions and/or gadolinium-enhanced lesions that developed later compared with baseline MRI. Course of the disease The period between the onset and the final observation was two months. The disease had a monophasic pattern, and considering the nadir of the symptoms, no recurrence was seen within at least three months. Company Comment: The event developed after the administration of ELASOMERAN and there is temporal relationship.							
	This regulatory authority case was reported by an other health care professional and describes the occurrence of ENCEPHALITIS (Encephalitis / Encephalomyelitis) and ENCEPHALOMYELITIS (Encephalitis / Encephalomyelitis) in a 53-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. Concurrent medical conditions included Hypertension. On 07-Mar-2022, the patient received third dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 24-Mar-2022, the patient experienced ENCEPHALITIS (Encephalitis / Encephalomyelitis) (seriousness criterion hospitalization) and ENCEPHALOMYELITIS (Encephalitis / Encephalomyelitis) (seriousness criterion hospitalization). At the time of the report, ENCEPHALITIS (Encephalitis / Encephalomyelitis) and ENCEPHALOMYELITIS (Encephalitis / Encephalomyelitis) was resolving. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Concomitant medication was not provided. On 07-Mar-2022, it was reported as patient received BNT vaccine on October 30 and December 12, 2021. Vaccination on March 7, 2022 (Moderna 3rd shot). He denied recent fever, infection, AGE, trauma, illicit drug use, and alcohol consumption. His baseline activity of daily life was total independent. He worked as a driver. Since March 24 evening about 17:00-18:00, his wife noticed him talking about strange thought (He said that when visiting his uncle who died a while ago, he saw the other dead people. He said that there had always been pictures in his mind and talked about the cycle of life and death of strange forces and gods, but he was still in the scope of carrying out conservation).	MRI brain: no infarction or hemorrhage. CSF analysis: negative for pathogens. WBC: 0	NOT a case of ADEM.	Level 4	Level 5	Unclassified	This is a regulatory authority reported case concerning a 53-year-old male patient with concurrent medical conditions including hypertension, no concomitant medication history provided. He received heterologous Spikevax third dose/booster (primary series - BNT/Pfizer) and 17 days post dose 3, reported changes in behavior, agitation, irrational speech and hallucination. Neurological examination showed no obvious focal weakness, except agitation. Diagnostic imaging not consistent with ADEM. This case is classified as NOT a case of ADEM. According to WHO-UMC causality assessment, this case is assessed as Unclassified, based on missing relevant information, that cannot be comple. More relevant information is needed for proper assessment. However, information can not be complemented.	

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	Besides, he was still able to communicate and do daily activities. On March 25 morning, he went to work. At about 14:00, his wife received his phone call saying "I just got stuck, and I cannot make it". Then she asked his company to go and look for him, finding him staying there doing nothing, then he was sent to hospital. After admission at neurological ward, aspirin was given. On the first day, his consciousness was shifting between clear and obtunded status. On 26-Mar-2022, at 01:00-02:00, his wife noticed him mumbling nonsense, agitation (four limbs shaking against control), shifting from elated mood to worrisome, and sexual hyperactivity [REDACTED]. Due to worsening condition, brain magnetic resonance images (MRI) was done at hospital and it showed no infarction, and hemorrhage. Then he was transferred to our emergent department for further evaluation, under the impression of suspect encephalitis. At emergent department of our hospital, neurological examination showed no obvious focal weakness, except agitation, and the patient tapped the mobile phone and claimed to be playing games, but it was stuck in the same picture. Cerebrospinal fluid showed no infection (WBC = 0), borderline elevated The Worldwide UID was reported as [REDACTED] Company Comment- This is a regulatory case concerning a 53-year-old male patient with no relevant medical history, who experienced the unexpected serious adverse events of special interest, Encephalitis and Encephalomyelitis. The events were medically significant and led to the hospitalization of the patient as reported by the regulatory authority and occurred 17 days after receiving the third dose of mRNA-1273 Vaccine. As reported, 17 days after receiving the vaccine, the patient had changes in behavior and became agitated, patient was then rushed at the hospital. Initial physical examination findings did not any focal weakness, diagnostic and laboratory examinations were all normal, patient was given supportive treatment and improved however it was noted still had problems with thinking and had an episode of chest pain with noted t-wave inversion in the EKG but with normal cardiac markers. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 25-Apr-2022: No new information received.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 18-Apr-2022 and was forwarded to Moderna on 18-Apr-2022.	No MRI brain report. SARS-CoV-2 test: negative	Level 4	Level 5	Level 4	Unlikely	This is a regulatory authority reported case concerning a 57-year-old male patient with a past medical history of cardiac failure, nephropathy requiring	

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	This regulatory authority case was reported by a physician and describes the occurrence of DEMYELINATING POLYNEUROPATHY (POLYNEUROPATHY OF DEMYELINATING SPECIES), MUSCULAR WEAKNESS (DECREASED MUSCLE STRENGTH (LOWER LEG), WHEELCHAIR-BOUND) and WHEELCHAIR USER (WHEELCHAIR-BOUND) in a 57-year-old male patient who received mRNA-1273 (Spikevax) (batch no. [REDACTED]) for COVID-19 vaccination. The patient's past medical history included Nephropathy, Cardiac failure (Skin rash 4 days after Tazocin insertion), Dialysis in March 2021, Skin rash (Skin rash 4 days after Tazocin insertion) and Sepsis. Concurrent medical conditions included Diabetes with unspecified complication (Diabetes mellitus type 2 with multiple complications, incl dialy-intensive renal failure), Renal failure (dialy-intensive renal failure) and Neuropathy. On 30-Mar-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) .5 milliliter. On 30-Mar-2021, the patient experienced MUSCULAR WEAKNESS (DECREASED MUSCLE STRENGTH (LOWER LEG), WHEELCHAIR-BOUND) (seriousness criterion disability) and WHEELCHAIR USER (WHEELCHAIR-BOUND) (seriousness criterion disability). On an unknown date, the patient experienced DEMYELINATING POLYNEUROPATHY (POLYNEUROPATHY OF DEMYELINATING SPECIES) (seriousness criterion disability). At the time of the report, DEMYELINATING POLYNEUROPATHY (POLYNEUROPATHY OF DEMYELINATING SPECIES), MUSCULAR WEAKNESS (DECREASED MUSCLE STRENGTH (LOWER LEG), WHEELCHAIR-BOUND) and WHEELCHAIR USER (WHEELCHAIR-BOUND) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, SARS-CoV-2 test: negative (Negative) negative. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medications were provided by the reporter. No treatment information was provided by the						dialysis; and concurrent medical conditions of type 2 diabetes mellitus with multiple complications including renal failure and neuropathy. No concomitant medication was reported. The patient received an unknown dose of Spikevax and on the same day, was reported to experience lower legs muscular weakness that required wheelchair use, and associated demyelinating polyneuropathy. Inadequate medical history and clinical course of events. No diagnostic results reported except for a negative COVID-19 test. No MRI brain report. This case is classified as Brighton's Level 4 ADEM due to insufficient evidence to meet level 1,2 or 3 of the case definition. The WHO-UMC causality assessment is Unlikely, based on the rather short time to onset that makes a relationship with the use of the product and the event improbable. Comorbidities (T2DM, renal failure, neuropathy) are strong confounders and provide plausible explanations.	

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	reporter. Company comment: This is a regulatory authority case concerning a 57-year-old male patient with medical history of cardiac failure and sepsis; and concurrent medical conditions of diabetes mellitus type 2 with multiple complications including dialysis, renal failure and neuropathy who experienced serious (disability), unexpected events of muscular weakness on lower legs and wheelchair user on the same date after the administration of mRNA-1273 vaccine. Additionally, on an unknown date, the patient experienced serious (disability) event of demyelinating polyneuropathy. No further details regarding clinical course, diagnostic tests or treatment performed were disclosed. Patient's medical history and concurrent medical conditions remain confounders. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.							
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 25-Apr-2022 and was forwarded to Moderna on 02-May-2022. This case was presented at "The 120th [REDACTED]" and since the proprietary name of the suspect drug was not specified, the drug is handled as a Takeda product in this case report. Acute disseminated encephalomyelitis was assessed as serious by the MAH. This case concerned a 51-year-old female patient. The patient received the 2nd dose of SARS-CoV-2 m-RNA vaccine (the proprietary name was unknown) on X-4 day. The patient experienced headache since X-2 day. The patient turned to the state of unrest and emergently transferred by ambulance on X day. Mild disturbed consciousness Neurologically categorized into JSC 1 was noted. The patient was Negative SARS-CoV-2 PCR test. Blood test revealed Negative for either AntiAQP4 antibody and AntiMOG antibody. Cerebrospinal fluid tests revealed Cell count, 1/mcL; Protein count, 55 mg/dL which indicated albuminocytologic dissociation, and negative for both Myelin basic protein and Oligoclonal band. Contrast-enhanced head MRI revealed T2 high signal lesion disseminated under cerebral cortex white matter, however, Gd contrast-enhanced effect was absent. Concluding from the clinical courses and neurological findings, the patient was diagnosed with acute disseminated encephalomyelitis. The symptoms were improved with steroid pulse therapy 2 courses. Follow-up investigation will be made. Company Comment: The event developed after the administration of elasomeran and there is temporal relationship.	MRI head: T2 high signal lesion disseminated under cerebral cortex white matter. SARS-CoV-2 PCR test: negative. AntiAQP4 antibody and AntiMOG antibody: negative. CSF: WBC- 1/mcL; Protein-55 mg/dL. Myelin basic protein and Oligoclonal band: negative	Level 2	Level 3	Level 5	Conditional	This regulatory authority reported case concerns a 51-year-old female patient with no reported medical history and concurrent medication, who received dose 2 Spikevax and 4 days post-vaccine, experienced restlessness and mildly distorted level of consciousness (JCS 1- awake without stimuli). Diagnostic reports: MRI brain: diffuse white matter lesion, ID panels: negative. Dx-ADEM. Treated with steroid. Event outcome not reported. This case is classified as Brighton's level 2 ADEM based on MRI brain report, and assessed as WHO-UMC Conditional due to insufficient medical history and concomitant medication information. More information for proper assessment is needed.	
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 31-May-2022 and was forwarded to Moderna on 31-May-2022. This regulatory authority case was reported by a consumer and describes the occurrence of	No MRI brain report	Level 4	Level 4	Level 4	Not assessable	A regulatory authority reported case concerning a 41-year-old female, with past medical history including hypoaesthesia, vitamin D deficiency and hypothyroidism; no reported concomitant medications; who received dose 2	

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	ENCEPHALOMYELITIS (Encephalomyelitis), ENCEPHALITIS (Encephalitis), HYPOAESTHESIA (Hypoesthesia on both sides and below without motor deficits) and DEMYELINATION (Demyelinating diseases of the central nervous system, unspecified) in a 41-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The patient's past medical history included Hypoesthesia (comorbid diagnosis), Vitamin D deficiency (comorbid diagnosis) and Hypothyroidism (comorbid diagnosis). On 12-Apr-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) .5 milliliter. On 02-Jun-2021, received second dose of mRNA-1273 (Spikevax) (Intramuscular) dosage was changed to .5 milliliter. On 05-Jun-2021, the patient experienced ENCEPHALOMYELITIS (Encephalomyelitis) (seriousness criteria hospitalization and medically significant), ENCEPHALITIS (Encephalitis) (seriousness criteria hospitalization and medically significant), HYPOAESTHESIA (Hypoesthesia on both sides and below without motor deficits) (seriousness criterion hospitalization) and DEMYELINATION (Demyelinating diseases of the central nervous system, unspecified) (seriousness criteria hospitalization and medically significant). At the time of the report, ENCEPHALOMYELITIS (Encephalomyelitis), ENCEPHALITIS (Encephalitis), HYPOAESTHESIA (Hypoesthesia on both sides and below without motor deficits) and DEMYELINATION (Demyelinating diseases of the central nervous system, unspecified) was resolving. No concomitant medication was reported. No treatment information was reported. Company Comment: This regulatory authority case concerns a 41-year-old female, with relevant past medical history of hypoesthesia, who experienced unexpected, serious (hospitalization and medically significant) AESI encephalitis, AESI encephalomyelitis and demyelination with hypoesthesia, around 3 days after receiving a second dose of mRNA-1273. Clinical course, labs, concomitant medications, and treatment details were not reported. The outcome of the events was recovering. The medical history of hypoesthesia could be confounding factor for hypoesthesia. In addition, the first and second doses of mRNA-1273 were given around 51 days apart (inappropriate schedule of vaccine administered). The benefit risk relationship of mRNA-1273 is not affected by this					Spikevax and 3 days post-vaccine, reported "encephalomyelitis, demyelination with hypoesthesia". Details of clinical features were not provided. The clinical course, diagnostic results/MRI and infectious disease panels, and treatment details were not reported. The outcome of the events was recovering. This case is classified as Brighton's level 4 ADEM due to insufficient evidence to meet any level of the case definition. According to WHO-UMC causality assessment, this case is NOT assessable, since it does not meet Brighton's levels 1-3 case definition for ADEM. The presence of comorbidities (hypoesthesia and hypothyroidism) are strong co-founders for the occurrence of the events.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	report. Event seriousness is assessed as per regulatory authority's report.							
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 06-Jun-2022 and was forwarded to Moderna on 09-Jun-2022. This case, initially reported to the [REDACTED] by a [REDACTED] (physician), was received via the [REDACTED]. Concomitant drugs: steroid 6 mg On an unknown date, the patient received the 1st dose of non-company coronavirus modified uridine RNA vaccine (SARS-CoV-2). On an unknown date, the patient received the 2nd dose of non-company coronavirus modified uridine RNA vaccine (SARS-CoV-2). On 26-Mar-2022, the patient received the 3rd vaccination with this vaccine. On 29-Mar-2022, acute disseminated encephalomyelitis (ADEM) developed. Limitation of eye movement and diplopia suddenly developed. On 04-Apr-2022, the patient visited an ophthalmologist, and MRI showed multiple lesions with high signal intensities in T2 in the brain. ADEM after vaccination with this vaccine or worsening of MOG antibody-associated disease was considered. On 05-Apr-2022, the patient was hospitalized in the neurology department of the reporting hospital for treatment. MRI showed lesions in many regions including the cerebral cortex, white matter, thalamus, brainstem, and right trigeminal nerve, but the patient had only diplopia as subjective symptoms. On an unknown date, while the patient was in the hospital, steroid pulse therapy was performed, and the diplopia tended to improve but did not fully improve; therefore, the second steroid pulse therapy was performed. Subsequently, oral administration of prednisolone was started with the dose of 60 mg, which was then tapered. On 06-May-2022, the symptoms were improving without worsening, and the patient was discharged from the hospital when the dose of prednisolone was reduced to 30 mg. The symptoms were resolving. The patient was going to be followed up on an outpatient basis. The outcome of limitation of eye movement, diplopia, acute disseminated encephalomyelitis, and worsening of MOG antibody-associated disease was reported as resolving. Follow-up investigation will be made. Clinical symptom. Inflammatory demyelination was presumed to be the cause. • The patient had a history of optic neuritis, a demyelinating disease of the central nervous system. • It was clinically multifocal central nervous system disorder (event). • As localized or multiple findings that could be attributed to the central nervous system, either single abnormality or multiple abnormalities of cranial nerves, changes in deep tendon reflexes (diminished or increased reflexes and asymmetry of reflexes), or cerebellar dysfunction (ataxia, dysmetria, cerebellar nystagmus, and others) developed on 29-Mar-2022. Course of the disease • The time from onset to last observation was one month. • The observation	MRI showed multiple lesions with high signal intensities in T2. Anti-aquaporin 4 (AQP4) antibody negative (r/o Neuromyelitis optica (NMO), anti-MOG antibody positive	NOT a case of ADEM. Case of MOGAD	Level 5	Level 5	Unlikely	This is a regulatory authority reported case concerning a 38 year-old male patient with a medical history of optic neuritis, and no reported concomitant medications, who received dose 3 Spikevax and 3 days post-vaccine, experienced limitation of eye movement and sudden onset of diplopia. Diagnostic results: MRI showed multiple lesions with high signal intensities in T2. Anti-aquaporin 4 (AQP4) antibody negative (r/o Neuromyelitis optica (NMO), anti-MOG antibody positive. The event resolved after one month. This case is classified as Brighton's level 5, NOT a case of ADEM, but rather a case of Myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOGAD) based on the positive anti-MOG antibody. According to WHO-UMC causality assessment, this case is Unlikely related to the product. The history of optic neuritis and MOGAD provide more plausible explanation for the occurrence of the events.	

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	period after onset was less than three months, which was insufficient to show a monophasic pattern of disease. Differential diagnosis • There were other obvious acute infections or other diseases that could explain the illness Testing for autoantibodies (Date of exam: 09-Jul-2021) • Anti-AQP4 antibody negative, anti-MOG antibody positive Reporter comments continuation: However, it is difficult to consider the effect of the dose reduction because almost one month had passed since the dose reduction. The symptoms developed in a few days after the vaccination with this vaccine, giving the impression that the onset and progress of the disease was earlier than those of common ADEM. It is difficult to judge clinically whether MOG antibody-associated disease, which relapses easily, recurred coincidentally at that time or it was related to this vaccine. Company Comment: The events developed after the administration of ELASOMERAN and there is temporal relationship.							
	This regulatory authority case was reported by an other health care professional and describes the occurrence of LETHARGY (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), ASTHENIA (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), GAIT DISTURBANCE (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), FALL (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), DIZZINESS (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), POLLAKIURIA (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), INCONTINENCE (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), CONSTIPATION (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no	MRI brain: expansile high signal on t2wi and faintly high Expansile high signal on T2WI and faintly high signal on T1WI suspected inflammation at bilateral pons and midbrain. CSF analysis: elevated protein (82.1), normal cell count (WBC 3), and negative PNS panel. Other panels negative.	Level 2	Level 5	Level 3	Conditional	This is a regulatory authority reported case concerning a 58-year-old female patient, with no reported medical history and concomitant medications, who received dose 3 Spikevax and 13 days post-vaccine, experienced lethargy, generalized weakness of lower limbs, gait disturbance, dizziness, urinary incontinence, constipation, no reported loss of consciousness. Diagnostic reports: MRI brain: suspected inflammation at bilateral pons and midbrain. CSF analysis: elevated protein (82.1), normal cell count (WBC 3), and negative PNS panel. Other panels negative. This case is classified as Brighton's level 2 ADEM based on MRI brain expansile high signal findings, and assessed as WHO Conditional, due to missing relevant information including medical history and concomitant medications. More information for proper assessment is needed.	

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	significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), ENCEPHALITIS (Encephalitis/ Encephalomyelitis), ENCEPHALOMYELITIS (Encephalitis/ Encephalomyelitis) and MUSCULAR WEAKNESS (Limb weakness) in a 58-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. No Medical History information was reported. On 02-Mar-2022, the patient received third dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) .25 milliliter. On 15-Mar-2022, the patient experienced LETHARGY (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), ASTHENIA (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), GAIT DISTURBANCE (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), FALL (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), DIZZINESS (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), POLLAKIURIA (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), INCONTINENCE (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), CONSTIPATION (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant							

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	injury), worsened dizziness, urinary frequency with occasional incontinence, consti) (seriousness criterion hospitalization), ENCEPHALITIS (Encephalitis/ Encephalomyelitis) (seriousness criterion hospitalization), ENCEPHALOMYELITIS (Encephalitis/ Encephalomyelitis) (seriousness criterion hospitalization) and MUSCULAR WEAKNESS (Limb weakness) (seriousness criterion hospitalization). The patient was treated with CEFTRIAXONE at an unspecified dose and frequency; PREDNISOLONE at an unspecified dose and frequency; BIPERIDEN at an unspecified dose and frequency; CLONAZEPAM at an unspecified dose and frequency; VITAMIN B12 [VITAMIN B12 NOS] at an unspecified dose and frequency and METHYLPREDNISOLONE (intravenous) from 25-May-2022 to 29-May-2022 at a dose of 1000 milligram once a day. At the time of the report, LETHARGY (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), worsened dizziness, urinary frequency with occasional incontinence, consti), ASTHENIA (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), GAIT DISTURBANCE (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), FALL (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), DIZZINESS (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), POLLAKIURIA (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), INCONTINENCE (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), CONSTIPATION (Lethargy, generalized weakness (weak lower limbs, and speech in a very low voice), gait disturbance with falling incidence twice (but no significant injury), worsened dizziness, urinary frequency with occasional incontinence, consti), ENCEPHALITIS (Encephalitis/ Encephalomyelitis), ENCEPHALOMYELITIS (Encephalitis/ Encephalomyelitis) and MUSCULAR							

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	WEAKNESS (Limb weakness) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 06-Apr-2022, Electroencephalogram: normal (normal) normal. On 06-Apr-2022, Laboratory test: normal (normal) normal. On 06-Apr-2022, Laryngoscopy: normal (normal) normal. On 29-Apr-2022, Magnetic resonance imaging head: high t2 signal and contrast enhancement High T2 signal and contrast enhancement over bilateral midbrain, pons, right thalamus and cerebellum. Favor post-viral infection lobar encephalitis. Malignancy is less likely (symmetry lesion)							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 18-Feb-2022 and was forwarded to Moderna on 18-Feb-2022. This regulatory authority case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 31-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 000105A) for COVID-19 vaccination. No Medical History information was reported. On 16-Dec-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 3 dosage form. On 17-Dec-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization and medically significant). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) had not resolved. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. Concomitant Medication use information was not provided by reporter. Treatment Medication use information was not provided by reporter Patient had already been vaccinated twice with Spikevax and unfortunately none further information available. Company comment-This is a regulatory case concerning a 31-year-old female patient with no medical history reported who experienced the unexpected and serious (medically significant and	No MRI report	Level 4	Level 4	Level 4	Unlikely	This is a regulatory authority reported case concerning a 31-year-old female patient with no medical history and concomitant medications reported, who received dose 3 Spikevax and one day post-vaccine, experienced unspecified symptoms and diagnosed with acute disseminated encephalomyelitis. No brain MRI or diagnostic reports were provided. Event had not resolved at the time of report. This case is missing relevant information including medical history, concomitant medications, and diagnostic results, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unlikely, based on the short time to onset that makes a relationship of the event with Spikevax improbable. The lack of relevant information is a challenge in assessing for causality in this case.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	hospitalization) event of acute disseminated encephalomyelitis the following day a third dose of mRNA-1273 vaccine was administered. The outcome was reported as not recovered. No further clinical information was provided for medical reviewing. The benefit-risk relationship of the mRNA-1273 vaccine is not affected by this report. Has already been vaccinated twice with Spikevax, unfortunately none further information available							
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 22-Feb-2022. The most recent information was received on 03-Mar-2022 and was forwarded to Moderna on 03-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 40-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The patient's past medical history included COVID-19 in November 2020. On 21-Dec-2021, the patient received second dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 22-Dec-2021, after starting mRNA-1273 (Spikevax), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criterion hospitalization). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) had resolved with sequelae. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medication was reported. No treatment information was provided. Company Comment: This regulatory authority report concerns a 40-year-old male patient, with a medical history of COVID-19, who experienced the unexpected serious (seriousness criterion-Caused/prolonged hospitalization) event of Acute disseminated encephalomyelitis (AESI). The event occurred 1 day after the second dose of mRNA-1273 vaccine. There is no available information regarding clinical course and treatment medication. At the time of report, event had resolved with sequelae (4 weeks duration). The patient's medical history of COVID-19, which can cause acute disseminated encephalomyelitis, remains a confounder. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.	No MRI report. Hx of COVID-19 infection	Level 4	Level 4	Level 4	Unlikely	This regulatory authority report concerns a 40-year-old male patient, with a medical history of COVID-19 (2020), no concomitant medications reported, who received dose 2 Spikevax and one day post-vaccine, experienced unspecified symptoms and diagnosed with acute disseminated encephalomyelitis. No report of clinical course and treatment medication. No brain MRI or diagnostic reports were provided. Event had resolved with sequelae at the time of report. This case is missing relevant information including concomitant medications, and diagnostic results, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unlikely, based on the short time to onset that makes a relationship of the event with Spikevax improbable. The medical history of COVID-19 infection is a confounder. The lack of relevant information is a challenge in assessing for causality in this case.	

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	Most recent FOLLOW-UP information incorporated above includes: On 03-Mar-2022: Significant Follow-up received: start date of medical history updated.							
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 21-Feb-2022 and was forwarded to Moderna on 28-Feb-2022. This case was reported by a physician via a medical representative. On an unknown date, the patient received the 1st dose of this vaccine. On an unknown date, the patient received the 2nd dose of this vaccine. Around 04-Feb-2022, the patient received the 3rd dose of this vaccine. Around 05-Feb-2022, pyrexia and headache developed. On 18-Feb-2022, encephalomyelitis developed. The patient had pyrexia of 39 degrees Celsius and headache and visited an emergency outpatient department. CT and MRI scan were performed. There were findings of brain swelling. Cerebral blood flow was confirmed. Herpes was negative. On an unknown date, the patient was hospitalized. The outcome of encephalomyelitis was unknown. Follow-up investigation will be made. Company Comment: The event developed after the administration of ELASOMERAN and there is temporal relationship. Sender's comments: The event developed after the administration of ELASOMERAN and there is temporal relationship. Sender's comments: The event developed after the administration of ELASOMERAN and there is temporal relationship.	CT & MRI: brain swelling. Herpes: negative	Level 4	Level 4	Level 4	Conditional	This is a regulatory authority reported case concerning a 66-year-old female patient with no medical history and concomitant medications reported, who received dose 3 Spikevax and 14 days post-vaccine, experienced unspecified symptoms and diagnosed with acute disseminated encephalomyelitis. Clinical course and treatment not provided. CT & MRI brain shows brain swelling (vague report). Herpes was negative. Event outcome was unknown. Follow-up investigation will be made. This case is missing relevant information including medical history, concomitant medications, and detailed MRI report, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Conditional. More data for proper assessment is needed.	
	This spontaneous case was reported by an other health care professional and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM (After the third vaccination)) in a 62-year-old male patient who received mRNA-1273 (COVID 19 Vaccine Moderna) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included Hepatitis C (Treatment was completed). On 15-Feb-2022, the patient received third dose of mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 16-Feb-2022, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM (After the third vaccination)) (seriousness criterion medically significant) and VACCINATION SITE PAIN (Pain at the vaccination site (After the third vaccination)). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM (After the third vaccination)) had not resolved and VACCINATION SITE PAIN (Pain at the vaccination site (After the third vaccination)) outcome was unknown.	Multiple white matter lesions in the cerebrum	Level 2	Level 4	Level 4	Possible	A Spontaneous reported case concerning a 62-years-old male patient with past medical history of clinical hepatitis C (completed treatment course), no concomitant medication reported, who one day post dose 3 Spikevax reported left hemiplegia predominantly in the upper extremity and diagnosed with ADEM. Brain MRI: diffuse white matter lesions in the cerebrum. This case is classified as Brighton's level 2 ADEM based on brain MRI finding. This case is assessed as WHO Possible, based on temporal association. However, the presence of alternative association (history of HCV infection), provide a more plausible explanation for the occurrence of the events. ADEM is associated with HCV infection.	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 16-Feb-2022, Nerve conduction studies: paralysis Test Result:Paralysis. On 16-Feb-2022, Reflex test: were observed changes. were observed changes.. On 16-Feb-2022, Sensory level: abnormalities Test Result: Abnormalities. On 25-Feb-2022, Alanine aminotransferase: 113 Test Result:113. On 25-Feb-2022, Aspartate aminotransferase: 71 Test Result:71. On 25-Feb-2022, Basophil count: 0.0 Test Result:0.0. On 25-Feb-2022, Blood alkaline phosphatase: 120 Test Result:120. On 25-Feb-2022, Blood chloride: 101 Test Result:101. On 25-Feb-2022, Blood creatine phosphokinase: 128 Test Result:128. On 25-Feb-2022, Blood creatinine: 0.82 Test Result:0.82. On 25-Feb-2022, Blood glucose: 107 Test Result:107. On 25-Feb-2022, Blood lactate dehydrogenase: 263 Test Result:263. On 25-Feb-2022, Blood potassium: 5.1 Test Result:5.1. On 25-Feb-2022, Blood sodium: 139 Test Result:139. On 25-Feb-2022, Blood triglycerides: 245 Test Result:245. On 25-Feb-2022, Blood urea: 15.2 Test Result:15.2. On 25-Feb-2022, Blood uric acid: 7.4 Test Result:7.4. On 25-Feb-2022, C-reactive protein: 0.09 Test Result:0.09. On 25-Feb-2022, Eosinophil count: 1.0 Test Result:1.0. On 25-Feb-2022, Erythroblast count: 0,0 Test Result:0,0. On 25-Feb-2022, Gamma-glutamyltransferase: 57 Test Result:57. On 25-Feb-2022, Grip strength: right 40 kg Test Result:Right 40 kg, left 32 kg Test Result:Left 32 kg and muscular weakness and sensory disturbance of the- Muscular weakness and sensory disturbance of the left upper extremity were noted.. On 25-Feb-2022, Haematocrit: 50.5 Test Result:50.5. On 25-Feb-2022, Haemoglobin: 18.1 Test Result:18.1. On 25-Feb-2022, High density lipoprotein: 49 Test Result:49. On 25-Feb-2022, Imaging procedure: abnormal • Diffuse or multiple white matter lesions were seen on T2-weighted, diffusion-weighted (DWI), or							

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	FLAIR images. • Diffuse, ill-defined, and large (larger than 1 to 2 centimeters) lesion was predominantly seen in the white matter of the cerebrum. • Both or either of the following criteria in MRI for multiple sclerosis were not met. <Proof of spatial multiplicity by MRI> • One or more T2 lesion(s) in at least two of the four CNS regions (periventricular, subcortical, subventricular, and spinal cord) (The lesion does not have to be a contrast-enhanced image. In patients presenting with symptoms of brainstem or spinal cord, the foci responsible for those symptoms should be excluded.) <Proof of temporal multiplicity by MRI> Asymptomatic gadolinium-enhanced lesion and asymptomatic non-enhanced lesion are present at the same time (at any point in time). Alternatively, new symptomatic or asymptomatic T2 lesions and/or gadolinium-enhanced lesions that appeared later (at any time) compared to the MRI at the reference time point. [Disease course] • The duration from onset to last observation was seven days.. On 25-Feb-2022, Laboratory test: 0.0 Test Result:0.0 and 0.0 Test Result:0.0. On 25-Feb-2022, Low density lipoprotein: 125 Test Result:125. On 25-Feb-2022, Lymphocyte count: 32.0 Test Result:32.0. On 25-Feb-2022, Magnetic resonance imaging head: abnormal A relatively new lesion was seen in the right thalamus, with high signal intensities in T2/FLAIR of 10.8 mm in major axis length, T1 iso, and slightly high signal intensities in DW.. On 25-Feb-2022, Mean cell haemoglobin: 32.1 Test Result:32.1. On 25-Feb-2022, Mean cell haemoglobin concentration: 35.8 Test Result:35.8. On 25-Feb-2022, Mean cell volume: 90 Test Result:90. On 25-Feb-2022, Monocyte count: 6.0 Test Result:6.0. On 25-Feb-2022, Neutrophil count: 3.0 Test Result:3.0 and 58.0 Test Result:58.0. On 25-Feb-2022, Platelet count: 15.1 Test Result:15.1. On 25-Feb-2022, Protein total: 8.3 Test Result:8.3. On 25-Feb-2022, Red blood cell count: 564 Test Result:564. On 25-Feb-2022, White blood cell count: 9460 Test Result:9460. On 01-Mar-2022, C-reactive protein: 0.09 Test Result:0.09. On 01-Mar-2022, White blood cell count: 9460 Test Result:9460. On 04-Mar-2022, Nerve conduction studies: abnormal The motor function of the fingers of the left hand was almost improved. Numbness remained a bit..							

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	For mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM (After the third vaccination)) and VACCINATION SITE PAIN (Pain at the vaccination site (After the third vaccination)) to be possibly related. COMPANY COMMENT: This is an Spontaneous case concerning a 62-years-old male patient with clinical history of hepatitis c who experienced the unexpected event of Acute disseminated encephalomyelitis (AESI) and other expected event 1 days after 3rd dose of mRNA-1273 vaccine. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Terms and onset were captured as provided. The case was assessed as serious by the Regulatory Authority's report due to IME Most recent FOLLOW-UP information incorporated above includes: On 23-Mar-2022: Follow-up received and updated: Patient Information, Lab Data, Product Information, Event Information, Narrative, Reporter Comments [Clinical condition]. Since the symptoms developed on the day after the administration of the vaccine, the occurrence of the adverse event is temporally related to the timing of the vaccine administration. On the following day of the third vaccination with this vaccine, left hemiplegia predominantly in the upper extremity appeared, and head MRI on the 10th day after the vaccination showed lesions suggestive of demyelination, which showed a rapid improving trend after steroid therapy. See "narrative" section							
	This case was received via an unknown source (no reference has been entered for a health authority or license partner) on 01-Mar-2022 and was forwarded to Moderna on 02-Mar-2022. This regulatory authority case was reported by an other health care professional and describes the occurrence of ENCEPHALITIS (Encephalitis/Encephalomyelitis) and ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis) in a 74-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for an unknown indication. Concurrent medical conditions included Diabetes mellitus, Hypertension and Hyperlipidemia. On 15-Feb-2022, the patient received third dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) .25 milliliter. On 15-Feb-2022, the patient experienced ENCEPHALITIS	No acute infarction or inflammatory lesion seen. MRI finding inconsistent with ADEM.	NOT a case of ADEM	Level 4	Level 4	Unlikely	A regulatory authority reported case concerning a 74-year-old elderly female patient, with concurrent medical conditions including diabetes mellitus, hypertension and hyperlipidemia; no concomitant medications reported, who was found to be unconscious, a day post dose 3 Spikevax. Diagnostic reports: MRI brain - no acute infarction or inflammatory lesion seen (MRI finding inconsistent with ADEM), CSF cytology: WBC < 5 /ML and protein 93.2 mg/dL. No treatment were reported. The event had not resolved at the time of report. This case is classified as Brighton's level 5: NOT a case of ADEM, based on MRI findings inconsistent of demyelination/ inflammation. And case is assessed as WHO "Unlikely" based on the short latency time that makes a relationship of the event with Spikevax improbable. The presence of comorbidities	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Encephalitis/Encephalomyelitis) (seriousness criterion life threatening) and ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis) (seriousness criterion life threatening). At the time of the report, ENCEPHALITIS (Encephalitis/Encephalomyelitis) and ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis) had not resolved. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No concomitant products were reported. On 16-02 the patient was found to be unconscious by family members and was admitted to the hospital through ER. During her hospitalization her condition did not significantly improve. On 17-02-2022, brain MRI was performed, no acute infarction or inflammatory lesion was observed. On 18-02-2022, patient's CSF: WBC < 5 /ML and protein 93.2 mg/dL. On 19-02 her left leg muscle strength recovered slightly and she was immediately transferred to another hospital On 21-02-2022 follow up carried out, patient's daughter mentioned that the patient was currently unconscious and was transferred to the intensive care unit of the hospital on 19-02, which is on Saturday morning. No treatment drugs were reported Company comment: This regulatory case concerns a 74-year-old elderly female patient, with medical history of Diabetes mellitus, experienced the unexpected serious(life-threatening) AESI events Encephalitis and Encephalomyelitis, on same day after third dose of mRNA-1273. It was reported that next day the patient was found to be unconscious by family members and was admitted to the hospital through ER. During her hospitalization her condition did not significantly improve. Brain MRI was performed, no acute infarction or inflammatory lesion was observed. Patient's CSF: WBC < 5 /ML and protein 93.2 mg/dL. Her left leg muscle strength recovered slightly, and she was immediately transferred to another hospital. Follow up carried out after six days, patient's daughter mentioned that the patient was currently unconscious and was transferred to the intensive care unit of the hospital. Medical history of Diabetes mellitus could be a confounder. At the time of reporting, the patient had not recovered from the events. The benefit-risk relationship of mRNA-1273 is not affected by this report. Event seriousness assessed as per Regulatory Authority reporting.						(DM,HTN,hyperlipidemia) provide plausible explanations.	
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 08-Mar-2022 and was forwarded to	No report	Level 4	Level 4	Level 4	Unassessable	A regulatory authority reported case concerning a 74 year-old, male patient with concurrent medical conditions	

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	Moderna on 08-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of ENCEPHALOMYELITIS (Encefalomyelit) in a 74-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 3001531) for COVID-19 vaccination. Concurrent medical conditions included Chronic renal failure, Ulcerative colitis, Depression and Anxiety. Concomitant products included MESALAZINE (ASACOL) for an unknown indication. On 14-Apr-2021, the patient received first dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 31-May-2021, the patient experienced ENCEPHALOMYELITIS (Encefalomyelit) (seriousness criteria hospitalization and disability). At the time of the report, ENCEPHALOMYELITIS (Encefalomyelit) had not resolved. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. Dosage text for Suspect vaccine Spikevax reported as Dose 1 (conflicting information with NVR it distinguishes one day, 2021-04-15). No treatment information was provided by the reporter. Company comment: This is a regulatory case concerning a 74 year-old, male patient with no relevant medical history, who experienced the serious (due to disability and hospitalization) unexpected, AESI of Encephalomyelitis, approximately 1 month 17 days after the first dose of mRNA-1273 vaccine. The outcome was reported as not recovered. No further clinical information was available for medical review. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.						including chronic renal failure, ulcerative colitis, depression and anxiety; and concomitant medication included mesalazine, who experienced encephalomyelitis 47 days post dose 1 Spikevax. Clinical course and treatment not provided. No diagnostic MRI report. Event was reported as not resolved at time of report. This case is missing relevant information including concomitant medications, and MRI report, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unassessable. Case cannot be assessed because information is insufficient.	
	This regulatory authority case was reported by an other health care professional and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 28-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for an unknown indication. No Medical History information was reported. On 22-Jan-2022, the patient received third dose of	CT & MRI brain done but no result.	Level 4	Level 4	Level 4	Unlikely	This regulatory authority case concerns a 28-year-old male patient with no medical history and concomitant medication provided, who received dose 3 Spikevax and 1 day later, experienced weakness of the left arm and foot. Was diagnosed with cervical compression and received rehabilitation treatment. Events worsened. MRI brain done but no report. Treated with steroids, with some improvement. This case is missing relevant information including medical history, concomitant	

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	mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 23-Jan-2022, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criterion hospitalization prolonged). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) was resolving. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) to be related. No concomitant medication was reported. The patient was engaged in business-related work. However, due to physical discomfort, except for specific business that needs to be handled by the patient himself (that is, the business requiring the patient to handle in person), most other businesses were now handled by his colleagues on his behalf. The information related to VICP was provided by email. 03/08/2022 The patient said that the numb feeling was still going on, and he kept seeing the doctor. It was expected that he would apply for VICP in the near future (to be sent to the Health Bureau in paper). This regulatory case concerns a 28-year-old, male patient with no medical history reported, who experienced the unexpected, serious (hospitalization) AESI of acute disseminated encephalomyelitis. The event occurred 1 day after administration of the third dose of the Moderna mRNA-1273 vaccine. The left half of the patient's body developed a 'paralytic reaction'. The left hand and left foot lost strength. He did not sought consult immediately, however, because he felt more and more uncomfortable he went to [REDACTED] Hospital for examination on the fourth day of lunar January. He was diagnosed with Cervical compression and received rehabilitation treatment. However, the discomfort did not improved. Gradually, the patient was unable to climb the stairs with his right foot. He was then referred to the Department of Neurology of [REDACTED] Hospital. The examination report was normal, but the patient became increasingly uncomfortable. Later, he was transferred to the Emergency department of [REDACTED] Hospital and was subsequently hospitalized for 9 days. Computerized Tomogram and Magnetic Resonance Imaging were done, however, the results were not provided. The					medications, and diagnostic results, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unlikely, based on the short latency time of one day, that makes a relationship of the event with Spikevax improbable. The lack of relevant information is a challenge in assessing for causality in this case.		

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	patient received intravenous drip (unspecified) and high-dose steroid treatment (unspecified). The left side of the patient's body felt somewhat numb, and his left hand was still weak while the strength of his right foot had improved. After discharge, the doctor prescribed steroids (unspecified) for 1 month. It was expected that the dose of steroids would be adjusted according to the examination results after the follow-up consultation in Apr2022. The event was resolving at the time of the report. The benefit-risk relationship of the Moderna mRNA-1273 vaccine is not affected by this report.							
	This regulatory authority case was reported by an other health care professional and describes the occurrence of CRYING (CRYING INCOERCIBLE), IRRITABILITY (IRRITABILITY), CONFUSIONAL STATE (CONFUSION), HEADACHE (HEADACHE) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM) in a 25-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 940885) for an unknown indication. No Medical History information was reported. On 27-Jan-2022, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 27-Jan-2022, the patient experienced CRYING (CRYING INCOERCIBLE) (seriousness criteria hospitalization and life threatening), IRRITABILITY (IRRITABILITY) (seriousness criteria hospitalization and life threatening), CONFUSIONAL STATE (CONFUSION) (seriousness criteria hospitalization and life threatening), HEADACHE (HEADACHE) (seriousness criteria hospitalization and life threatening) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM) (seriousness criteria hospitalization and life threatening). At the time of the report, CRYING (CRYING INCOERCIBLE), IRRITABILITY (IRRITABILITY), CONFUSIONAL STATE (CONFUSION), HEADACHE (HEADACHE) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, SARS-CoV-2 test: negative (Negative) Negative. For mRNA-1273 (Spikevax) (Unknown), the reporter did not provide any causality assessments. Patient did not receive any previous dose. No concomitant medications were reported.	No report. SARS-CoV-2 test: negative	Level 4	Level 4	Level 4	Unlikely	This is a regulatory authority case concerning a 25-year-old female patient with no reported medical history, concomitant medications, who received dose 3 Spikevax and on the same day (Day 0), experienced confusional state, headache, crying, irritability, and ?ADEM. Other information regarding clinical course, diagnostic tests/MRI brain and treatment details were not provided. This case is missing relevant information including medical history, concomitant medications, clinical course and diagnostic results, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unlikely, based on the short time to onset of day 0, that makes a relationship of the event with Spikevax improbable. The lack of relevant information is a challenge in assessing for causality in this case.	

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	No treatment medications were reported. It was reported that patient did not have swelling, pain, erythema, induration, ulceration, abscess, seizures, hypotonia, rash, diarrhea, invagination intestinal, fever, syncope vasovagal. No sequelae. Company comment: This is a regulatory case concerning a 25-year-old female patient with no reported medical history, who experienced the serious (hospitalization and life threatening) unexpected AESI Acute disseminated encephalomyelitis (ADEM), the same day after receiving booster dose of mRNA-1273. Confusional state, headache and crying incoercible were reported as events. SARS-CoV-2 test was negative. Other information regarding clinical course, diagnostic tests and treatment details were not provided. Events seriousness captured as per Regulatory Authority assessment in Source Document. The benefit-risk relationship of mRNA-1273 is not affected by this report.							
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 16-Mar-2022. The most recent information was received on 18-Mar-2022 and was forwarded to Moderna on 18-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of ENCEPHALOMYELITIS (suspected encephalomyelitis) in a 47-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3002622) for COVID-19 vaccination. The patient's past medical history included Alopecia areata (In treatment with dexamethasone.). On 14-Jun-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 01-Jul-2021, after starting mRNA-1273 (Spikevax), the patient experienced ENCEPHALOMYELITIS (suspected encephalomyelitis) (seriousness criterion medically significant). At the time of the report, ENCEPHALOMYELITIS (suspected encephalomyelitis) had not resolved. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medications were reported. No treatment medications were reported. Company comment: This regulatory authority case concerns a 47-year-	No report.	Level 4	Level 4	Level 4	Unassessable	This regulatory authority reported case concerns a 47-year-old, female patient with no relevant medical history and no concomitant medications reported, who received an unknown dose of Spikevax and 17 days post-vaccine, reported to experience ADEM. No detailed reports of clinical course of events, no MRI brain and diagnostic results provided. Event was reported as not resolved at time of report. This case is missing relevant information, hence classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unassessable. Case cannot be assessed because information is insufficient.	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	old, female patient with no relevant medical history reported, who experienced the unexpected serious AESI event of Encephalomyelitis (seriousness criteria medically significant) which occurred 17 days after a dose of mRNA-1273 vaccine (dose number not specified). The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Event seriousness assessed as per Regulatory Authority's report. Most recent FOLLOW-UP information incorporated above includes: On 18-Mar-2022: Significant Follow up received. Patient demographics were added, Medical History was added and Suspect product action taken was added.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 17-Mar-2022 and was forwarded to Moderna on 17-Mar-2022. This regulatory authority case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM), GUILLAIN-BARRE SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM), CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) and OVERLAP SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) in a 34-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. No Medical History information was reported. On 14-Dec-2021, the patient received third dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On an unknown date, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) (seriousness criterion hospitalization), GUILLAIN-BARRE SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) (seriousness criterion hospitalization), CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) (seriousness criterion hospitalization) and OVERLAP SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP +	No report	Level 4	Level 5	Level 4	Unlikely	This regulatory authority reported case concerns a 34- year-old male patient with no medical history and concomitant medication reported, who 9 days prior to dose 3 Spikevax, experienced acute and rapidly progressing painful tingling paresthesia. Differential diagnoses included ADEM, Guillain-Barre syndrome, Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multiple sclerosis. No diagnostic results provided. Treated with cortisone. The events were resolved with sequelae at the time of report. This case is missing relevant information including medical history, concomitant medications, and diagnostic results, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unlikely, based on the occurrence of events prior to receiving dose 3 Spikevax, that makes a relationship of the event with Spikevax improbable.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	additional ADEM) (seriousness criterion hospitalization). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM), GUILAIN-BARRE SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM), CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) and OVERLAP SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) had resolved with sequelae. Concomitant medication was not provided. Treatment information was not provided. Diagnosis DD CIDP and then also ADEM DD MS in the examinations; inpatient admission with cortisone boost, ocrelizumab plan. On 05-Dec-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) (seriousness criterion hospitalization), GUILAIN-BARRE SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) (seriousness criterion hospitalization), CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) (seriousness criterion hospitalization) and OVERLAP SYNDROME (Overlap syndrome with PNS and CNS affection in the sense of an AIDP/CIDP + additional ADEM) (seriousness criterion hospitalization). Company comment-This regulatory case concerns a 34- year-old male patient with no relevant medical history reported, who experienced the unexpected serious (Hospitalization) events of Acute disseminated encephalomyelitis (AESI), Guillain-Barre syndrome (AESI), Chronic inflammatory demyelinating polyradiculoneuropathy (AESI) and Overlap syndrome 9 days prior to third dose of mRNA-1273 Vaccine administration. It was reported that acute and rapidly increasing, painful tingling paresthesia -> diagnosis DD CIDP and then also ADEM DD MS in the examinations; Hospitalized and treated with cortisone boost, ocrelizumab is planned. The events were resolved with sequel at the time of report. Benefit risk relationship of mRNA-1273 Vaccine is not affected by this report. Event seriousness assessed as per							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	Regulatory Authority reporting, This regulatory authority case was reported by a physician and describes the occurrence of DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) in a 71-year-old male patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for COVID-19 vaccination. The patient's past medical history included Cigarette smoker (Alcohol: 4-5 cigarettes for 52 years). Concomitant products included RIVAROXABAN (XARELTO), NEBIVOLOL HYDROCHLORIDE (NEBILET), ATORVASTATIN CALCIUM (ATORVASTATINE PFIZER), LISINOPRIL, PANTOPRAZOLE (PANTOZOLE) and PARACETAMOL (DAFALGAN) for an unknown indication. On 05-Jan-2022, the patient received dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 50 microgram. On 07-Jan-2022, after starting mRNA-1273 (COVID-19 Vaccine Moderna), the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criterion hospitalization). At the time of the report, DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Laboratory test: abnormal (abnormal) TEST: Spine MRI on 02/15/2022: No elements that would explain spinal cord compression. Degenerative realignment of the cervical, thoracic, and lumbar spine, with a greater narrowing of the spinal canal at C3-C4, without signs of associated cervical-thoracic myelopathy. Lower neck mass at a height of 4.8 cm, thyroid goiter. Chest scan on 02/21/2022: Mild cardiomegaly with no signs of fluid overload or cardiac consolidation. No pleural effusion or pulmonary focus. Serological tests dated 02/14/2022 and 02/18/2022: - Lyme IgG 69.4 UA/mL, IgM 0.10 UA/mL; syphilis and HIV: negative. - EBV: IgG for prior infection; CMV, HSV 1 and 2 negative. Blood test: - Sedimentation rate, TSH, rheumatoid factors normal - Protein electrophoresis: alpha-2-globulins 13.0%, beta-1-2 globulins 16.0% - Campylobacter jejuni serological test: negative. For mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular), the reporter considered DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) to be possibly related. The patient received COVID-19 Vaccine Moderna	Brain MRI: no report. Spine MRI: Degenerative realignment of the cervical, thoracic, and lumbar spine, with a greater narrowing of the spinal canal at C3-C4, without signs of associated cervical-thoracic myelopathy. Lower neck mass: thyroid goiter. Negative results for syphilis, HIV, CMV, HSV 1 and 2 and Campylobacter jejuni, EBV: IgG for prior infection; negative.	NOT a case of ADEM	Level 5	Level 4	Unlikely	This is a regulatory authority reported case concerning a 71 year-old male patient with past medical history of chronic tobacco use, concomitant medications included XARELTO; NEBILET; statins; LISINOPRIL; PANTOZOLE; DAFALGAN, who received dose 2 Spikevax and 2 days later, experienced demyelinating polyneuropathy. Diagnostic report: Spine MRI: Degenerative realignment of the cervical, thoracic, and lumbar spine, with a greater narrowing of the spinal canal at C3-C4, without signs of associated cervical-thoracic myelopathy. Lower neck mass: thyroid goiter. The event outcome was reported as recovering. This case is missing relevant information including complete medical history, and CSF results; classified as NOT a case of ADEM based on the absence of encephalopathy and imaging finding inconsistent with ADEM. This case is assessed as WHO Unlikely, based on imaging results of degenerative bone disease with compression, that makes a relationship of the event with Spikevax improbable. The medical history of chronic tobacco use is a confounder. The lack of relevant information is a challenge in assessing for causality in this case.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Spikevax) 3rd vaccination (COVID-19 vaccine), a dosage of 50 microgram. No treatment information was provided. Company comment: This is a regulatory case concerning a 71 year-old, male patient with no relevant medical history, who experienced the serious due to hospitalization, unexpected, AESI of demyelinating polyneuropathy, approximately 2 days after the 3rd dose of mRNA-1273 vaccine. The outcome was reported as recovering. The reporter assessed the event as possibly related to the vaccine. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 29-Mar-2022: Translation received on 01-Apr-2022, contains significant information. Lab test results updated. The case was serious and unlabelled. Due to temporal relationship and the known safety profile of the vaccine, the causality was assessed as possible.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 31-Mar-2022 and was forwarded to Moderna on 31-Mar-2022. This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 32-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The patient's past medical history included Pregnancy and Gastrectomy. Concurrent medical conditions included Obesity and Ex-tobacco user. Concomitant products included ENOXAPARIN SODIUM (LOVENOX HP) from 09-Feb-2022 to an unknown date for Thrombosis prophylaxis. On 05-Jan-2022, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 12-Feb-2022, after starting mRNA-1273 (Spikevax), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criterion life threatening). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) had not resolved. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the	No report	Level 4	Level 4	Level 4	Unassessable	This regulatory authority reported case concerns a 32-year-old, female patient with no relevant medical history reported, concomitant medications included enoxaparin, who received an unknown dose of Spikevax and 38 days post-vaccine, reported to experience ADEM. No detailed reports of clinical course of events, no MRI brain and other diagnostic results provided. Event was reported as not resolved at time of report. This case is missing relevant information, hence classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unassessable. Case cannot be assessed because information is insufficient.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	reporter did not provide any causality assessments. No concomitant medication reported. No treatment medication reported. Dosage text was reported as R1. COMPANY COMMENT : This regulatory authority case concerns a 32-year-old, female patient with no relevant medical history reported, who experienced the unexpected serious (seriousness criteria life threatening). AESI event of acute disseminate encephalomyelitis, which occurred 38 days after a dose (dose number not specified) of mRNA-1273 vaccine. The benefit-risk relationship of mRNA-1273 is not affected by this report. The event were assessed as serious as per Regulatory Authority's report. Most recent FOLLOW-UP information incorporated above includes: On 04-Apr-2022: Follow-up received with no new information.							
	This regulatory authority case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 28-year-old male patient who received mRNA-1273 (COVID-19 Vaccine Moderna) (batch no. 3004215) for COVID-19 vaccination. The patient's past medical history included SARS-CoV-2 infection. On 04-Aug-2021, the patient received dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 04-Dec-2021, after starting mRNA-1273 (COVID-19 Vaccine Moderna), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criterion life threatening). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 14-Dec-2021, Computerised tomogram head: inconclusive (Inconclusive) Inconclusive. On 14-Dec-2021, Electroencephalogram: inconclusive (Inconclusive) Inconclusive. On 14-Dec-2021, Magnetic resonance imaging spinal: inconclusive (Inconclusive) Inconclusive. On 17-Dec-2021, Magnetic resonance imaging head: inconclusive (Inconclusive) Inconclusive. No concomitant products were reported.	MRI brain (medullary MRI): showed extensive myelitis. CT brain & spine: inconclusive. EEG: inconclusive. ID panels: negative (negative serology for Lyme, HIV, CMV, HTLV-1 and 2, syphilis, malaria, anguillulosis, Whipple, Rickettsia, Q fever)	NOT a case of ADEM	Level 5	Level 2	Unlikely	This regulatory authority case concerns a 28-year-old male patient with a past medical history of COVID-19 infection, no concomitant medication reported, who received an unknown dose of Spikevax and 123 days later, experienced fever, headache, neck pain, rapidly progressive paraparesis and bladder and sphincter dysfunction with symptoms of dysuria and constipation. These events occurred 32 days after a 15 days trip to [REDACTED]. Diagnostic reports include: extensive infectious diseases panels were negative, imaging inconclusive, medullary MRI showed extensive myelitis, CSF analysis: proteinemia, and Positive anti-MOG antibodies. Treatment included oral steroid. Events outcome was complete motor recovery with persistence of vesico-sphincter disorders. This case is missing relevant information including complete travel history, and concomitant medications. Case is classified as NOT a case of ADEM, but rather, a MOGAD, based on positive anti-MOG, absence of encephalopathy and imaging finding inconsistent with ADEM. Also, this case is assessed as WHO Unlikely, based on the prolonged 123 days time to onset (outside the risk window) that makes a relationship of the events with Spikevax improbable. The medical history of COVID-19 infection, and the travel history overseas are strong confounders, that provide a more plausible explanation for the occurrence of the events.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	It was reported that patient experienced disseminated acute encephalomyelitis with anti-MOG antibodies, with initial symptoms occurring approximately 4 months after vaccination with Spikevax. According to a medical report, the patient was hospitalized in intensive care and then in acute care in a hospital in [REDACTED] from 12-Dec-2021 to 23-Dec-2021. The patient developed in early December 2021, following a 15-day trip to [REDACTED] with return on 02-Nov-2021, febrile headaches and neck pain (max. 38.8°) complicated by rapidly progressive paraparesis and bladder and sphincter disorders (dysuria, constipation). A diagnosis of disseminated acute encephalomyelitis was retained. Treatment included: Methylprednisolone (Solumedrol) 1g 1x/d was started and provided complete motor recovery with the persistence of vesico-sphincter disorders. The patient was then transferred to a rehabilitation stay on 23-Dec-2021 with continued treatment of prednisone (Cortancyl) in a degressive scheme (end 03-Jan-2022). Laboratory tests included: Clinical examination which confirmed proximal paraparesis with tetra-pyramidal syndrome (osteotendinous hyperreflexia, possible bilateral Babinsky sign). A broad assessment was carried out with the following additional examinations: multiple blood tests, 2-fold lumbar puncture, electroencephalogram (EEG), medullary and cerebral MRI, cerebral CT scan. These examinations showed extensive myelitis (medullary MRI) and the lumbar puncture regained hyperproteinorrhagia. A large infectious balance returned negative (including negative serology for Lyme, HIV, CMV, HTLV-1 and 2, syphilis, malaria, anguillolosis, Whipple, Rickettsia, Q fever, CSF and sterile blood cultures). The patient was reviewed on 17-Jan-2022. In the meantime anti-MOG antibodies returned positive posing the indication to oral corticosteroid therapy for a minimum of 6 months. Spinal cord and cerebral MRI of 14-Dec-2021 showed aspect in favor of myelitis especially with regard to the cervical spinal cord and the terminal cone.; Brain CT-scan of 14-Dec-2021 showed no thrombophlebitis or intracranial abscess.; Brain MRI of 17-Dec-2021 showed some T2 FLAIR hypersignals, in particular from the posterior arm of the left internal capsule, superior frontal cortical juxta.; EEG of 14-Dec-2021 showed irregular tracing. Important activity of delta elements of the hi-frontocentral topography, which can diffuse at the level of the anterior temporal electrodes. These elements never take on a periodic character and are reactive. No appearance of latent illness. Company comment: This regulatory authority case concerns a 28-year-old male patient with no relevant medical history who experienced serious due to life-threatening, unexpected AESI of acute disseminated encephalomyelitis, that occurred approximately 4							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	months after the dose of the mRNA-1273. According to a medical report, the patient was hospitalized for 11 days. Reportedly, the patient developed febrile headaches and neck pain after [REDACTED] trip, further aggravated with rapidly progressive paraparesis and bladder and sphincter dysfunction with symptoms of dysuria and constipation. A broad assessment was carried out with the following additional examinations: multiple blood tests, 2-fold lumbar puncture, electroencephalogram (EEG), medullary and cerebral MRI, cerebral CT scan. Medullary MRI showed extensive myelitis, lumbar puncture showed hyperproteinorrhagia, whereas infectious studies came back negative. The patient had positive anti-MOG antibodies and was started on oral corticosteroid therapy. The patient showed completed motor recovery with persistence of vesico-sphincter disorders. The benefit-risk relationship of mRNA-1273 is not affected by this report. Seriousness assessment retained as per regulatory authority reporting.							
[REDACTED]	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 07-Apr-2022 and was forwarded to Moderna on 12-Apr-2022. This case, initially reported to the [REDACTED] by a pharmacist, was received via the [REDACTED]. The vaccine recipient was making visits to a hospital because of postoperative both femur fracture. On an unknown date, the patient received the 1st dose of a COVID-19 vaccine (product name unknown). On an unspecified date in Aug-2021, the patient received the 2nd dose of a COVID-19 vaccine (product name unknown). On 30-Mar-2022, at 15:30, the patient received the 3rd vaccination with this vaccine. There were no abnormalities after the patient returned home. On 31-Mar-2022, in the morning, the patient experienced headache and felt feverish. At 09:00, the patient was in bed without having breakfast. Around 10:00, encephalomyelitis developed. After getting up and going to the bathroom, the patient made a gesture like tracing a rice bowl and a bowl on the table in the standing position without speaking, and the family members felt suspicious about it. After that, the patient collapsed and unable to stand up, and thus a physician was requested to visit the patients house. The patient received drip infusion, and two persons tried to pull the patient up, but it was impossible. Thus, the condition was judged to be beyond their control, and an emergency call was made. After 11:00, the patient was transported to another hospital. Head MRI showed high signal intensities in the brain-stem area, and encephalitis and encephalopathy after vaccination with this vaccine were suspected. Therefore, the patient was transported to the reporting hospital and hospitalized. On 01-Apr-2022, the symptoms were resolving. On 06-Apr-2022, the symptoms	MRI brain: high signal intensities in brain-stem.(Inconclusive)	Level 4	Level 4	Level 4	Unlikely	A regulatory authority reported case concerning an 80 year-old female patient with concurrent medical conditions including rectosigmoid cancer stage III; hypertension; cholelithiasis; fibromyalgia, femur fracture and post surgery, with no reported concomitant medications; who received dose 3 Spikevax and one day post vaccine, was reported to have collapsed with weakness of lower limbs. Diagnostic results: MRI brain: high signal intensities in brain-stem (often seen in MRI of older patients). Treatment included IV infusion. Event outcomes were resolving. This case is missing relevant information including concomitant medications, and other diagnostic results, hence it is classified as Brighton's level 4 ADEM: reported event of ADEM with insufficient evidence to meet level 1,2 or 3 of the case definition. According to the WHO causality assessment, this case is assessed as Unlikely, based on the short time to onset of one day, that makes a relationship of the event with Spikevax improbable. The lack of relevant information is a challenge in assessing for causality in this case. The medical history of advanced cancer, surgery, HHD are strong confounders, that provide a more plausible explanation for the occurrence of the events.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	improved, and the patient was discharged from the hospital. The outcome of encephalomyelitis was reported as resolving. Follow-up investigation will be made. Company Comment: The event developed after the administration of ELASOMERAN and there is temporal relationship. Although the patient did not experience adverse reactions after the 1st and the 2nd vaccinations, it is considered that the patient was hospitalized this time because of adverse reactions to the 3rd vaccination as no medical practice other than vaccination with this vaccine and no changes in medication were performed. The symptoms improved with fluid replacement and rehabilitation at the reporting hospital, and no sequelae were left. The event developed after the administration of ELASOMERAN and there is temporal relationship.							
	This literature-non-study case was reported in a literature article and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in an 81-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. LITERATURE REFERENCE: Ballout AA, Babaie A, Kolesnik M, Li JY, Hameed N, Waldman G, et al.. A single-health system case series of new-onset CNS inflammatory disorders temporally associated with mRNA-based SARS-CoV-2 vaccines. Front Neurol. 2022;13:796882 No Medical History information was reported. On an unknown date, the patient received first dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On an unknown date, after starting mRNA-1273 (Spikevax), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria death and medically significant). The patient was treated with METHYLPREDNISOLONE (METHYLPREDNISOLONE NATIV) (intravenous) for Acute disseminated encephalomyelitis, at an unspecified dose and frequency; IMMUNOGLOBULINS NOS (IMMUNOGLOBULIN I.V) (intravenous) for Acute disseminated encephalomyelitis, at an unspecified dose and frequency and VANCOMYCIN (oral) for Clostridium difficile infection, at an unspecified dose and frequency. The reported cause of death was Acute disseminated encephalomyelitis and Hemorrhagic shock. It is unknown if an autopsy was performed. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available):	Biopsy brain: inflammatory demyelinating process. Brain MRI: multiple, non-enhancing, T2 hyperintense lesions. Clostridium difficile infection: positive. Other infectious disease workup was negative. Mild leukocytosis. CSF pleocytosis with relative lymphocytosis, protein of 45 mg/dL, and significantly elevated myelin basic protein (MBP)	Level 2	Level 5	Level 5	Conditional	A literature-non-study reported case with fatal outcome, concerning a 81 year-old male patient with no reported medical history and concomitant medications, who received dose 1 Spikevax and 13 days post-vaccination, experienced rapid-onset acute change in mental status with severe encephalopathy. This was preceded by prodromal symptoms of viral-like illness (low-grade fever, fatigue, and myalgia). Diagnostic reports included: brain MRI: multiple non-enhancing, T2 hyperintense lesions. Infectious diseases workup: positive for Clostridium difficile infection, CSF pleocytosis with relative lymphocytosis, and proteinuria; negative for other infectious diseases. Treatment included high-dose IV methylprednisolone, IVIG therapy, and vancomycin and plasmapheresis. The patient died 39 days post vaccination (hospital day 26) due to hemorrhagic shock. No autopsy report was provided. This case is missing relevant information including medical history, concomitant medications. This case is classified as Brighton's level 2 ADEM based on brain MRI finding. According to the WHO causality assessment, this case is assessed as Conditional. More data for proper assessment is needed.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On an unknown date, Anti-aquaporin-4 antibody: negative (Negative) Negative and negative (Negative) Negative. On an unknown date, Biopsy brain: inflammatory demyelinating (abnormal) leptomeninges and cortex, and showed an acute inflammatory demyelinating process. On an unknown date, C-reactive protein (Unknown-<4.9 mg/l): 10.8 mg/l (High) 10.8 mg/L. On an unknown date, CSF glucose (40mg/dl-70 mg/dl): 69 mg/dl 69 mg/dL. On an unknown date, CSF granulocyte count (0cells/μl-5 cells/μl): 3 cells/μl (normal) 3 cells/μL, 11 cells/μl (High) 11 cells/μL mild lymphocytic pleocytosis and 69 cells/μl (High) 69 cells/μL. On an unknown date, CSF myelin basic protein: >167.0 ng/ml >167.0 ng/mL. On an unknown date, CSF protein (5mg/dl-45mg/dl): 45 mg/dl (normal) 45 mg/dL, 52 mg/dl (High) 52mg/dL and 45 mg/dl (normal) 45 mg/dL. On an unknown date, Clostridium difficile infection: positive (Positive) positive. On an unknown date, HIV antibody: negative (Negative) Negative. On an unknown date, Magnetic resonance imaging: possible inflammatory or infectious process. (abnormal) diffusion restricting lesion involving the right dorsal medulla with corresponding T2 FLAIR hyperintensity very faint left pontine, midbrain, and thalamic T2 FLAIR hyperintensity and minimal T2 sulcal hyperintensity without apparent enhancement and adem (abnormal) multiple, non-enhancing, T2 hyperintense lesions involving bilateral frontoparietal lobes, lentiform nuclei, thalami, cerebral peduncles, pons, and right posterior medulla.The clinical and neuroradiological findings were deemed most consistent with ADEM. On an unknown date, Neurological examination: minimal response to noxious stimuli (abnormal) minimal response to noxious stimuli, right gaze preference. On an unknown date, Red blood cell sedimentation rate (1mm/h-15 mm/h): 86 mm/hr (High) 86 mm/hr. On an unknown date, SARS-CoV-2 test: negative (Negative) negative. On an unknown date, White blood cell count (3.8 k/μl-10.5k/μl): 12.5 k/μl mild leukocytosis 12.5 K/μL. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. For mRNA-1273 (Spikevax) (Unknown), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) to be related. No concomitant medications were reported. Patient							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	undergone plasmapheresis (PLEX) for 4days. Patient had prodromal symptoms of viral-like illness marked by several days of low-grade fever, fatigue, and myalgia and fever of 102°F without skin rashes or nuchal rigidity and new neurological symptoms like Severe confusion. Oculocephalic testing shows absent pupillary response to light, absent right corneal reflex, diffuse hypertonicity, and extensor plantar responses bilaterally. Head CT and CT angiogram of the head and neck were unremarkable. There was Brain involvement includes brainstem and thalamus and Spinal cord involvement was Unknown. Lab data includes Anti-MOG CSF ab was negative and Anti-MOG Serum ab was unknown. Infectious workup was negative. It included urine culture, urine legionella, respiratory virus panel PCR, encompassing influenza, parainfluenza, adenovirus, respiratory syncytial virus, Chlamydia pneumoniae, Mycoplasma pneumoniae, and enterovirus. Blood cultures drawn on admission (day 1) and twice afterwards (day 5 and 10) were without growth. CSF infectious workup was negative which included HSV PCR, bacterial cultures, gram stain, cryptococcal antigen, VDRL titer, fungal culture, and listeria antibody. Serologies for blastomycosis, cryptococcus, coccidioides, and galactomannan were negative. QuantiFERON testing was performed twice and was indeterminate (however titers were low), imaging was negative for tuberculoma, and CSF glucose and total nucleated cell count was normal lowering suspicion of tuberculosis meningitis. His neurological condition deteriorated rapidly to a comatose state within the subsequent 24 h and required emergent intubation. He continued to spike fevers despite broad-spectrum antibiotics and a negative infectious . Stains for infectious agents were negative, including bacterial, fungal, and viral sources (including JC virus). This case was linked to [REDACTED] (Patient Link). Most recent FOLLOW-UP information incorporated above includes: On 13-Apr-2022: Follow up received by safety on 13-Apr-2022 has Email with FTA received from SARA team and contains significant information: Literature information, lab data and treatment drugs were updated.							
[REDACTED]	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 05-Jan-2022. The most recent information was received on 18-Jan-2022 and was forwarded to Moderna on 18-Jan-2022. This regulatory authority case was reported by a pharmacist and describes the occurrence of VISUAL IMPAIRMENT (bilateral hypovision with pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis), ENCEPHALOMYELITIS (bilateral hypovision with	No report	Level 4	Level 5	Level 5	Not applicable (Unassessable)	A regulatory authority reported case with fatal outcome, concerning a 50-year-old male with a past medical history of alcoholism, no information on concomitant medications and treatment provided, who after an unknown dose of Spikevax, with an unknown time to onset (TTO), experienced visual impairment, craniocerebral injury, was diagnosed with encephalomyelitis/disseminated encephalomyelitis with a fatal outcome. It	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis), CRANIOCEREBRAL INJURY (bilateral hypovisus with pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis) and PUPILLARY REFLEX IMPAIRED (bilateral hypovisus with pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis) in a 50-year-old male patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. The patient's past medical history included Alcoholism. On an unknown date, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 01-Jun-2021, the patient experienced VISUAL IMPAIRMENT (bilateral hypovisus with pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis) (seriousness criterion death), ENCEPHALOMYELITIS (bilateral hypovisus with pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis) (seriousness criterion death), CRANIOCEREBRAL INJURY (bilateral hypovisus with pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis) (seriousness criterion death) and PUPILLARY REFLEX IMPAIRED (bilateral hypovisus with pupillary ariflexia, cranio-facial trauma, disseminated encephalomyelitis) (seriousness criterion death). It is unknown if an autopsy was performed. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medications were reported. No treatment information was provided. Company Comment: This regulatory case concerns a 50-year-old, male patient with a relevant medical history of Alcoholism, who experienced the unexpected serious AESI event of Encephalomyelitis and unexpected serious events of Visual impairment, Craniocerebral injury and Pupillary reflex impaired. The events occurred after an unknown dose of mRNA-1273 with a fatal outcome. (The dose sequence and date of vaccination not provided). The clinician believes there is no correlation with the vaccine per information in the SD. The medical history of Alcoholism is a confounder. The benefit-risk relationship of mRNA-1273 is not affected by this report.						is unknown if an autopsy was performed. No imaging report or LD/tumor/autoimmune panel was provided. Relevant information missing in the report included concomitant medications, TTO, dose, imaging, and laboratory tests. This case is classified as Brighton's level 4, due to insufficient information provided. According to the WHO-UMC causality assessment, this report is considered Unassessable based on inadequate information to assess the case. A casual relationship cannot be excluded due to lack of other information.	
	This regulatory authority case was reported by a physician and describes the occurrence of DEPRESSED LEVEL OF CONSCIOUSNESS	Imaging (type not specified): Mass with swelling of the right thalamus and hippocampus. Inconclusive.	Level 5: NOT a case of ADEM	Level 5	Level 5	Not applicable (Unlikely)	This is a fatal report by a regulatory authority concerning a 82-year-old male with unknown medical history and	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Disturbance of consciousness and epileptic seizure with subsequent focal neurological failures), EPILEPSY (Disturbance of consciousness and epileptic seizure with subsequent focal neurological failures), DEATH (Death) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute demyelinating encephalomyelitis (ADEM)) in an 82-year-old male patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for COVID-19 vaccination. No Medical History information was reported. On 23-Mar-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form once a day. On 24-Mar-2021, the patient experienced DEPRESSED LEVEL OF CONSCIOUSNESS (Disturbance of consciousness and epileptic seizure with subsequent focal neurological failures) (seriousness criteria death, hospitalization, disability and medically significant), EPILEPSY (Disturbance of consciousness and epileptic seizure with subsequent focal neurological failures) (seriousness criteria death, hospitalization, disability and medically significant) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute demyelinating encephalomyelitis (ADEM)) (seriousness criteria death, hospitalization, disability and medically significant). The patient died in September 2021. It is unknown if an autopsy was performed. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In March 2021, Imaging procedure: inconclusive (Inconclusive) Inconclusive. In March 2021, Lumbar puncture: negative (Negative) Negative. On an unknown date, Bacterial test: negative (Negative) Culture on bacteria & mycobacteria- Negative. On an unknown date, Imaging procedure: abnormal (abnormal) TEST 10068979 (RESUL1) imaging (202103) [In the Imaging shows a space requirement with swelling of the thalamus and hippocampus on the right.]: Imaging shows a space requirement with swelling of the thalamus and hippocampus on the right. and negative (Negative) TEST 10024999 (24.1) LP (202103) [RESULT: no indication of infection]: LP: 1 cell (monocytic), protein and glucose, multiplex PCR, CNS pathogen negative. On an unknown date, Polymerase chain reaction: negative (Negative) Negative. For mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular), the reporter considered DEPRESSED LEVEL OF CONSCIOUSNESS	Negative ID serology					concomitant medications, who one day post-dose 1 Spikevax experienced depressed level of consciousness and seizure/epilepsy and subsequent focal neurological deficits; was diagnosed with Acute demyelinating encephalomyelitis (ADEM), with a fatal outcome six months later. It is unknown if an autopsy was performed. Diagnostic results included imaging that showed a mass with swelling of the right thalamus and hippocampus. Infectious disease panels/serology were negative. This case is classified as Brighton's level 5: NOT a case of ADEM based on imaging report inconsistent with ADEM, and considered WHO Unlikely, with a time to onset of one day that makes a relationship with the product improbable. A causal relationship cannot be excluded due to the lack of medical history and concomitant medications information that could provide plausible explanations.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	(Disturbance of consciousness and epileptic seizure with subsequent focal neurological failures), EPILEPSY (Disturbance of consciousness and epileptic seizure with subsequent focal neurological failures), DEATH (Death) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute demyelinating encephalomyelitis (ADEM)) to be unlikely related. No concomitant drug therapy and Treatment medications were reported. The patient was in EMERGENCY with impaired consciousness, epileptic seizure. The imaging showed a mass with swelling of the thalamus and hippocampus on the right. Only moderate improvement in focal clinic under high-dose steroids. An LP gives no indication of an infection. The pictures were assessed by the Inselspital during the process. In ADEM after vaccination would be the cause and possible DD. No further known course, no further information or diagnostic findings were provided. As a result of the consequences of ADEM, the patient died, 6 months after the event. ADEM was caused by an inflammatory reaction in the brain and spinal cord. The onset of encephalopathy and multifocal neurologic deficits was acute and often rapidly progressive. The patient had swelling/edema in the right thalamus and hippocampus, while pathogens were excluded. Not known if a COVID-19 swab was taken. Company comment This case concerns an 82-year-old male patient, with no reported medical history, who experienced the unexpected serious fatal events of DEPRESSED LEVEL OF CONSCIOUSNESS, EPILEPSY, DEATH and ACUTE DISSEMINATED ENCEPHALOMYELITIS (AESI). Events DEPRESSED LEVEL OF CONSCIOUSNESS, EPILEPSY, and ACUTE DISSEMINATED ENCEPHALOMYELITIS occurred on the following day after the administration of the first dose of mRNA-1273 vaccine, on 24-Mar-2021. Patient died in September 2021. It is unknown if an autopsy was performed. The reporter considered the events to be unlikely related to mRNA-1273 vaccine. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report.							
	This case was received via European Medicines Agency (Reference number [REDACTED]) on 02-Feb-2022 and was forwarded to Moderna on 02-Feb-2022. This regulatory authority case was reported by a physician and describes the occurrence of ENCEPHALOMYELITIS (encephalomyelitis) in a 22-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 3004672) for COVID-19 vaccination. No Medical History information was reported.	No report	Level 4	Level 5	Level 5	Not applicable (Unassessable)	A regulatory authority reported case concerning a 22-year-old male with no medical history reported and no information on concomitant medications and treatment provided; 8 days post-dose 1 Spikevax, patient was reported to experienced unspecified symptoms and was diagnosed with encephalomyelitis. No imaging report or ID/tumor/autoimmune panel was provided. At the time of the report, events had resolved. Relevant information missing in the report included medical history, concomitant medications, time to	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	On 27-Jul-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On an unknown date, after starting mRNA-1273 (Spikevax), the patient experienced ENCEPHALOMYELITIS (encefalomielitis) (seriousness criterion hospitalization). At the time of the report, ENCEPHALOMYELITIS (encefalomielitis) had resolved. mRNA-1273 (Spikevax) (Intramuscular) was withdrawn on 27-Jul-2021. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Concomitant medication information was not provided by the reporter. Treatment information was not provided by the reporter. Company Comment: This case concerns a 22-year-old male patient, with no medical history reported, who experienced the unexpected serious AESI event of Encephalomyelitis. The event occurred approximately 8 days after receiving the first dose of mRNA-1273 Vaccine and resulted in hospitalization. At the time of the report the outcome of the event was resolved. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report.						onset, clinical course, and imaging and laboratory tests. This case is classified as Brighton's level 4 ADEM, due to insufficient information provided to assess the case. A casual relationship cannot be excluded due to lack of other information.	
	This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Encefalomiélitis diseminada aguda) and CEREBRAL INFARCTION (Infarto cerebral por vasculitis) in a 59-year-old male patient who received mRNA-1273 (Moderna CoviD-19 Vaccine) for COVID-19 vaccination. Concurrent medical conditions included Hypertension arterial (HTA). On 21-Jan-2021, the patient received first dose of mRNA-1273 (Moderna CoviD-19 Vaccine) (unknown route) 1 dosage form. On 24-Jan-2021, the patient experienced CEREBRAL INFARCTION (Infarto cerebral por vasculitis) (seriousness criteria hospitalization prolonged, disability, medically significant and life threatening). On 25-Jan-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Encefalomiélitis diseminada aguda) (seriousness criteria hospitalization prolonged, medically significant and life threatening). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS	0	Level 4	Level 4	0	conditional	This is report is for a 59 years old male with history of hypertension and no other medical history or concomitant medications provide, who 4 days after receiving the 1st dose of Spikevax developed ADEM. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4 (not enough information to classify in any level); according to the Brighton classification for Encephalitis is also classified as Level 4 (Not enough information for its Level classification), and accoring to the WHO causality assessment this case is considered conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	(Encefalomiелitis diseminada aguda) outcome was unknown and CEREBRAL INFARCTION (Infarto cerebral por vasculitis) was resolving. For mRNA-1273 (Moderna CoviD-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Concomitant product use was not provided. Treatment information was not provided. This is a 59 year old male who experienced cerebral infarction and acute disseminated encephalomyelitis three and four days after the first dose of the vaccine respectively. Patient's history of arterial hypertension is a confounder for cerebral infarction. Very limited information regarding this event has been provided at this time. No further information is expected in this regulatory report case. This is a 59 year old male who experienced cerebral infarction and acute disseminated encephalomyelitis three and four days after the first dose of the vaccine respectively. Patient's history of arterial hypertension is a confounder for cerebral infarction. Very limited information regarding this event has been provided at this time. No further information is expected in this regulatory report case. Most recent FOLLOW-UP information incorporated above includes: On 01-Jul-2021: Follow-up containing additional event							
	A regulatory authority report [REDACTED] was received from healthcare facility staff concerning a 42-year-old, female patient who received Moderna's COVID-19 vaccine and developed autoimmune demyelinating disease, Cauda equina syndrome, Gait disturbance, Guillain-Barre syndrome, Injection site erythema, Injection site reaction, Injection site warmth, Paraesthesia, Peripheral motor neuropathy, Peripheral sensory neuropathy, Plasmapheresis and Pruritus, The patient's medical history included Sjogren's syndrome, hypothyroidism, anemia, allergy to latex, and allergy to tramadol. Concomitant product use was not provided by the reporter. On 15 Jan 2021, approximately eight days prior to the onset of the symptoms, the patient received the first of two planned doses of mRNA-1273 (Batch number: 039K20A) intramuscularly in the left arm for prophylaxis of COVID-19 infection. The patient had a delayed injection site reaction which was warm and erythematous one week after	0	Level 5	Level 5	0	possible	This report is for a 42 years old female with medical history of Sjogren's syndrome, and hypothyroidism. No information on concomitant medications was provided. Eight days after receiving the 1st dose of Spikevax the patient developed injection site reactions, pruritus, as well as paraesthesia, peripheral motor and sensory neuropathy, Cauda equina syndrome, Gait disturbance, and Guillain-Barre syndrome. CT and MRI of the brain were normal, but Spinal MRI and lumbar puncture were abnormal with protein total increased, and White blood cell count decreased. The patient was later diagnosed with GBS. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5 (not a case), according to the Brighton classification for Encephalitis is also classified as Level 5 (Not a case), and according to the WHO causality assessment this case is considered possible. The medical history of this patient constitute an important risk factor	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	vaccination on left arm for which she was seen by the PCP and prescribed sulfamethoxazole-trimethoprim for 10 days. On 22 Jan 2021, the patient developed Autoimmune demyelinating disease, Cauda equina syndrome, Gait disturbance, Guillain-Barre syndrome, Injection site erythema, Injection site reaction, Injection site warmth, Paraesthesia, Peripheral motor neuropathy, Peripheral sensory neuropathy, Plasmapheresis and Pruritus. On 22-JAN-2021 the patient had a Computerised tomogram of the head and a Magnetic resonance imaging of the brain, which were both normal. On 22-JAN-2021, the patient had a Magnetic resonance imaging spinal, which was abnormal. Other tests on 22-JAN-2021 included CSF white blood cell count, which was negative; Lumbar puncture which was abnormal; protein total increased; White blood cell count was decreased. On 03 Feb 2021 the patient experienced itchiness in hands and feet with pins and needles sensation. The patient was seen by a PCP on 04 Feb 2021 and was started on methylprednisolone for pruritis and paresthesias. The patient went to the Emergency Department on 10 Feb 2021 and presented with progressive sensory motor polyneuropathy and early gait dysfunction. The Patient started plasmapheresis treatment for suspected Guillan-Barre Syndrome on 11 Feb 2021. Action taken with mRNA-1273 in response to the event(s) was not provided. The outcome of the event(s) was not reported.						as well as the diagnosis of cauda equina syndrome which is a rare condition that involve extreme pressure and swelling of the nerves at the end of the spinal cord. This diagnosis provides a more plausible explanation for the symptoms presented by this patient. There is very little additional information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	
	A Regulatory Authority report from [REDACTED] was received from a Healthcare Professional concerning a 60 years old female patient who received Moderna's COVID-19 vaccine (mRNA-1273) and the patient experienced swelling/inflammation in the brain (acute disseminated encephalomyelitis), brain oedema, noninfective encephalitis, double vision (diplopia), immediate post-injection reaction, pyrexia, chills, fatigue and achy/joint pain (arthralgia). The patient's medical history was not provided. The patient was allergic to latex. The patient was taking lisinopril-hctz 20/25, vitamin D, 81 mg aspirin, and multivitamin as concomitant medication. On 19 Jan 2021, prior to the onset of the events, the patient received second dose of planned doses of mRNA-1273 batch no: 028L20A in the left arm for prophylaxis of COVID-19 infection.	swelling/ inflammation of the brain.	Level 2	Level 3A	0	Conditional	This report is for a 60 years old female with no medical history or complete concomitant medication information provided, who 22 days after the 2nd dose of Spikevax developed double vision. The patient had previously experience fever, chills, fatigue, malaise within 24 hours after the 2nd dose of Spikevax. MRI of the brain performed 6 days later showed swelling/ inflammation of the brain. Patient was diagnosed with ADEM by a neurologist. This case according to the Brighton collaboration case definition for ADEM is classified as Level 2. According to the WHO causality assessment this case is considered Conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted.	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On 20 Jan 2021, the patient experienced fever within 24 hours, chills, achy, fatigue. Fever lasted for 4 days. Fatigue and achy/joint pain lasted for at least a couple weeks. On February 11/12, 2021, the patient started with double vision, which had progressively worsened and was constant starting on 2/17. Magnetic resonance imaging (MRI) results showed swelling/inflammation in the brain, specifically on the left side. Post testing the Neurologist diagnosis was acute disseminated encephalomyelitis (ADEM). Treatment included antiviral medication, saw specialists - Ophthalmologist and Neurologist on 24 Feb and 25 Feb respectively, intravenous immune globulin (IVIG) started on 01 Mar for 3 consecutive days as treatment medication. The patient was also quarantined for a maximum of 30 days post the first IVG treatment, a repeat MRI, potential lumbar puncture (LP). Action taken with mRNA-1273 in response to the events was not reported. On an unspecified date the event of pyrexia, fatigue and achy/joint pain (arthralgia) were resolved. The outcome of the events of swelling/inflammation in the brain (acute disseminated encephalomyelitis), brain oedema, noninfective encephalitis, double vision (diplopia), immediate post-injection reaction, and chills were reported as not resolved.							
	This spontaneous case was reported by a pharmacist and describes the occurrence of SINUS NODE DYSFUNCTION (Sick sinus syndrome), ENCEPHALOMYELITIS (Encephalomyelitis), APHASIA (Expressive aphasia) and ENCEPHALITIS (Encephalitis) in an 83-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch nos. 027A21A and 031M20A) for COVID-19 vaccination. The patient's past medical history included DVT prophylaxis (Lovenox), Gastrointestinal disorder prophylaxis (Protonix), Skin graft (Right hand excisional debridement of degloving crush injury with application of allogenic skin graft), Right hand excisional debridement and Permanent cardiac pacemaker insertion on 12-Apr-2021. Concurrent medical conditions included Drug allergy (Codeine), Milk allergy (Allergy to milk products), AV block (Unspecified atrioventricular block), Hyperlipidemia (Unspecified Hyperlipidemia, Continue statin therapy), Dyslipidemia, Hypertension and Wolff-Parkinson-White syndrome. Concomitant products included NAPROXEN SODIUM (ALEVE), AMLODIPINE, ATORVASTATIN and PANTOPRAZOLE for an	Abnormal enhancement in the white matter of the posterior left parietal lobe	Level 2	Level 4	Level4	Possible	This is a case of an 83-year-old female patient, with a relevant history of hypertension, Wolff Parkinson white, and AV block, and on treatment with high doses corticosteroids, multiple anticonvulsant medications (valproate, phenytoin) and antihypertensive medication (amlodipine), who received the second dose of Spikevax and 19 days later reported poorly described symptoms "encephalitis, encephalomyelitis and sinus node dysfunction" and aphasia. MRI: enhancement in the white matter of the posterior left parietal lobe. Infectious disease workups were negative. This case is classified as Brighton's Level 2 of diagnostic certainty and considered WHO Possible based on temporal association, but the event could also be explained by cofounders including, medical history of Wolff Parkinson White syndrome, hypertension, AV block and multiple medications.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	unknown indication. On 08-Feb-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 08-Mar-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On 26-Mar-2021, the patient experienced ENCEPHALOMYELITIS (Encephalomyelitis) (seriousness criteria hospitalization and medically significant) and ENCEPHALITIS (Encephalitis) (seriousness criteria hospitalization and medically significant). On 08-Apr-2021, the patient experienced SINUS NODE DYSFUNCTION (Sick sinus syndrome) (seriousness criteria hospitalization and medically significant). On an unknown date, the patient experienced APHASIA (Expressive aphasia) (seriousness criterion hospitalization). The patient was hospitalized from 08-Apr-2021 to 13-Apr-2021 due to APHASIA and SINUS NODE DYSFUNCTION, then from 08-Apr-2021 to 19-Apr-2021 due to ENCEPHALITIS and ENCEPHALOMYELITIS. The patient was treated with PREDNISONE (oral) on 31-Mar-2021 at a dose of 10 mg once a day; PREDNISONE (oral) on 31-Mar-2021 at a dose of 20 mg twice a day; PREDNISONE (oral) on 31-Mar-2021 at a dose of 5 mg once a day; PREDNISONE (oral) on 31-Mar-2021 at a dose of 50 UNK, Every morning; FOSPHENYTOIN SODIUM (CEREBYX) at an unspecified dose and frequency; LORAZEPAM (ATTIVAN) at an unspecified dose and frequency; ASPIRIN [ACETYLSALICYLIC ACID] (oral) at a dose of 325 mg four times per day; LEVETIRACETAM (oral) at a dose of 500 mg twice a day; VALPROATE SEMISODIUM (DIVALPROEX) (oral) at a dose of 500 mg twice a day; LEVETIRACETAM (KEPPRA [LEVETIRACETAM]) (oral) at a dose of 1000 mg twice a day; MICONAZOLE NITRATE on 15-Apr-2021 at a dose of UNK, bid and NOREPINEPHRINE BITARTRATE (LEVOPHED) ongoing since an unknown date for Hypotension, at an unspecified dose and frequency. On 13-Apr-2021, SINUS NODE DYSFUNCTION (Sick sinus syndrome) had resolved. On 19-Apr-2021, ENCEPHALITIS (Encephalitis) was resolving. At the time of the report, ENCEPHALOMYELITIS (Encephalomyelitis) was resolving and APHASIA (Expressive aphasia) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 26-Mar-2021, Magnetic resonance imaging: abnormal (abnormal) Abnormal enhancement in the white matter of the posterior left parietal lobe with no significant abnormality on t1 unenhanced images. Subtle restricted diffusion on diffusion weighted sequences. Encephalomyelitis is favoured.							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	On 08-Apr-2021, Body mass index: 24 (normal) 24. On 08-Apr-2021, Magnetic resonance imaging: abnormal (abnormal) Encephalitis. On 09-Apr-2021, Blood pressure measurement: stable (normal) Stable. On 09-Apr-2021, Heart rate: 32 (Low) 32. On 09-Apr-2021, Oxygen saturation: normal (normal) Normal. On 10-Apr-2021, Heart rate: 50 (Low) 50. On 12-Apr-2021, Blood pressure measurement: 70/40 (Low) 70/40. On 12-Apr-2021, Heart rate: 40 (Low) Improved to 50 after awaking. On 18-Apr-2021, Blood glucose (80-120): 131 (High) at 16: 52 blood glucose was 131 mg dl at 11: 41 blood glucose was 101 mg dl. On 19-Apr-2021, Blood pressure measurement: 113/65 (Low) 113/65. On 19-Apr-2021, Body temperature: 97 (normal) 97 F. On 19-Apr-2021, Heart rate: 70 (Low) 70. On 19-Apr-2021, Oxygen saturation: 100 (normal) 100 %. On 19-Apr-2021, Respiratory rate: 22 (abnormal) 22. On an unknown date, Anti-myelin-associated glycoprotein associated polyneuropathy: negative (Negative) Negative with MOG ab screen. On an unknown date, CSF test: abnormal (abnormal) CSF studies were relatively benign. On an unknown date, Computerised tomogram head: normal (normal) There Is no evidence of an acute intracranial process or alignment change from previous. On an unknown date, Human anti-human antibody test: negative (Negative) Negative with paraneoplastic syndrome with negative HU ab screen. On an unknown date, Physical examination: normal (normal) Normal. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter considered SINUS NODE DYSFUNCTION (Sick sinus syndrome), ENCEPHALOMYELITIS (Encephalomyelitis) and ENCEPHALITIS (Encephalitis) to be possibly related. No further causality assessment was provided for APHASIA (Expressive aphasia). She had no significant issues with first vaccine. Patient was admitted to hospital services, placed on telemetry and steroids increased. Neurosurgery was consulted. She became hypotensive and levophed was initiated and improved with a short period time. Patient took keppra and addition of depakote were made and her mentation improved point where she was at her baseline prior to any symptoms started nearly a month ago. Initially they planned to send							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	her to the inpatient rehabilitation but the patient was improved. The patient received IVIG x5 doses and prednisone, along with seizure meds for treatment. After a lumbar puncture she was worked up for possible metastasis. Patient done Physical, occupational and speech therapy. Patient condition was stable and she following low carb, low sodium diet. Company Comment: This case concerns a 83 year-old female patient, with a relevant history of hypertension, Wolff Parkinson white and AV block, and in treatment with corticosteroids in high doses, multiple anti convulsivant medications (valproate, phenytoin) and antihypertensive medication (amlodipine), who experienced the serious unexpected events of Encephalitis (AESI), Encephalomyelitis (AESI) and Sinus node dysfunction. The events Encephalitis and Encephalomyelitis started 19 days after the second dose of a proper schedule of administration of Moderna covid-19 vaccine (30 days between doses). The event Sinus node dysfunction started 31 days after the same second dose of Covid-19 moderna vaccine. The rechallenge is not applicable for all the events since no further doses are expected. Advanced age of the patient, medical history of Wolff Parkinson white syndrome, hypertension, AV block and multiple medications prescribed (concomitant and as treatment of the diagnosed Encephalitis and Encephalomyelitis) remain confounders for the event Sinus node dysfunction. The benefit-risk relationship of Covid-19 Vaccine moderna is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 26-Jun-2021: Follow up document received contains Events, medical history, lab investigation and concomitant medication were added and the inarrative was updated On 26-Jun-2021: Follow up document received contains no new information							
	This spontaneous case was reported by a physician assistant and describes the occurrence of RESPIRATORY FAILURE (Respiratory failure), ACUTE RESPIRATORY FAILURE (Acute hypoxic respiratory failure), ILEUS PARALYTIC (adynamic ileus), PNEUMONIA (Pneumonia), DEMYELINATING POLYNEUROPATHY (Demyelinating neuropathy), BULBAR PALSY (Bulbar weakness) and MUSCULAR WEAKNESS (Progressive Extremity Weakness) in a 51-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Diabetes mellitus, Hypertension, Glaucoma and Hyperlipidemia. Concomitant products included ATORVASTATIN	No report provided	Level 3	Level 4	0	Conditional	This report is for a 51 years old male with medical history of diabetes, hypertension, and hyperlipidemia, and concomitant medications of atorvastatin, metformin, and lisinopril, who 13 days after the 1st dose of Spikevax reported respiratory failure, and bulhar palsy. Nine days later the patient reported experiencing demyelinating neuropathy, acute respiratory failure, muscular weakness, pneumonia, and ileus paralytic. An Electromyogram was reported as abnormal consistent with demyelinating neuropathy. No other information was provided. This case according to the Brighton collaboration case definition for ADEM is classified as Level 3. According to the WHO causality assessment this case is considered Conditional. The	

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	for Cholesterol, METFORMIN for Diabetes, LISINAPRIL for Hypertension. On 21-Feb-2021 at 9:15 AM, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Subcutaneous) 1 dosage form. On 06-Mar-2021, the patient experienced RESPIRATORY FAILURE (Respiratory failure) (seriousness criteria hospitalization prolonged and medically significant) and BULBAR PALSY (Bulbar weakness) (seriousness criteria hospitalization prolonged and medically significant). On 15-Mar-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating neuropathy) (seriousness criterion hospitalization prolonged). On an unknown date, the patient experienced ACUTE RESPIRATORY FAILURE (Acute hypoxic respiratory failure) (seriousness criterion hospitalization), ILEUS PARALYTIC (adynamic ileus) (seriousness criteria hospitalization prolonged and medically significant), PNEUMONIA (Pneumonia) (seriousness criteria hospitalization prolonged and medically significant), MUSCULAR WEAKNESS (Progressive Extremity Weakness) (seriousness criterion hospitalization prolonged), ASTHENIA (Weakness), GAIT DISTURBANCE (Trouble walking), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Impaired mobility and ADLs), OBESITY (Obesity), ANAEMIA (Anemia) and GLAUCOMA (Glaucoma). The patient was hospitalized from 06-Mar-2021 to 31-Mar-2021 due to ACUTE RESPIRATORY FAILURE, BULBAR PALSY, DEMYELINATING POLYNEUROPATHY, ILEUS PARALYTIC, MUSCULAR WEAKNESS, PNEUMONIA and RESPIRATORY FAILURE. The patient was treated with AZITHROMYCIN for Pneumonia, at an unspecified dose and frequency; PARACETAMOL (TYLENOL) for Pain, at a dose of UNK, prn; DORZOLAMIDE (ophthalmic) ongoing since an unknown date for Glaucoma, at a dose of 1 drop every twelve hours; TIMOLOL (ophthalmic) ongoing since an unknown date for Glaucoma, at a dose of .5 % every twelve hours; BRIMONIDINE (ophthalmic) ongoing since an unknown date for Glaucoma, at a dose of .2 % every twelve hours; PILOCARPINE (ophthalmic) ongoing since an unknown date for Glaucoma, at a dose of 1 drop every twelve hours; LABETALOL (oral) ongoing since an unknown date for Hypertension, at a dose of 100 mg every twelve hours; NIFEDIPINE for Hypertension, at a dose of 30 mg once a day; FORMOTEROL FUMARATE, MOMETASONE FUROATE (DULERA) for Obesity, at an unspecified dose and frequency; TIOTROPIUM BROMIDE MONOHYDRATE (SPIRIVA RESPIMAT) ongoing since an unknown date for Obesity, at a dose of UNK UNK, qd; ALBUTEROL [SALBUTAMOL] ongoing since an unknown date for Obesity, at a dose of UNK, prn;						medical history of this patient constitute an important risk factor as well as the diagnosis of pneumonia and bulbar palsy before the event of demyelinating polyneuropathy. There is very little additional information provided for this report including patient's full medical history and concomitant medications history. TThere was no MRI report provided.	

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	ALLOPURINOL (oral) ongoing since an unknown date at a dose of 100 mg once a day; POLYVINYL ALCOHOL (ARTIFICIAL TEARS [POLYVINYL ALCOHOL]) (ophthalmic) ongoing since an unknown date at a dose of 1 drop as required; CHOLECALCIFEROL (oral) ongoing since an unknown date at a dose of 125 mcg once a day; CYCLOBENZAPRINE (oral) ongoing since an unknown date for Spasms, at a dose of 5 mg every eight hours; DOCUSATE SODIUM (oral) ongoing since an unknown date at a dose of 100 mg twice a day; FOLIC ACID (oral) ongoing since an unknown date at a dose of 1 mg once a day; GABAPENTINE (oral) ongoing since an unknown date at a dose of 300 mg; LATANOPROST (ophthalmic) ongoing since an unknown date at a dose of 1 drop and SENNA [SENNA ALEXANDRINA] (oral) ongoing since an unknown date at a dose of 8.6 mg. At the time of the report, RESPIRATORY FAILURE (Respiratory failure) had resolved with sequelae, ACUTE RESPIRATORY FAILURE (Acute hypoxic respiratory failure), PNEUMONIA (Pneumonia), BULBAR PALSY (Bulbar weakness), MUSCULAR WEAKNESS (Progressive Extremity Weakness), ASTHENIA (Weakness), GAIT DISTURBANCE (Trouble walking), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Impaired mobility and ADLs), OBESITY (Obesity), ANAEMIA (Anemia) and GLAUCOMA (Glaucoma) outcome was unknown, ILEUS PARALYTIC (adynamic ileus) was resolving and DEMYELINATING POLYNEUROPATHY (Demyelinating neuropathy) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 15-Mar-2021, Electromyogram: abnormal (abnormal) consistent with demyelinating neuropathy.. On 30-Mar-2021, SARS-CoV-2 test: negative (Negative) Negative. On 14-May-2021, Blood pressure diastolic: 81 mmhg (Inconclusive) Unknown. On 14-May-2021, Blood pressure systolic: 123 mmhg (Inconclusive) Unknown. On 14-May-2021, Body temperature: 36.4 degree Celsius (Inconclusive) Unknown. On 14-May-2021, Heart rate: 83 breaths per minute (Inconclusive) Unknown. On 14-May-2021, Oxygen saturation: 98 percent (Inconclusive) Unknown. On 14-May-2021, Respiratory rate: 20 breaths per minute (Inconclusive) Unknown. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Subcutaneous) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine)							

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	(Subcutaneous), the reporter considered RESPIRATORY FAILURE (Respiratory failure) and DEMYELINATING POLYNEUROPATHY (Demyelinating neuropathy) to have an unknown relationship. No further causality assessments were provided for ACUTE RESPIRATORY FAILURE (Acute hypoxic respiratory failure), ILEUS PARALYTIC (adynamic ileus), PNEUMONIA (Pneumonia), BULBAR PALSY (Bulbar weakness), MUSCULAR WEAKNESS (Progressive Extremity Weakness), ASTHENIA (Weakness), GAIT DISTURBANCE (Trouble walking), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Impaired mobility and ADLs), OBESITY (Obesity), ANAEMIA (Anemia) and GLAUCOMA (Glaucoma). It was reported that once medically stable he was deemed appropriate for inpatient rehabilitation and was transferred from hospital to rehabilitation on 31-MAR-2021 under care. Patient was instructed to follow diet with controlled carbohydrate, low fat/low cholesterol. Company comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. Patient's comorbidities and advanced age may confound the event. Unlikely, that the events are related to the vaccine. Most recent FOLLOW-UP information incorporated above includes: On 24-May-2021: Follow-up received on 24-May-2021 included updated dose vaccination information, additional medical history, lab data, concomitant medications, treatment medications, new events, updated onset dates, event outcomes, and reporter causality. On 25-May-2021: Follow up received on 25-MAY-2021 included no new information.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 11-May-2021 and was forwarded to Moderna on 11-May-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), HAEMORRHAGIC INFARCTION (Haemorrhagic infarction), PLEOCYTOSIS (Pleocytosis), HEADACHE (Headache) and INTRACRANIAL PRESSURE INCREASED (Elevated opening pressure) in a 30-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below.	No report provided	Not a case of ADEM	0	0	Unlikely	This report is for a 30 years old female with unknown medical history or concomitant medications who the same day she received the 1st dose of Spikevax was reported with ADEM, haemorrhagic infarction, pleocytosis, and intracranial pressure increased. The patient had EVD placement 11 days later and was intubated and sedated. Infectious diseases evaluation/workup negative. This report is heavily confounded by the history of ongoing headaches for several weeks before receiving the vaccine. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5, NOT a case of ADEM, rather a case of hemorrhagic cerebrovascular injury. According to the WHO causality assessment this case is considered	

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	The patient's past medical history included Ventricular drainage on 26-Mar-2021 and Endotracheal intubation on 26-Mar-2021. Concomitant products included PARACETAMOL (TYLENOL) for an unknown indication. On 26-Mar-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 26-Mar-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization, medically significant and life threatening), HAEMORRHAGIC INFARCTION (Haemorrhagic infarction) (seriousness criteria hospitalization, medically significant and life threatening), PLEOCYTOSIS (Pleocytosis) (seriousness criteria hospitalization and life threatening) and HEADACHE (Headache) (seriousness criteria hospitalization and life threatening). On an unknown date, the patient experienced MENTAL STATUS CHANGES (AMS) and INTRACRANIAL PRESSURE INCREASED (Elevated opening pressure) (seriousness criterion medically significant). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), HAEMORRHAGIC INFARCTION (Haemorrhagic infarction), PLEOCYTOSIS (Pleocytosis) and HEADACHE (Headache) had not resolved and MENTAL STATUS CHANGES (AMS) and INTRACRANIAL PRESSURE INCREASED (Elevated opening pressure) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 26-Mar-2021, CSF culture: negative (Negative) Negative. On 26-Mar-2021, CSF lymphocyte count: high (High) high. On 26-Mar-2021, CSF monocyte count: low (Low) low. On 26-Mar-2021, CSF red blood cell count: positive (Positive) Positive. On 26-Mar-2021, Cytomegalovirus test: negative (Negative) Negative. On 26-Mar-2021, Enterovirus test: negative (Negative) Negative. On 26-Mar-2021, Escherichia test: negative (Negative) Negative. On 26-Mar-2021, Herpes simplex test: negative (Negative) Negative. On 26-Mar-2021, Human herpes virus 6 serology: negative (Negative) Negative. On 26-Mar-2021, Influenza virus test: negative (Negative) Negative. On 26-Mar-2021, Protein total: high (High) high. On 26-Mar-2021, Streptococcus test: negative					unlikely. There is very little additional information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding MRI result.		

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	(Negative) Negative. On 26-Mar-2021, Varicella virus test: negative (Negative) Negative. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), HAEMORRHAGIC INFARCTION (Haemorrhagic infarction), PLEOCYTOSIS (Pleocytosis), HEADACHE (Headache), MENTAL STATUS CHANGES (AMS) and INTRACRANIAL PRESSURE INCREASED (Elevated opening pressure) to be possibly related. The patient was transferred for workup of headache, AMS, and found to have CSF lymphocytic pleocytosis along with elevated opening pressure and parietal and occipital infarcts in the setting of multiple recent presentations to the ED over the past several weeks for ongoing headache. The patient had EVD placement on 07APR2021 and was intubated and sedated. All workup had remained negative so far, but some studies were still pending. Diagnosis clinically most consistent with ADEM but unclear trigger. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This case was received via an unknown source (no reference has been entered for a health authority or license partner) on 23-May-2021 and was forwarded to Moderna on 23-May-2021. This regulatory authority case was reported by a physician and describes the occurrence of GUILLAIN-BARRE SYNDROME (guillain barre syndrome) and DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) in a patient of an unknown age and gender who received mRNA-1273 (Moderna Covid-19 Vaccine) for COVID-19 vaccination. The patient's past medical history included Guillain Barre syndrome. On an unknown date, the patient received first dose of mRNA-1273 (Moderna Covid-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, the patient experienced GUILLAIN-BARRE SYNDROME (guillain barre syndrome) (seriousness criteria hospitalization, disability and medically significant) and DEMYELINATING POLYNEUROPATHY (Demyelinating	0	Level 4	Level 4	0	conditional	This report is for a patient of unknown age and gender, and with previous medical history of GBS. No other information was provided including any additional medical history or concomitant medications. The patient after receiving the 1st dose of the vaccine experienced GBS at an unknown time after the vaccine and demyelinating neuropathy. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4 (not enough information to classify in any level); according to the Brighton classification for Encephalitis is also classified as Level 4 (Not enough information for its Level classification), and according to the WHO causality assessment this case is considered conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

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	polyneuropathy) (seriousness criteria hospitalization, disability and medically significant). At the time of the report, GUILLAIN-BARRE SYNDROME (guillain barre syndrome) outcome was unknown and DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, SARS-CoV-2 test: negative (Negative) Negative COVID-19 test. The action taken with mRNA-1273 (Moderna Covid-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna Covid-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. No concomitant medication was reported. Treatment drug information was not given. Company comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This case was received via United States FDA VAERS (Reference number: [REDACTED]) on 01-Jun-2021 and was forwarded to Moderna on 01-Jun-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), OSMOTIC DEMYELINATION SYNDROME (Osmotic demyelination syndrome), BRAIN STEM INFARCTION (Brain stem infarction), CEREBROVASCULAR DISORDER (Cerebrovascular disorder), DYSPHAGIA (Dysphagia), ISCHAEMIA (Ischaemia) and GENERAL PHYSICAL HEALTH DETERIORATION (General physical health deterioration) in an 82-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The patient's past medical history included Hyperlipidemia, Hypertension, Obesity, Obstructive sleep apnea syndrome and CPAP. Concurrent medical conditions included Drug allergy (Piperidine), Lactose intolerance (Epoxy resin Lactose) and Diabetes. Concomitant products included AZELASTINE HYDROCHLORIDE (ASTELIN [AZELASTINE	0	Level 4	Level 4	0	possible	This is a regulatory report concerning an 82-year-old male patient with medical history of hypertension, obesity, hyperlipidemia, and on several antihypertensive, statins concomitant medications. Eight days after receiving the second dose of Spikevax, the patient reported experiencing dysarthria, ischemia, CV disorder and was diagnosed with ADEM and osmotic demyelination syndrome. The patient died 3 months later. On 17-Mar-2021, Magnetic resonance imaging head showed osmotic demyelination; Ischemia cannot be entirely excluded given the high signal on diffusion-weighted imaging. Abnormal signal in brainstem and right occipital lobe appears to show mainly T2 shine through rather than restricted diffusion; Given configuration pons lesion and appearance of right occipital lesion, demyelination such as related to osmotic demyelination considered. The patient's neurologist documented in the medical record " Cannot rule out autoimmune reaction after a COVID-19 vaccination (symptoms started 3 weeks after the 2nd vaccine shot with moderna)" Originally started with dysarthria approximately 3 weeks prior to	

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	HYDROCHLORIDE]), OMEPRAZOLE (PROTONIX [OMEPRAZOLE]), ATORVASTATIN CALCIUM (LIPITOR), CALCIUM CARBONATE, DOXAZOSIN MESILATE (CARDURA), MOMETASONE FUROATE (FLONASE [MOMETASONE FUROATE]), DEXTROMETHORPHAN HYDROBROMIDE (ROBITUSSIN [DEXTROMETHORPHAN HYDROBROMIDE]), INSULIN GLARGINE (LANTUS), METOPROLOL TARTRATE (LOPRESSOR), MIRTAZAPINE (REMERNON), OLANZAPINE (ZYPREXA), ONDANSETRON (ZOFTRAN [ONDANSETRON]), MACROGOL 3350 (MIRALAX) and LACTOBACILLUS ACIDOPHILUS (FLORASTOR [LACTOBACILLUS ACIDOPHILUS]) for an unknown indication. On 17-Feb-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 25-Feb-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria death, hospitalization and medically significant), OSMOTIC DEMYELINATION SYNDROME (Osmotic demyelination syndrome) (seriousness criteria death, hospitalization and medically significant), BRAIN STEM INFARCTION (Brain stem infarction) (seriousness criteria death, hospitalization and medically significant), CEREBROVASCULAR DISORDER (Cerebrovascular disorder) (seriousness criteria death and hospitalization), DYSARTHRIA (Dysarthria) (seriousness criteria death and hospitalization), ISCHAEMIA (Ischaemia) (seriousness criteria death and hospitalization) and GENERAL PHYSICAL HEALTH DETERIORATION (General physical health deterioration) (seriousness criteria death and hospitalization). The patient was hospitalized on 13-Apr-2021 due to ACUTE DISSEMINATED ENCEPHALOMYELITIS, BRAIN STEM INFARCTION, CEREBROVASCULAR DISORDER, DYSARTHRIA, GENERAL PHYSICAL HEALTH DETERIORATION, ISCHAEMIA and OSMOTIC DEMYELINATION SYNDROME. The patient died on 01-May-2021. The cause of death was not reported. It is unknown if an autopsy was performed. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 17-Mar-2021, Magnetic resonance imaging head: abnormal (abnormal) osmotic demyelination; Ischemia cannot be entirely excluded given the high signal on diffusion-weighted imaging. On 18-Apr-2021, Magnetic resonance imaging head: abnormal (abnormal) Abnormal signal in					presentation. The patient was diagnosed with a brain stem CVA. Continued to progressively worsen and readmitted and eventually diagnosed with Acute disseminated encephalomyelitis (ADEM) on top of neurovascular disease. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4 (not enough information to classify in any level); according to the Brighton classification for Encephalitis is also classified as Level 4 (Not enough information for its Level classification), and accoring to the WHO causality assessment this case is considered possible. The concurrent diagnosis of osmotic demyelination syndrome provides a more plausible explanation for the adverse events. The osmotic demyelination syndrome (ODS) has been a recognized complication of the rapid correction of hyponatremia as well as a variety of other medical conditions have been associated with the development of ODS, independent of changes in serum sodium. It is suggested that the pathogenesis of ODS may involve the inability of brain cells to respond to rapid changes in osmolality of the interstitial (extracellular) compartment of the brain, leading to dehydration of energy-depleted cells with subsequent axonal damage that occurs in characteristic areas. Features of the syndrome include quadriplegia and neurocognitive changes in the presence of characteristic lesions found on magnetic resonance imaging of the brain. There is very little additional information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.		

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	brainstem and right occipital lobe appears to show mainly T2 shine through rather than restricted diffusion; Given configuration pons lesion and appearance of right occipital lesion, demyelination such as related to osmotic demyelination considered. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No treatment medications were reported. The patient's neurologist documented in the medical record " Cannot rule out autoimmune reaction after a COVID-19 vaccination (symptoms started 3 weeks after the 2nd vaccine shot with moderna)" Originally started with dysarthria approximately 3 weeks prior to presentation on 18-Mar-2021 (exact date of onset unknown). The patient was diagnosed with a brain stem CVA. Continued to progressively worsen and readmitted on 13-Apr-2021. Eventually diagnosed with Acute disseminated encephalomyelitis (ADEM) on top of neurovascular disease. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 01-Jun-2021 and was forwarded to Moderna on 01-Jun-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of ASTHENIA (Asthenia), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), GAIT DISTURBANCE (Gait disturbance), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) and MUSCULAR WEAKNESS (Muscular weakness) in a 69-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. Concurrent medical conditions included Hypertension, Anxiety, Lumbar puncture since 19-Mar-2021 and Immunoglobulin therapy since 19-Mar-2021. Concomitant products included HCTZ for an unknown indication. On 18-Mar-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 19-Mar-2021, the patient experienced ASTHENIA (Asthenia) (seriousness criteria hospitalization and disability),	0	Level 5	Level 5	0	possible	This report is for a 69 years old female with medical history of hypertension, and anxiety. Patient was taking HCTZ. The next day after the patient received the 1st dose of Spikevax the patient experienced asthenia, gait disturbance, demyelinating neuropathy, muscular weakness and was diagnosed with GBS. According to the reporter the patient's Na was low on hospital admission, attributed to SIADH and HCTZ. Patient's HCTZ was discontinued and Na gradually corrected to the 130s. Patient received 4 doses of IVIG with marked improvement in symptoms. Test results showed Blood sodium: decreased; CSF glucose increased, CSF protein increased; and Electromyogram abnormal. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5 (not case); according to the Brighton classification for Encephalitis is also classified as Level 5, and according to the WHO causality assessment this case is considered possible. There are important risk factors associated with this report including the patient's medical history of hypertension and low Na. This patient was diagnosed with GBS instead of	

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	DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization, disability and medically significant), GAIT DISTURBANCE (Gait disturbance) (seriousness criteria hospitalization and disability), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criteria hospitalization, disability and medically significant) and MUSCULAR WEAKNESS (Muscular weakness) (seriousness criteria hospitalization and disability). At the time of the report, ASTHENIA (Asthenia), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), GAIT DISTURBANCE (Gait disturbance), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) and MUSCULAR WEAKNESS (Muscular weakness) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 19-Mar-2021, Blood sodium: decreased (Low) decreased. On 19-Mar-2021, CSF glucose: increased (High) increased. On 19-Mar-2021, CSF protein: increased (High) increased. On 19-Mar-2021, Electromyogram: abnormal (abnormal) abnormal. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Patient was admitted to the hospital for evaluation. Patient's Na was low on admission, attributed to SIADH and HCTZ. Patient's HCTZ was discontinued and Na gradually corrected to the 130s. Patient received 4 doses of IVIG with marked improvement in symptoms. The concern is that her GBS was possible vaccine induced given the sequence of events and patient being completely mobile, ambulatory before the vaccine was administered. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.						ADEM but at this point there is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	
	This case was received via [REDACTED] Reference number: [REDACTED] on 01-Jun-2021 and was forwarded to Moderna on 01-Jun-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of DEMYELINATING	0	Level 5	Level 5	0	conditional	This report is for a 67 years old female for which medical history and concomitant medication information was not provided and who 25 days after receiving the 2nd dose of the vaccine developed severe numbness and tingling in her extremities, and she was then diagnosed with chronic	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	POLYNEUROPATHY (Demyelinating polyneuropathy), HYPOAESTHESIA (Hypoaesthesia) and PARAESTHESIA (Paraesthesia) in a 67-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch nos. 004M20A and 029A21A) for COVID-19 vaccination. No Medical History information was reported. On 31-Jan-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 25-Feb-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization, disability and medically significant), HYPOAESTHESIA (Hypoaesthesia) (seriousness criteria hospitalization and disability) and PARAESTHESIA (Paraesthesia) (seriousness criteria hospitalization and disability). At the time of the report, DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), HYPOAESTHESIA (Hypoaesthesia) and PARAESTHESIA (Paraesthesia) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 25-Feb-2021, Electroencephalogram: inconclusive (Inconclusive) inconclusive.. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medication information was provided. No treatment information provided. Action taken with mRNA-1273 in response to the drug was not applicable. The patient developed severe numbness and tingling in her extremities, she was then diagnosed with chronic demyelinating polyneuropathy. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.						demyelinating polyneuropathy. Test result information was not provided, only inconclusive results from an EEG. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5 (not case); according to the Brighton classification for Encephalitis is also classified as Level 5, and according to the WHO causality assessment this case is considered conditional. The diagnosis of chronic demyelinating polyneuropathy provides a more plausible explanation for the AE described for this patient. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course,	
	This case was received via [REDACTED] (Reference number [REDACTED]) on 08-Jun-2021 and was forwarded to Moderna on 08-Jun-2021. This regulatory authority case was reported by an [REDACTED]	MRI head, neck & spine: abnormal. No details provided	Level 3	Level 2	0	Conditional	This report is for an 82 years old male with medical history of hypersensitivity lung disease, CVA, diverticulitis, obesity, hypertension, diabetes, chronic kidney disease and hyperlipidemia, and a long	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	other health care professional and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), ASTHENIA (Asthenia/progressive generalized weakness) and CRANIAL NERVE DISORDER (Cranial nerve disorder) in an 82-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The patient's past medical history included Lung disease (Hypersensitivity lung disease). Concurrent medical conditions included Sleep apnea, Cerebrovascular accident, Diverticulitis, Obesity, Milk allergy (Lactose allergy), Allergy (Epoxy resin), Hypertension, Diabetes mellitus, Chronic kidney disease and Hyperlipidemia. Concomitant products included ATORVASTATIN, METOPROLOL, PANTOPRAZOLE, CALCIUM GLUCONATE, PROBIOTICS NOS, DOXAZOSIN MESILATE (CARDURA) and INSULIN for an unknown indication. On 01-Feb-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 01-Mar-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization, disability, medically significant and life threatening), ASTHENIA (Asthenia/progressive generalized weakness) (seriousness criteria hospitalization, disability and life threatening) and CRANIAL NERVE DISORDER (Cranial nerve disorder) (seriousness criteria hospitalization, disability and life threatening). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), ASTHENIA (Asthenia/progressive generalized weakness) and CRANIAL NERVE DISORDER (Cranial nerve disorder) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 01-Mar-2021, Blood test: inconclusive (Inconclusive) Inconclusive. On 01-Mar-2021, Electromyogram: abnormal (abnormal) Result-Abnormal. On 01-Mar-2021, Lumbar puncture: abnormal (abnormal) Result-Abnormal. On 01-Mar-2021, Magnetic resonance imaging head: abnormal (abnormal) Result-Abnormal. On 01-Mar-2021, Magnetic resonance imaging neck: abnormal (abnormal) Result-Abnormal. On 01-Mar-2021, Magnetic resonance imaging spinal: abnormal (abnormal) Result- Abnormal.					list of concomitant medications, who 28 days after receiving the 1st dose of the vaccine developed ADEM, asthenia, and cranial nerve disorder. No other information was provided. Test result information showed abnormal Electromyogram, lumbar puncture, MRI of the head, and neck, and spine. But no details of findings provided. This case according to the Brighton collaboration case definition for ADEM is classified as Level 3. No MRI findings reported. According to the WHO causality assessment this case is considered Conditional. More information for proper assessment needed. There is very little information provided about the MRI and infectious diseases evaluation reports.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No treatment products reported. Company Comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This case was received via [REDACTED] Reference number: [REDACTED] on 15-Jun-2021 and was forwarded to Moderna on 15-Jun-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of RESPIRATORY FAILURE (Respiratory failure), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), ASTHENIA (Asthenia), MUSCULAR WEAKNESS (Muscular weakness), SPEECH DISORDER (Speech disorder), GAIT INABILITY (Gait inability), MYALGIA (Myalgia) and FATIGUE (Fatigue) in a 51-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Hypertension, Diabetes, Hypocholesteremia and Glaucoma. Concomitant products included LISINAPRIL, ATORVASTATIN, METFORMIN, DORZOLAMIDE, LATANOPROST, BRIMONIDINE, PILOCARPINE and TIMOLOL for an unknown indication. On 21-Feb-2021, the patient received dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Subcutaneous) 1 dosage form. On 21-Feb-2021, the patient experienced RESPIRATORY FAILURE (Respiratory failure) (seriousness criteria hospitalization, disability and medically significant), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization, disability and medically significant), ASTHENIA (Asthenia) (seriousness criteria hospitalization and disability), MUSCULAR WEAKNESS (Muscular weakness) (seriousness criteria hospitalization and disability), SPEECH DISORDER (Speech disorder) (seriousness criteria hospitalization and disability), GAIT INABILITY (Gait inability) (seriousness criteria hospitalization and disability), MYALGIA (Myalgia) (seriousness	No MRI report available	Level 2	Level 4	0	Conditional	This report is for a 51 years old male with medical history of hypertension, diabetes, hcholesteremia and a long list of concomitant medications, who the same day after receiving the 1st dose of the vaccine he immediately experienced weakness, myalgias, fatigue. The progressive weakness in limbs continued and by day 13 reported difficulty speaking and inability to walk. Admitted to acute care hospital for progressive extremity weakness, bulbar weakness, and respiratory failure. EMG testing demonstrated findings of demyelinating neuropathy. This case according to the Brighton collaboration case definition for ADEM is classified as Level 2. According to the WHO causality assessment this case is considered Conditional. More data for proper assessment needed. There are also other important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	criteria hospitalization and disability) and FATIGUE (Fatigue) (seriousness criteria hospitalization and disability). 21-Feb-2021, the patient experienced INCORRECT ROUTE OF PRODUCT ADMINISTRATION (Inappropriate route of vaccination). At the time of the report, RESPIRATORY FAILURE (Respiratory failure), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), ASTHENIA (Asthenia), MUSCULAR WEAKNESS (Muscular weakness), SPEECH DISORDER (Speech disorder), GAIT INABILITY (Gait inability), MYALGIA (Myalgia) and FATIGUE (Fatigue) had not resolved and INCORRECT ROUTE OF PRODUCT ADMINISTRATION (Inappropriate route of vaccination) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 21-Feb-2021, Electromyogram: abnormal (abnormal) Demyelinating polyneuropathy. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Subcutaneous) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Subcutaneous), the reporter did not provide any causality assessments. The patient received first dose of Moderna vaccine after which he immediately experienced weakness, myalgias, fatigue. The progressive weakness in limbs continued and by day 13 following his vaccine patient presented to hospital with difficulty speaking and inability to walk. Admitted to acute care hospital for progressive extremity weakness, bulbar weakness, and respiratory failure. EMG testing demonstrated findings of demyelinating neuropathy. Patient was transferred for intensive inpatient rehabilitation on 31-Mar-2021 and remains currently hospitalized. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. The causality for the event of inappropriate route of product administration remains as not applicable.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 15-Jun-2021 and was forwarded to Moderna on 15-Jun-2021. This regulatory authority case was reported by a health care professional and describes the occurrence of DEMYELINATING	No MRI report available	Level 3	Level 4	0	Conditional	This report is for a 33 years old female with medical history of hypertension and concomitant use of chlorthalidone, who 17 days after receiving the 1st dose of the vaccine reported demyelinating polyneuropathy, acute polyneuropathy, Weakness, Bronchitis and Paraesthesia. CSF analysis: protein high, and Lumbar	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	POLYNEUROPATHY (Demyelinating polyneuropathy), ACUTE POLYNEUROPATHY (Acute polyneuropathy), ASTHENIA (Weakness), BRONCHITIS (Bronchitis) and PARAESTHESIA (Paraesthesia) in a 33-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 026A21A) for COVID-19 vaccination. Concurrent medical conditions included Hypertension, Allergy to nuts (Peanut allergy) and Allergy to chemicals (Allergy to hydrogen peroxide). Concomitant products included CHLORTHALIDONE for an unknown indication. On 11-Mar-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 28-Mar-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization and medically significant), ACUTE POLYNEUROPATHY (Acute polyneuropathy) (seriousness criteria hospitalization and medically significant), ASTHENIA (Weakness) (seriousness criterion hospitalization), BRONCHITIS (Bronchitis) (seriousness criterion hospitalization) and PARAESTHESIA (Paraesthesia) (seriousness criterion hospitalization). At the time of the report, DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), ACUTE POLYNEUROPATHY (Acute polyneuropathy), ASTHENIA (Weakness), BRONCHITIS (Bronchitis) and PARAESTHESIA (Paraesthesia) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 28-Mar-2021, CSF protein: high (High) high. On 28-Mar-2021, Lumbar puncture: abnormal (abnormal) abnormal. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No Treatment medicines were not provided by the reporter. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.					puncture abnormal. This case according to the Brighton collaboration case definition for ADEM is classified as Level 3; according to the Brighton classification for Encephalitis is also classified as Level 4, and according to the WHO causality assessment this case is considered Conditional, needs more information to assess this case.. The diagnosis of bronchitis is an important confounder and risk factor for for the AE described for this patient. There is very little information provided for this report including patient’s full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	This case was initially received via [REDACTED] on 15-Jun-2021. (Reference number: [REDACTED]) The most recent information was received on 15-Jun-2021 and was forwarded to Moderna on an unknown date. This regulatory authority case was reported by a health care professional and describes the occurrence of ENCEPHALOMYELITIS (Encephalomyelitis) in a 64-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 019B21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Drug allergy (Amlodipine-Rash), Shellfish allergy, Hypertension, Hyperlipidemia, Angioedema (Sulfa) and Drug allergy (Sulfa). Concomitant products included HYDROCHLOROTHIAZIDE, LISINAPRIL (LISINAPRIL HCTZ) and ATENOLOL for an unknown indication. On 13-Apr-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 14-Apr-2021, the patient experienced ENCEPHALOMYELITIS (Encephalomyelitis) (seriousness criterion medically significant), DISTURBANCE IN ATTENTION (Disturbance in attention), HYPOAESTHESIA (Hypoaesthesia), ASTHENIA (Asthenia), PAIN (Pain), FATIGUE (Fatigue), CHILLS (Chills) and HEADACHE (Headache). The patient was treated with METHYLPREDNISOLONE SODIUM SUCCINATE (SOLUMEDROL) at a dose of 1 dosage form. At the time of the report, ENCEPHALOMYELITIS (Encephalomyelitis), DISTURBANCE IN ATTENTION (Disturbance in attention), HYPOAESTHESIA (Hypoaesthesia), ASTHENIA (Asthenia), PAIN (Pain), FATIGUE (Fatigue), CHILLS (Chills) and HEADACHE (Headache) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 05-May-2021, Magnetic resonance imaging head: abnormal (abnormal) Abnormal signal intensities within the corpus callosum and left hippocampus that may represent acute disseminated encephalomyelitis (ADEM). The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments.	0	Level 4	Level 4	0	possible	This report is for a 64 years old female with medical history of hypertension, hyperlipidemia, angioedema and taking HCTZ, lisinopril, and atenolol, who the next day after receiving the 1st dose of the vaccine developed Disturbance in attention, Hypoaesthesia, Asthenia, Pain, Fatigue, Chills and Headache, and was diagnosed with Encephalomyelitis. The patient was treated with METHYLPREDNISOLONE SODIUM SUCCINATE (SOLUMEDROL) at a dose of 1 dosage form. Test results conducted a month and a half later, showed an abnormal MRI indicating the possibility of an ADEM diagnosis but not conclusive. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4; according to the Brighton classification for Encephalitis is classified as Level , and according to the WHO causality assessment this case is considered possible. Information provided in this report does not provide clear indications of this been a case of ADEM or encephalitis. The fact that the patient was treated with solumedrol indicates more a hypersensitivity reaction. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	Laboratory tests include MRV Brain on 20-05-2021 with Normal Results , Normal MRV Head Company Comment : Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. Most recent FOLLOW-UP information incorporated above includes: On 15-Jun-2021: Upon internal review on 09-SEP-2021 Results for Laboratory data Magnetic resonance imaging Head was added, Laboratory data of MRV Brain was added to the narrative							
	This case was received via [REDACTED] on 15-Jun-2021 and was forwarded to Moderna on 15-Jun-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of ENCEPHALOMYELITIS (Encephalomyelitis) in a 61-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. No Medical History information was reported. On 16-Apr-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 23-Apr-2021, the patient experienced ENCEPHALOMYELITIS (Encephalomyelitis) (seriousness criteria hospitalization prolonged and medically significant). At the time of the report, ENCEPHALOMYELITIS (Encephalomyelitis) had not resolved. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. On an unknown date, an MRI was performed, however the results were not provided. No concomitant medication details was provided. No treatment medication details was provided. Based on the current available information and temporal association between the use of the product and the start date of the event, a causal relationship cannot be excluded.	0	Level 4	Level 4	0	conditional	This report is for a 61 years old female for which medical history and concomitant medication information was not provided and who 7 days after receiving the 1st dose of the vaccine developed encephalomyelitis. No other information was provided. Test result information was not provided, only that a MRI was conducted. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4; according to the Brighton classification for Encephalitis is also classified as Level 4, and according to the WHO causality assessment this case is considered conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding laboratory tests conducted, results, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 15-Jun-2021 and was forwarded to Moderna on 15-Jun-2021. This regulatory authority case was reported by a health care professional and describes the occurrence of ACUTE POLYNEUROPATHY (Acute polyneuropathy), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), GAIT DISTURBANCE (Gait disturbance), HYPOAESTHESIA (Hypoesthesia), INFLAMMATION (Inflammation), MUSCULAR WEAKNESS (Muscular weakness), PAIN (Pain), PRURITUS (Pruritus) and SENSORIMOTOR DISORDER (Sensorimotor disorder) in a 38-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. Concomitant products included MULTIVITAMIN [VITAMINS NOS] for an unknown indication. On 03-May-2021, the patient received dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 04-May-2021, the patient experienced ACUTE POLYNEUROPATHY (Acute polyneuropathy) (seriousness criterion hospitalization and medically significant), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criterion hospitalization and medically significant), GAIT DISTURBANCE (Gait disturbance) (seriousness criterion hospitalization), HYPOAESTHESIA (Hypoesthesia) (seriousness criterion hospitalization), INFLAMMATION (Inflammation) (seriousness criterion hospitalization), MUSCULAR WEAKNESS (Muscular weakness) (seriousness criterion hospitalization), PAIN (Pain) (seriousness criterion hospitalization), PRURITUS (Pruritus) (seriousness criterion hospitalization) and SENSORIMOTOR DISORDER (Sensorimotor disorder) (seriousness criterion hospitalization). The patient was treated with IMMUNOGLOBULIN G HUMAN (intravascular) ongoing from 24-May-2021 at an unspecified dose and frequency. At the time of the report, ACUTE POLYNEUROPATHY (Acute polyneuropathy), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), GAIT DISTURBANCE (Gait disturbance), HYPOAESTHESIA (Hypoesthesia), INFLAMMATION (Inflammation), MUSCULAR WEAKNESS (Muscular weakness), PAIN (Pain), PRURITUS (Pruritus) and SENSORIMOTOR DISORDER (Sensorimotor disorder) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 04-May-2021, CSF glucose: 51 (normal)	0	Level 5	Level 5	0	Unlikely	This report is for a 38 years old female for which medical history and concomitant medication information was not provided and who the next day after receiving the 1st dose of the vaccine developed progressive sensorimotor changes. The patient initially experienced itching in palms of her hands and feet then gradually ascending pain and numbness, with weakness starting in right lower extremity first noted 16 days later and gradually progressed such that she had difficulty ambulating independently. Patient was diagnosed with acute inflammatory demyelinating polyneuropathy 20 days after the vaccine, and was started on a five days treatment with Intravenous immunoglobulin (IVIG). Lumbar Puncture performed with CSF results as follows: protein slightly elevated at 57, glucose normal at 51, WBC 4 and RBC less than 1 in tube 4. MRI Brain was unremarkable and MRI C spine notes possible mild enhancement involving nerve roots at multiple levels. The diagnosis was acute polyneuropathy, probably related to the findings mentioned in the MRI of the spine. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5 (not an ADEM case); according to the Brighton classification for Encephalitis is also classified as Level 5 (Not an Encephalitis case), and according to the WHO causality assessment this case is considered unlikely. The diagnosis of acute polyneuropathy provides a more plausible explanation for the AEs described for this patient. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course,	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Caosality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	normal. On 04-May-2021, CSF protein: 57 (High) Slightly elevated. On 04-May-2021, CSF red blood cell count: less than1 in tube (Positive) Positive. On 04-May-2021, CSF white blood cell count: 4 (Positive) Positive. On 04-May-2021, Magnetic resonance imaging head: unremarkable (normal) normal. On 04-May-2021, Magnetic resonance imaging neck: c-spine possible mild enhancement involving nerve (Inconclusive) C-Spine possible mild enhancement involving nerve roots at multiple levels.. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. The patient experienced progressive sensorimotor changes first starting one day after Moderna COVID vaccine on 03-May-2021, She initially experienced itching in palms of her hands and feet then gradually ascending pain and numbness, with weakness starting in right lower extremity first noted on 20-May-2021 and gradually progressed such that she had difficulty ambulating independently since 23-May-2021. Diagnosed with acute inflammatory demyelinating polyneuropathy on 24-May-2021, starting five days of treatment with Intravenous immunoglobulin (IVIG). On 23-May-2021 patient pass for the procedure lumbar puncture. Treatment included IVIG. Company comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This case was received via [REDACTED] (Reference number [REDACTED]) on 29-Jun-2021 and was forwarded to Moderna on 29-Jun-2021. This regulatory authority case was reported by a health care professional and describes the occurrence of DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) in a 64-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 020B21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Previously administered products included for an unreported indication: Influenza vaccine (in the fall	No MRI report available	Level 3	Level 4	0	Conditional	This report is for a 64 years old male with medical history of GBS after the influenza vaccine recently, hyperlipidemi, hypertension and diabetes and concomitant medication informations including amitriptiline, aspirin, dulixerine, gabapenting, and glimepiride who 2 days after receveing the 1st dose of the vaccine developed muscular wekness, paraesthesia, and sensory loss. Patient was diagnosed with recurrence of distal muscle weakness and worsening of length dependent sensory loss/paresthesias consistent with recurrent acute polyneuropathy. Test results included EMG/NCS testing consistent with acute demvelinating polyneuronopathy. This case	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	of 2020 following the influenza vaccine but had recovered very well with minimal deficits). Concurrent medical conditions included Hyperlipidemia, Diabetes mellitus and Hypertension. Concomitant products included AMITRIPTYLINE, ACETYLSALICYLIC ACID (ASPIRIN 81), DULOXETINE, GABAPENTIN and GLIMEPIRIDE for an unknown indication. On 01-Apr-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 03-Apr-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criterion medically significant), MUSCULAR WEAKNESS (Muscular weakness), PARAESTHESIA (Paraesthesia) and SENSORY LOSS (Sensory loss). At the time of the report, DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), MUSCULAR WEAKNESS (Muscular weakness), PARAESTHESIA (Paraesthesia) and SENSORY LOSS (Sensory loss) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 03-Apr-2021, Electromyogram: abnormal (abnormal) Testing consistent with acute demyelinating polyneuropathy.. On 03-Apr-2021, Nerve conduction studies: testing consistent with acute demyelinating polyn (abnormal) Testing consistent with acute demyelinating polyneuropathy.. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Treatment medication were not reported/unknown. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.						according to the Brighton collaboration case definition for ADEM is classified as Level 3, since there is no results of brain MRI. According to the WHO causality assessment this case is considered Conditional. More information needed to assess this case. The diagnosis of GBS after the influenza vaccine constitutes an important confounder for this report. There is also very little information provided for this report including patient's full medical history and concomitant medications history, as well as information missing regarding other laboratory tests conducted, test results, treatment, medical course, etc.	
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 29-Jun-2021 and was forwarded to Moderna on 29-Jun-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy) in a 41-year-old male patient who received mRNA-	No report provided	Level 5	Level 5	0	Unlikely	This report is for a 41 years old male with medical history of anxiety, repressioon, obesity, fatty liver and IgA nephropathy with several concomitant medications who the next day after receiving the 2nd dose of the vaccine developed proteinuria, hematuria, fever and malaise. Patient had similar proteinuria and hematuria in response to viral infections (influenza)	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	1273 (Moderna COVID-19 Vaccine) (batch no. 022C21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Anxiety, Depression, Obesity, Nonalcoholic fatty liver disease and IgA nephropathy (suspected IgA nephropathy). Concomitant products included SERTRALINE, FAMOTIDINE, OMEPRAZOLE, LORATADINE and COLECALCIFEROL (VITAMIN D [COLECALCIFEROL]) for an unknown indication. On 27-May-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 28-May-2021, the patient experienced IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy) (seriousness criterion medically significant), HAEMATURIA (Haematuria), PROTEINURIA (Proteinuria) and PYREXIA (Pyrexia). The patient was treated with PARACETAMOL (TYLENOL) for Fever, at an unspecified dose and frequency. At the time of the report, IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy), HAEMATURIA (Haematuria), PROTEINURIA (Proteinuria) and PYREXIA (Pyrexia) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 28-May-2021, Urine analysis: unknown (Inconclusive) Proteinuria about 0.5g/L. Hematuria about 200 ery/uL. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Action taken with mRNA-1273 in response to the event was not applicable. Patient had proteinuria about 0.5g/L, hematuria about 200 ery/uL, fever of 100.5F oral and malaise. Patient had similar proteinuria and hematuria in response to viral infections (influenza) before but it had resolved and not been seen in the last year prior to the vaccination. Patient had suspected mild IgA nephropathy but not confirmed. Fever and malaise resolved in 36 hours, hematuria resolved in about 4 days and proteinuria in about 6 days. No treatment other than tylenol for fever. Company Comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a					before but it had resolved and not been seen in the last year prior to the vaccination. Patient had suspected mild IgA nephropathy but not confirmed. Fever and malaise resolved in 36 hours, hematuria resolved in about 4 days and proteinuria in about 6 days. No treatment other than tylenol for fever. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5 (not case); according to the Brighton classification for Encephalitis is also classified as Level 5, and according to the WHO causality assessment this case is considered unlikely. The diagnosis of suspected IgA proteinuria provides a more plausible explanation for the AE described for this patient. There is very little information provided for this report including patient’s full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course,		

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	causal relationship cannot be excluded. However, more information is required for further assessment.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 06-Jul-2021 and was forwarded to Moderna on 06-Jul-2021. This regulatory authority case was reported by a health care professional and describes the occurrence of DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), CEREBRAL INFARCTION (Cerebral infarction), RESPIRATORY DISTRESS (Respiratory distress), PLASMAPHERESIS (Plasmapheresis), ENDOTRACHEAL INTUBATION (Endotracheal intubation), IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy), ASTHENIA (Asthenia), HYPOAESTHESIA (Hypoesthesia), MOBILITY DECREASED (Mobility decreased) and PARAESTHESIA (Paraesthesia) in a 58-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. Unknown) for COVID-19 vaccination. No Medical History information was reported. On 30-May-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 10-Jun-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization, disability, medically significant and life threatening), CEREBRAL INFARCTION (Cerebral infarction) (seriousness criteria hospitalization, disability, medically significant and life threatening), RESPIRATORY DISTRESS (Respiratory distress) (seriousness criteria hospitalization, disability, medically significant and life threatening), PLASMAPHERESIS (Plasmapheresis) (seriousness criteria hospitalization, disability and life threatening), ENDOTRACHEAL INTUBATION (Endotracheal intubation) (seriousness criteria hospitalization, disability and life threatening), IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy) (seriousness criteria hospitalization, disability and life threatening), ASTHENIA (Asthenia) (seriousness criteria hospitalization, disability and life threatening), HYPOAESTHESIA (Hypoesthesia) (seriousness criteria hospitalization, disability and life threatening), MOBILITY DECREASED (Mobility decreased) (seriousness criteria hospitalization, disability and life threatening) and PARAESTHESIA (Paraesthesia) (seriousness criteria hospitalization, disability and life threatening). At the time of the report, DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), CEREBRAL	0	Level 3	Level 4	0	conditional	This is a case of a 58-year-old male patient with no medical history information reported, who received the first dose of Spikevax vaccine and 11 days later experienced demyelinating polyneuropathy, cerebral infarction, asthenia, decreased, mobility, paraesthesia, hypoesthesia and respiratory distress. Concomitant medication information was not provided and treatment information was not provided. Diagnostic results for infective causes were negative, Antinuclear antibody was positive. Electromyogram: abnormal, Lumbar puncture abnormal; Magnetic resonance imaging head abnormal. This case according to the Brighton collaboration case definition for ADEM is classified as Level 3 (possible case); according to the Brighton classification for Encephalitis is classified as Level 4 (Not enough information for its Level classification), and according to the WHO causality assessment this case is considered conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	INFARCTION (Cerebral infarction), RESPIRATORY DISTRESS (Respiratory distress), PLASMAPHERESIS (Plasmapheresis), ENDOTRACHEAL INTUBATION (Endotracheal intubation), IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy), ASTHENIA (Asthenia), HYPOAESTHESIA (Hypoaesthesia), MOBILITY DECREASED (Mobility decreased) and PARAESTHESIA (Paraesthesia) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 10-Jul-2021, Ammonia: normal (normal) Normal. On 10-Jul-2021, Antibody test: negative (Negative) Negative. On 10-Jul-2021, Antinuclear antibody: positive (Positive) Positive. On 10-Jul-2021, CSF culture: negative (Negative) Negative. On 10-Jul-2021, Electromyogram: abnormal (abnormal) Abnormal. On 10-Jul-2021, Lumbar puncture: abnormal (abnormal) Abnormal. On 10-Jul-2021, Magnetic resonance imaging head abnormal: abnormal (abnormal) Abnormal. On 10-Jul-2021, Rheumatoid factor: negative (Negative) Negative. On 10-Jul-2021, Treponema test: negative (Negative) Negative. On 10-Jul-2021, Viral test negative: negative (Negative) Negative. On 10-Jul-2021, Vitamin B12: normal (normal) Normal. On 10-Jul-2021, Vitamin B6 normal: normal (normal) Normal. On an unknown date, Amyloidosis senile: negative (Negative) Negative. On an unknown date, Lyme disease: negative (Negative) Negative. On an unknown date, Respiratory papilloma: negative (Negative) reactive but syphilis screen neg. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Concomitant product was not provided by the reporter. Treatment information was not provided. Based on the current available information and temporal association between the use of the product							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	and the start date of the events, a causal relationship cannot be excluded.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 06-Jul-2021 and was forwarded to Moderna on 06-Jul-2021. This regulatory authority case was reported by a health care professional and describes the occurrence of DYSPNOEA (Dyspnoea), PLEURAL EFFUSION (Pleural effusion), PULMONARY OEDEMA (Pulmonary oedema), STATUS EPILEPTICUS (Status epilepticus), UNRESPONSIVE TO STIMULI (Unresponsive to stimuli), VACCINATION COMPLICATION (Vaccination complication), WHITE MATTER LESION (White matter lesion), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), APHASIA (Aphasia) and ASCITES (Ascites) in a 57-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 036-V21A) for COVID-19 vaccination. Concurrent medical conditions included Allergy to antibiotic (Avelox), Type 2 diabetes mellitus, COPD, Hypertension, Brain injury (H/P anoxic brain injury (was able to speak and answer questions at rehab facility)) and Hyperlipidaemia. Concomitant products included METOPROLOL TARTRATE for Hypertension, ALOGLIPTIN, ATORVASTATIN, CLONIDINE, DIPHENHYDRAMINE, FUROSEMIDE, IPRATROPIUM BROMIDE, SALBUTAMOL SULFATE (DUONEB), METFORMIN, PREDNISONE, SIMVASTATIN and SITAGLIPTIN for an unknown indication. On 27-Apr-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 14-Jun-2021, the patient experienced DYSPNOEA (Dyspnoea) (seriousness criteria hospitalization and life threatening), PLEURAL EFFUSION (Pleural effusion) (seriousness criteria hospitalization and life threatening), PULMONARY OEDEMA (Pulmonary oedema) (seriousness criteria hospitalization, medically significant and life threatening), STATUS EPILEPTICUS (Status epilepticus) (seriousness criteria hospitalization, medically significant and life threatening), UNRESPONSIVE TO STIMULI (Unresponsive to stimuli) (seriousness criteria hospitalization, medically significant and life threatening), VACCINATION COMPLICATION (Vaccination complication) (seriousness criteria hospitalization and life threatening), WHITE MATTER LESION (White matter lesion) (seriousness criteria hospitalization and life threatening), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis)	Multifocal white matter changes involving the periventricular and subcortical white matter to include multiple locations of U fiber involvement. No MR evidence of meningitis.	Level 2	Level 2	0	Possible	This is a case of a 57-year-old female patient with concurrent medical conditions of Type 2 diabetes mellitus, COPD, Hypertension, Brain injury (H/P anoxic brain injury), and Hyperlipidaemia. Who 48 days after receiving the second dose of Spikevax vaccine, reported 'experienced dyspnoea, pleural effusion, pulmonary oedema, status epilepticus, aphasia and was unresponsive to stimuli'. MRI head showed Multifocal white matter changes involving the periventricular and subcortical white matter to include multiple locations of U fiber involvement (white matter lesion). A diagnosis of ADEM was made. The patient was treated with furosemide, methylprednisolone, levetiracetam, propofol, and oxygen. Concomitant medications included metoprolol, alogliptin, atorvastatin, clonidine, diphenhydramine, furosemide, metformin. This case according to the Brighton collaboration case definition for ADEM is classified as Level 2A (case meets both level 2 ADEM & encephalitis). According to the WHO causality assessment this case is considered possible, due to temporal association with pikevax. However, event could also be explained by cofounders including risk factors of concurrent pulmonary edema, pleural effusion.	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(seriousness criteria hospitalization, medically significant and life threatening), APHASIA (Aphasia) (seriousness criteria hospitalization and life threatening) and ASCITES (Ascites) (seriousness criteria hospitalization, medically significant and life threatening). The patient was treated with FUROSEMIDE (LASIX [FUROSEMIDE]) (intravenous) ongoing since an unknown date for Pulmonary edema, at a dose of 1 dosage form; METHYLPREDNISOLONE ongoing since an unknown date for Adverse event, at a dose of 1 gram once a day; LEVETIRACETAM DIHYDROCHLORIDE (KEPPRA [LEVETIRACETAM DIHYDROCHLORIDE]) ongoing since an unknown date for Adverse event, at a dose of 1 gram three times a day; PROPOFOL ongoing since an unknown date for Adverse event, at a dose of 1 dosage form and OXYGEN ongoing since an unknown date for Adverse event, at a dose of 1 dosage form. At the time of the report, DYSPNOEA (Dyspnoea), PLEURAL EFFUSION (Pleural effusion), PULMONARY OEDEMA (Pulmonary oedema), STATUS EPILEPTICUS (Status epilepticus), UNRESPONSIVE TO STIMULI (Unresponsive to stimuli), VACCINATION COMPLICATION (Vaccination complication), WHITE MATTER LESION (White matter lesion), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), APHASIA (Aphasia) and ASCITES (Ascites) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 14-Jun-2021, Angiogram cerebral: normal (normal) normal. On 14-Jun-2021, Blood bicarbonate: 37 (High) 37. On 14-Jun-2021, Blood creatinine: 1.3 (High) 1.3. On 14-Jun-2021, Blood electrolytes: normal (normal) normal. On 14-Jun-2021, Blood glucose: 135 (High) 135. On 14-Jun-2021, Blood lactic acid: normal (normal) normal. On 14-Jun-2021, Blood magnesium: 1.5 (normal) 1.5. On 14-Jun-2021, Blood pH: 7.35 (normal) 7.35. On 14-Jun-2021, Blood urea: 27 (High) 27. On 14-Jun-2021, Brain natriuretic peptide: 111,902 (High) 111,902. On 14-Jun-2021, CSF oligoclonal band: present (Inconclusive) present. On 14-Jun-2021, Computerised tomogram thorax: abnormal (abnormal) and negative for evidence of PE..Demonstrated bilateral pleural effusions body wall edema and ascites.. On 14-Jun-2021, Electroencephalogram: abnormal (abnormal) status epilepticus. On 14-Jun-2021, Flow cytometry: normal (normal) Normal. On 14-Jun-2021, Full blood count: normal (normal)							

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	normal. On 14-Jun-2021, Lumbar puncture: normal (normal) normal. On 14-Jun-2021, Magnetic resonance imaging head: abnormal (abnormal) Impression: 1. Multifocal white matter changes involving the periventricular and subcortical white matter to include multiple locations of U fiber involvement. 2. No MR evidence of meningitis.. On 14-Jun-2021, Oxygen saturation: 77 (Low) 77. On 14-Jun-2021, PCO2: 64 (High) 64. On 14-Jun-2021, PO2: 49 (Low) 49. On 14-Jun-2021, Procalcitonin: normal (normal) normal and normal (normal) normal. On 14-Jun-2021, SARS-CoV-2 test: negative (Negative) Negative. On 14-Jun-2021, Troponin: 87 (High) 87. On 14-Jun-2021, Urine analysis: abnormal (abnormal) abnormal. On 14-Jun-2021, Urine leukocyte esterase: positive (Positive) positive. On 14-Jun-2021, Vitamin D: decreased to 15 (Low) decreased to 15. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) to be possibly related. No further causality assessments were provided for DYSPNOEA (Dyspnoea), PLEURAL EFFUSION (Pleural effusion), PULMONARY OEDEMA (Pulmonary oedema), STATUS EPILEPTICUS (Status epilepticus), UNRESPONSIVE TO STIMULI (Unresponsive to stimuli), VACCINATION COMPLICATION (Vaccination complication), WHITE MATTER LESION (White matter lesion), APHASIA (Aphasia) and ASCITES (Ascites). Patient was having difficulty maintaining O2 saturation. Her oxygen levels were 77% . Patient had other labs ordered like Brain Natriuretic peptide (BNP) result was value of 90,000+, Blood urine and MRI of Brain parenchyma the results was Multifocal areas of increased rounded subcortical and periventricular T2 white matter changes and there are multiple small curvilinear subcortical foci with similar imaging characteristics seen in the superior frontal and parietal locations bilaterally (consistent with U these foci do not demonstrate enhancement on postcontrast images. These foci do not demonstrate diffusion restriction characteristics. No abnormal enhancement of the meninges to suggest meningitis. There was no evidence of acute infarct or hemorrhage. There was no midline shift or mass effect. There was no diffusion-weighted signal abnormality. There are no areas of abnormal enhancement. Ventricles and extra-axial spaces: No abnormal extra-axial fluid collection was identified.							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	No hydrocephalus. Major intracranial vasculature: Expected flow voids demonstrated. She was treated with dose of IV Lasix at facility for pulmonary edema and alternated between nasal cannula, Continuous Positive Airway Pressure(CPAP), nonrebreather's and Venti mask. She was finally achieved 85% sat on Ventimask subsequently transported to ED in the morning. Patient reported that she was admitted to Neuro Department. She was at nursing home when she started having desaturations. Her Lab investigations were BNP was elevated. She has had no clinical seizures and she was moving all 4 extremities. MD. Working diagnosis Acute disseminated encephalomyelitis associated with COVID 19 Vaccine. She was Extubated, and alert and oriented. Responded to commands. She stated that she was still in ICU but preparing for transfer to lower level of care. Company comment: Very limited information regarding these events has been provided at this time. No further follow-up information is expected.							
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 09-Jul-2021. The most recent information was received on 09-Jul-2021 and was forwarded to Moderna on 15-Jul-2021. This regulatory authority case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS [REDACTED] ADEM [REDACTED] in a 39-year-old female patient who received mRNA-1273 (COVID 19 Vaccine Moderna) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. No Medical History information was reported. On 15-Jun-2021, the patient received second dose of mRNA-1273 (COVID 19 Vaccine Moderna) (unknown route) dosage was changed to 1 dosage form. On an unknown date, the patient received first dose of mRNA-1273 (COVID 19 Vaccine Moderna) (unknown route) 1 dosage form. On 15-Jun-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS [REDACTED] V.a. ADEM ([REDACTED]) (seriousness criterion medically significant) and HEADACHE (Headache). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS [REDACTED] V.a. ADEM [REDACTED] and HEADACHE (Headache) had not resolved.	0	Level 4	Level 4	0	conditional	This is report is for a 39 years old female with no medical history or concomitant medications provide, who the same day after receving the 2nd dose of Spikevax developed ADEM, encephalomyelitis and headache. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4 (not enough information to classify in any level); according to the Brighton classification for Encephalitis is also classified as Level 4 (Not enough information for its Level classification), and accoring to the WHO causality assessment this case is considered conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	Concomitant medication were not provided. Treatment medication were not reported. Company Comment: Based on the current available information and temporal association between the use of the product and the start date of the event, a causal relationship cannot be excluded. Most recent FOLLOW-UP information incorporated above includes: On 09-Jul-2021: Translation uploaded for initial SD. An event headache was added. On 25-Aug-2021: Follow up document include no new information.							
	This case was initially received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 07-Jul-2021. The most recent information was received on 08-Sep-2021 and was forwarded to Moderna on 21-Sep-2021. This case, reported by a physician, was received by Takeda via Moderna's adverse reaction reporting site ([REDACTED]), and reported to the [REDACTED] by a physician, was received via the [REDACTED], and then was reported by a physician via a medical representative. On 08-Sep-2021, additional information was received from the physician. On an unknown date, body temperature before the vaccination: unknown. On 20-Jun-2021, the patient received the 1st dose of the vaccine. On 27-Jun-2021, the patient experienced numbness in the left forearm when carrying heavy things and difference in temperature sensation between the right and left sides. After bathing, the patient felt heat only in forearms. On 29-Jun-2021, tingling pain in the left precordium and left back occurred during breathing. On 30-Jun-2021, the patient visited the internal medicine department of the reporting hospital because the patient was aware of decreased grip strength in the left hand. In the early evening, the patient walked dragging the left foot unconsciously. The patient's left hand grip strength at that time was 7 kg. Alterations in primitive reflexes, motor palsies, sensory disturbances, and deep tendon reflexes were noted, but the observation period was insufficient to indicate an ADEM study (course of disease) disease.	0	Level 5	Level 5	0	conditional	This report is for a 33 years old female with no reported medical history or concomitant medications, who 7 days after receiving the 1st dose of Spikevac, experience numbness and muscular weakness in both upper limbs, muscular weakness in the left lower limb. Two days later the patient developed Left precordial pain and back pain. The patient was hospitalized two days later and was diagnosed with suspected ADEM. MRI showed no obvious focus of the disease and the spinal fluid findings showed no obvious abnormality. The symptoms were not stabilized after the hospitalization. Four days later the patient experienced numbness and weakness in the right upper limb. Three days later, the patient was discharged from the hospital. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5 (Not an ADEM case); according to the Brighton classification for Encephalitis is also classified as Level 5 (Not a case of encephalitis), and according to the WHO causality assessment this case is considered conditional. MRI and spinal exam do not correlate with ADEM or encephalitis findings. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On 01-Jul-2021, the patient was hospitalized for treatment and detailed examination. The lesion was not clear in the MRI, and there was no clear abnormality in the cerebrospinal fluid opinion either. The patient's symptoms fluctuated after admission. On 05-Jul-2021, decreased sensation in the left buccal region, numbness in the right upper extremity, and weakness developed. On 06-Jul-2021, treatment with pregabalin 25 mg 3T in 3 divided doses after each meal was started, and the numbness was then improving. There was no progress of muscular weakness in the left upper and lower extremities. The left grip strength also improved to 15 kg. On 08-Jul-2021, the patient was discharged from the hospital. On 26-Jul-2021, the patient was seen by the neurologist of the reporting hospital. The remission of the symptoms was confirmed. Grip strength was 41 kg in the right, and 36 kg in the left. Anesthesia remained in the left buccal region and right and left upper lip. Pregabalin 25 mg was prescribed. The patient completed treatment with pregabalin. The outcome of acute disseminated encephalomyelitis was reported as resolved with sequelae. No follow-up investigation will be made. Reporter comments continuation: Although the patient was originally healthy and had no pre-existing medical conditions, the symptoms started a week after the vaccination and were considered to be temporally related to the vaccine, because there were no other signs suggestive of infection. CSF examination, blood test, nerve conduction studies, head MRI, and cervical spinal cord MRI did not show any abnormalities, but the extent of the sensory disturbance was partially consistent with the root predominance, suggesting pathologies such as ADEM or inflammation of the cerebrospinal nerve roots. One week after vaccination is the period when adverse reactions appear most commonly, and a causal relationship cannot be ruled out. Follow-up received on 08-SEP-2021 Updated: Patient Information, Product Information, Event Information, Narrative, Reporter Comments							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	Company Comment; The event developed after the administration of COVID-19 vaccine mRNA (mRNA 1273) and there is temporal relationship.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 13-Jul-2021 and was forwarded to Moderna on 13-Jul-2021. This regulatory authority case was reported by a health care professional and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (acute disseminated encephalomyelitis), POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (Posterior reversible encephalopathy syndrome), SUBARACHNOID HAEMORRHAGE (Subarachnoid hemorrhage), WHITE MATTER LESION (multifocal white matter changes.), VOMITING (emesis), LABORATORY TEST ABNORMAL (Laboratory test abnormal), MAGNETIC RESONANCE IMAGING ABNORMAL (Magnetic resonance imaging abnormal), HEADACHE (Headache) and NAUSEA (Nausea) in a 53-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The patient's past medical history included COVID-19 in 2021, Stroke, Pulmonary embolus, Obesity and Macrocytic anemia. Concurrent medical conditions included Chronic kidney disease. Concomitant products included WARFARIN, FERROUS FUMARATE, PANTOPRAZOLE and ATORVASTATIN CALCIUM (ATORVASTATIN [ATORVASTATIN CALCIUM]) for an unknown indication. On 10-Jun-2021, the patient received dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 13-Jun-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (acute disseminated encephalomyelitis) (seriousness criteria hospitalization and medically significant), POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (Posterior reversible encephalopathy syndrome) (seriousness criteria hospitalization and medically significant), SUBARACHNOID HAEMORRHAGE (Subarachnoid hemorrhage) (seriousness criteria hospitalization and medically significant), WHITE MATTER LESION (multifocal white matter changes.) (seriousness criterion hospitalization), VOMITING (emesis) (seriousness criterion hospitalization), LABORATORY TEST ABNORMAL (Laboratory test abnormal)	T2 FLAIR changes in the bifrontal, biparietal, and bioccipital white matter mostly in addition to the SAH..	Level 2	Level 5	0	Possible	This report is for a 53 years old female with medical history of COVID-19 infection sometime in 2021, stroke, pulmonary embolous, obesity, chronic kidney disease, and macrocytic anemia, who 3 days after receiving an unknown dose of Spikevax, reported headache, nausea, vomiting, posterior reversible encephalopathy syndrome, subarachnoid haemorrhage, and ADEM. Test results showed MRI with T2 FLAIR changes in the bifrontal, biparietal, and bioccipital white matter mostly in addition to the SAH. This case according to the Brighton collaboration case definition for ADEM is classified as Level 2. According to the WHO causality assessment this case is considered possible due to the temporal association, but event could also be explained by cofounders including risk factors of COVID-19 infection as well as the history of CVA, pulmonary embolism, obesity, and chronic kidney disease. It is acknowledged that COVID-19 has been linked to neurological pathologies, including ADEM.	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(seriousness criterion hospitalization), MAGNETIC RESONANCE IMAGING ABNORMAL (Magnetic resonance imaging abnormal) (seriousness criterion hospitalization), HEADACHE (Headache) (seriousness criterion hospitalization) and NAUSEA (Nausea) (seriousness criterion hospitalization). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (acute disseminated encephalomyelitis), POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (Posterior reversible encephalopathy syndrome), SUBARACHNOID HAEMORRHAGE (Subarachnoid hemorrhage), WHITE MATTER LESION (multifocal white matter changes.), VOMITING (emesis), LABORATORY TEST ABNORMAL (Laboratory test abnormal), MAGNETIC RESONANCE IMAGING ABNORMAL (Magnetic resonance imaging abnormal), HEADACHE (Headache) and NAUSEA (Nausea) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 13-Jun-2021, Laboratory test: abnormal (abnormal) abnormal. On 13-Jun-2021, Magnetic resonance imaging: (Inconclusive) T2 FLAIR changes in the bifrontal, biparietal, and bioccipital white matter mostly in addition to the SAH.. On 13-Jun-2021, Magnetic resonance imaging abnormal: abnormal (abnormal) abnormal. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Treatment information was not provided. It was reported that patient had CKD as medical history. Patient had headache, nausea, emesis after 3 days of vaccination and was hospitalized. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Suspected acute disseminated encephalomyelitis (ADEM) (pyrexia, inability to move the leg)) in a 32-year-old male patient who received mRNA-1273 (COVID 19 Vaccine Moderna) (batch no. 3003189) for COVID-19 vaccination. The occurrence of	0	Level 4	Level 4	0	conditional	This is report is for a 32 years old male with no medical history or concomitant medications provide, who 8 days after receiving the 1st dose of Spikevax developed suspected ADEM, pyrexia, and movement disorder. This case according to the Brighton collaboration case definition for ADEM is classified as	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	additional non-serious events is detailed below. No Medical History information was reported. On 06-Jul-2021, the patient received first dose of mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 14-Jul-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Suspected acute disseminated encephalomyelitis (ADEM) (pyrexia, inability to move the leg)) (seriousness criteria hospitalization and medically significant), MOVEMENT DISORDER (Inability to move the leg) and PYREXIA (Pyrexia). The patient was hospitalized on 14-Jun-2021 due to ACUTE DISSEMINATED ENCEPHALOMYELITIS. At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Suspected acute disseminated encephalomyelitis (ADEM) (pyrexia, inability to move the leg)), MOVEMENT DISORDER (Inability to move the leg) and PYREXIA (Pyrexia) outcome was unknown. For mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Suspected acute disseminated encephalomyelitis (ADEM) (pyrexia, inability to move the leg)), MOVEMENT DISORDER (Inability to move the leg) and PYREXIA (Pyrexia) to be possibly related. No concomitant medications were provided by the reporter. Treatment information was not provided by the reporter. The reporter stated that on an unknown date, body temperature before the vaccination was 36.6 degrees Celsius. The reporter stated that the patient was admitted to hospital for suspected ADEM, and that tests and treatments were being performed. No dates or results were provided. Based on the current available information and temporal association between the use of the product, and the start date of the events, a causal relationship cannot be excluded. However, no information is available regarding medical history/medications that could be confounders/co-suspects for the events.						Level 4 (not enough information to classify in any level); according to the Brighton classification for Encephalitis is also classified as Level 4 (Not enough information for its Level classification), and according to the WHO causality assessment this case is considered conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.	
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 20-Jul-2021 and was forwarded to Moderna on 20-Jul-2021. This regulatory authority case was reported by a health care professional and describes the	0	Level 4	Level 4	0	conditional	This is report is for a 60 years old male with no medical history or concomitant medications provide, who 32 days after receiving the 2nd dose of Spikevax developed demyelinating polyneuropathy and paraesthesias. This case according to	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Caosality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	occurrence of DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) in a 60-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. No Medical History information was reported. On 31-Dec-2020, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 01-Feb-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criterion medically significant) and PARAESTHESIA (Paraesthesia). At the time of the report, DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) and PARAESTHESIA (Paraesthesia) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 01-Feb-2021, Electromyogram: abnormal (abnormal) abnormal. On 01-Feb-2021, Nerve conduction studies: normal (normal) normal. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter considered DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) and PARAESTHESIA (Paraesthesia) to be possibly related. No concomitant medications were reported. Unspecific treatment information was reported. In February, the patient had a sudden onset of severe paresthesia. Symptoms are slowly improving with medical treatment. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.					the Brighton collaboration case definition for ADEM is classified as Level 4 (not enough information to classify in any level); according to the Brighton classification for Encephalitis is also classified as Level 4 (Not enough information for its Level classification), and accoring to the WHO causality assessment this case is considered conditional. There is very little information provided for this report including patient's full medical history and concomitant medications history. There is also important information missing regarding other laboratory tests conducted, treatment, medical course, etc.		
	This case was initially received via European Medicines Agency (Reference number:) on 22-Jul-2021. The most recent information was received on 22-Jul-2021 and was forwarded to Moderna on 29-Jul-2021. This regulatory authority case was reported by a phvsician and describes the occurrence of	No detailed report available	Level 3	Level 3A	0	Conditional	This report is for a 61 years old female, with medical history of Pigmented purpuric dermatosis, Hepatitis B carrier, Arthritis rheumatoid, Leiomyoma, Uveitis NOS, Uterine fibroma, Cryoglobulinaemia and Hepatic steatosis, who developed amnesia transitoria,	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	ENCEPHALOMYELITIS (2/7 [REDACTED], RADICULOPATHY (2/7 [REDACTED], ATAXIA (2/7 [REDACTED], DIZZINESS (2/7 [REDACTED], AMNESIA (2/7 [REDACTED], DIPLOPIA (2/7 [REDACTED], PYREXIA (2/7 [REDACTED], NAUSEA (2/7 [REDACTED], HEADACHE (2/7 [REDACTED] and ARTHRALGIA (2/7 [REDACTED] [REDACTED] in a 61-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3001655) for SARS-CoV-2 vaccination. The patient's past medical history included Cataract (right). Concurrent medical conditions included Pigmented purpuric dermatosis, Hepatitis B carrier, Arthritis rheumatoid on 01-Jan-2013, Leiomyoma, Uveitis NOS, Uterine fibroma, Cryoglobulinaemia and Hepatic steatosis. Concomitant products included CALCIUM CARBONATE, LANSOPRAZOLE, SULFAMETHOXAZOLE, TRIMETHOPRIM (BACTRIM), COLCHICINE, LAMIVUDINE, ALENDRONATE SODIUM and HYDROXYCHLOROQUINE SULFATE for an unknown indication. On 13-May-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) .5 milliliter in total. On 02-Jul-2021, the patient experienced ENCEPHALOMYELITIS (2/7 [REDACTED] (seriousness criteria hospitalization and medically significant), RADICULOPATHY (2/7 [REDACTED] (seriousness criterion hospitalization), ATAXIA (2/7 encefalomieleradiculite, diplopia, ataxia ad esordio subacuto, amnesia					Arthralgia, ataxia, diplopia, dizziness, encephalomyelitis, headache, nausea, pyrexia, radiculopathy 49 days after receiving an unknown dose of Spikevax vaccine. Relevant concomitant medications include lansoprazole, colchicine, lamivudine, alendronate sodium, and hydrochloroquine sulphate. Lab data included: Chest X-ray, SARS-CoV-2 PCR test, MRI (no report provided), CT scan & CSF, with no results. This case according to the Brighton collaboration case definition for ADEM is classified as Level 3 (no MRI result). According to the WHO causality assessment this case is considered Conditional. There are important risk factors associated with this report including history of arthritis rheumatoid, as well as malignancies and hepatic steatosis. Very little information was provided for this report including patient's full medical history and concomitant medications history.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(seriousness criterion hospitalization), DIZZINESS (2/7 (seriousness criterion hospitalization), AMNESIA (2/7 (seriousness criterion hospitalization), DIPLOPIA (2/7 (seriousness criterion hospitalization), PYREXIA (2/7 (seriousness criterion hospitalization), NAUSEA (2/7 (seriousness criterion hospitalization), HEADACHE (2/7 (seriousness criterion hospitalization) and ARTHRALGIA (2/7 (seriousness criterion hospitalization). The patient was treated with IMMUNOGLOBULIN HUMAN NORMAL (IMMUNOGLOBULIN HUMAN) at an unspecified dose and frequency. At the time of the report, ENCEPHALOMYELITIS (2/7 RADICULOPATHY (2/7 DIZZINESS (2/7 AMNESIA (2/7 , PYREXIA (2/7 NAUSEA (2/7 HEADACHE (2/7 and ARTHRALGIA (2/7 had not resolved and ATAXIA (2/7 and DIPLOPIA (2/7 was resolving. For mRNA-1273 (Spikevax) (Intramuscular), the							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	reporter did not provide any causality assessments. Lab data included: Chest X-ray, SARS-CoV-2 PCR test on 3-JUL-2021, Magnetic resonance imaging brain on 7-JUL-2021, Computerized axial tomogram on 4-JUL-2021 and Spinal tap on an unknown date with no results. The patient was hospitalized due to diplopia and ataxia of sub-acute onset and had improved after IVIg treatment. Company comment: Very Limited information regarding the events has been provided at this time and a causal relationship cannot be excluded. Follow-up received on 2-sep-2021 included no new information Most recent FOLLOW-UP information incorporated above includes: On 22-Jul-2021: Translation source received on 29-Jul-2021: Outcome and treatment for the events diplopia and ataxia was updated. On 02-Sep-2021: Follow up received included no new information. On 07-Sep-2021: Follow up received and included no new information.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 27-Jul-2021 and was forwarded to Moderna on 27-Jul-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of MULTIPLE SCLEROSIS (Multiple sclerosis) and AUTOIMMUNE DEMYELINATING DISEASE (Autoimmune demyelinating disease) in a 46-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included Appendectomy. Concurrent medical conditions included Sinus bradycardia. Concomitant products included LACTULOSE and DUCSATE SODIUM (COLACE) for an unknown indication. On 12-Feb-2021, the patient received dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 17-Feb-2021, the patient experienced MULTIPLE SCLEROSIS (Multiple sclerosis) (seriousness criterion medically significant), AUTOIMMUNE DEMYELINATING	0	Level 5	Level 5	0	unlikely	This report is for a 46 years old female with concurrent medical history of sinus bradycardia, who 5 days after the 1st dose of Spikevax developed Asthenia, Autoimmune demyelinating disease, Central nervous system lesion, Hypoaesthesia, paraesthesia, and Multiple sclerosis. Test results showed oligonal bands positive in her CSF, and MRI was consistent with demyelinating disease. According to the reported it was originally thought patient had ADEM, however, it was determined she had multiple sclerosis. This case according to the Brighton collaboration case definition for ADEM is classified as Level 5 (not an ADEM case); according to the Brighton classification for Encephalitis is also classified as Level 5 (Not an Encephalitis case), and according to the WHO causality assessment this case is considered unlikely. Multiple sclerosis (MS) is the most frequently seen demyelinating disease, and it is considered a chronic, inflammatory, demyelinating and neurodegenerative disease of the central nervous system. There is very little additional information provided for this report including patient's full medical history and concomitant medications history. There is also important	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	DISEASE (Autoimmune demyelinating disease) (seriousness criterion medically significant), ASTHENIA (Asthenia), CENTRAL NERVOUS SYSTEM LESION (Central nervous system lesion), HYPOAESTHESIA (Hypoaesthesia) and PARAESTHESIA (Paraesthesia). At the time of the report, MULTIPLE SCLEROSIS (Multiple sclerosis), AUTOIMMUNE DEMYELINATING DISEASE (Autoimmune demyelinating disease), ASTHENIA (Asthenia), CENTRAL NERVOUS SYSTEM LESION (Central nervous system lesion), HYPOAESTHESIA (Hypoaesthesia) and PARAESTHESIA (Paraesthesia) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 17-Feb-2021, Anti-aquaporin-4 antibody: negative (Negative) Negative. On 17-Feb-2021, Autoantibody test: negative (Negative) Negative. On 17-Feb-2021, CSF oligoclonal band: present (Positive) Positive. On 17-Feb-2021, Magnetic resonance imaging head: abnormal (abnormal) MRI brain consistent with demyelinating disease. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Lab test also included neg Anti-MOG; Multiple sclerosis panel: The patient's CSF contains 2 well defined gamma restriction bands that are not present in the patient's corresponding serum sample; NI IgG synthesis and index; CSF immunoglobulin G index. Result not provided. On 17 Feb 2021, approximately 5 days after the 1st dose of the moderna vaccine, the patient experienced numbness and tingling in the hands which spread to her feet. Patient was found to have MRI brain consistent with demyelinating disease and was originally thought to have ADEM. However, she subsequently developed RU weakness and had new MRI lesions and was diagnosed with multiple sclerosis (which is accurate). It is unclear if this is a true vaccine related event given very short onset after the vaccine Treatment information was unknown. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.					information missing regarding other laboratory tests conducted, treatment, medical course, etc.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	This case was received via [REDACTED] on 03-Aug-2021 and was forwarded to Moderna on 03-Aug-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of PARAESTHESIA (Paraesthesia), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), SJOGREN'S SYNDROME (Sjogren's syndrome), MEMORY IMPAIRMENT (Memory impairment), DEMYELINATION (Demyelination), APHASIA (Aphasia), COGNITIVE DISORDER (Cognitive disorder), CONDITION AGGRAVATED (Condition aggravated), FEELING ABNORMAL (Feeling abnormal), IMPAIRED WORK ABILITY (Impaired work ability), FEELING ABNORMAL (brain fog), PARAESTHESIA (tingling of scalp) and PARAESTHESIA (tingling of feet) in a 60-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The patient's past medical history included Abdominal bloating, Abdominal distension gaseous (abnormal posture), Weight gain, Anxiety disorder, Arthritis (first carpometacarpal joint of left hand), Benign neoplasm (parotid gland), Hematuria, Lymphadenopathy (Cervical), Hypertrophy of tongue papillae, Demyelinating disease of central nervous system, unspecified, Dental restoration failure (Dental restoration status diverticular disease of colon), Diverticulosis (Diverticulosis of large intestine without perforation or abscess without bleeding dry eyes), Dysphagia, Essential fatty acid deficiency, Exposure to mold, Fatigue, Fatty stools, Stress incontinence, female, Gastroesophageal reflux disease, Hyperglycemia, Hyperreflexia (Abnormal reflex impaired vibration sensation of foot), Female orgasmic disorder, Insomnia, Kidney stone (kidney liver cyst), Cognitive disorder (Mild cognitive impairment), Hyperhidrosis, Non-alcoholic fatty liver (Fatty (change of) liver), Osteopenia (oropharyngeal phase), Paget's disease of bone (Skull), Paresthesia skin, Rheumatoid arthritis, Sicca syndrome, Incontinence of urine, Vaginal dryness (noninflammatory disorders of vagina), Vitamin D deficiency and Xerostomia. Concurrent medical conditions included Drug allergy (Bactrim itching), Allergy to antibiotic (TobraDex eye swelling) and Tuberculosis. Concomitant products included LACTOBACILLUS ACIDOPHILUS (FLORASTOR [LACTOBACILLUS ACIDOPHILUS]), UBIDECARENONE (COQ10 [UBIDECARENONE]), DOCOSAHEXAENOIC ACID (DHA), OMEGA-3 NOS and COLECALCIFEROL, KRILL OIL, LINUM USITATISSIMUM OIL (KRILL COMPLEX & VITAMIN D) for an unknown indication.	0	Level 4	Level 4	0	unlikely	This report is for a 60 years old female with an extensive medical history including Arthritis, Benign neoplasm of the parotid gland, Hematuria, Lymphadenopathy (Cervical), Hypertrophy of tongue papillae, Demyelinating disease of central nervous system, unspecified, diverticulosis, Dysphagia, Essential fatty acid deficiency, Gastroesophageal reflux disease, Hyperglycemia, Hyperreflexia (Abnormal reflex impaired vibration sensation of foot), kidney liver cyst, Cognitive disorder (Mild cognitive impairment), Hyperhidrosis, Non-alcoholic fatty liver (Fatty (change of) liver), Osteopenia (oropharyngeal phase), Paget's disease of bone (Skull), Paresthesia skin, Rheumatoid arthritis, Sicca syndrome (Sjogren's syndrome), Incontinence of urine, Xerostomia, and concurrent tuberculosis. 49 days after receiving the 2nd dose of the vaccine the patient developed Paraesthesia, Memory impairment, Demyelination, Aphasia, Cognitive disorder, Impaired work ability, and was diagnosed with ADEM. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and according to the WHO causality assessment this case is considered unlikely. There are very important risk factors associated with this patient and her very long list of conditions that are part of her medical history, including Sjogren's syndrome, paresthesias, and her ongoing tuberculosis. These conditions provides a more plausible explanation for the reported events. Additionally there is very little information provided for the course of the patient's full medical history as well as information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On 11-Feb-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 01-Apr-2021, the patient experienced PARAESTHESIA (Paraesthesia) (seriousness criteria hospitalization and disability), SJOGREN'S SYNDROME (Sjogren's syndrome) (seriousness criteria hospitalization, disability and medically significant), MEMORY IMPAIRMENT (Memory impairment) (seriousness criteria hospitalization and disability), DEMYELINATION (Demyelination) (seriousness criteria hospitalization, disability and medically significant), APHASIA (Aphasia) (seriousness criteria hospitalization and disability), COGNITIVE DISORDER (Cognitive disorder) (seriousness criteria hospitalization and disability), CONDITION AGGRAVATED (Condition aggravated) (seriousness criteria hospitalization and disability), FEELING ABNORMAL (Feeling abnormal) (seriousness criteria hospitalization and disability) and IMPAIRED WORK ABILITY (Impaired work ability) (seriousness criteria hospitalization and disability). On an unknown date, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization, disability and medically significant), FEELING ABNORMAL (brain fog) (seriousness criteria hospitalization and disability), PARAESTHESIA (tingling of scalp) (seriousness criteria hospitalization and disability) and PARAESTHESIA (tingling of feet) (seriousness criteria hospitalization and disability). The patient was treated with PREDNISONE for Adverse event, at an unspecified dose and frequency and METHYLPREDNISOLONE SODIUM SUCCINATE (SOLU-MEDROL) for Adverse event, at an unspecified dose and frequency. At the time of the report, PARAESTHESIA (Paraesthesia), SJOGREN'S SYNDROME (Sjogren's syndrome), MEMORY IMPAIRMENT (Memory impairment), DEMYELINATION (Demyelination), APHASIA (Aphasia), COGNITIVE DISORDER (Cognitive disorder), CONDITION AGGRAVATED (Condition aggravated), FEELING ABNORMAL (Feeling abnormal) and IMPAIRED WORK ABILITY (Impaired work ability) had not resolved and ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), FEELING ABNORMAL (brain fog), PARAESTHESIA (tingling of scalp) and PARAESTHESIA (tingling of feet) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available):							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On 01-Apr-2021, Blood alkaline phosphatase: high (High) alkaline phosphatase raised. On 01-Apr-2021, CSF immunoglobulin: high (High) High. On 01-Apr-2021, Magnetic resonance imaging head: abnormal (abnormal) Acute demyelination. On an unknown date, Blood immunoglobulin G: high (High) elevate IgG levels.. On an unknown date, C-reactive protein: high (High) C-reactive protein Elevated. On an unknown date, CSF oligoclonal band: inconclusive (Inconclusive) Inconclusive. On an unknown date, Lumbar puncture: abnormal (abnormal) likely a Sjogrens flare rather than a new onset of MS. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Patient was treated with 5 days of iv steroid infusion. Patient has a Rheum follow up in 3 weeks but was unable to find any one who could see her sooner. patient also has an appointment but not until September. Patient ordered repeat imaging of the head. Based upon the results, she was called by Neurology who admitted her directly for plasmapheresis therapy. So they started plasmapheresis (PLEX) and she did just complete the 5th one and now the team is meeting to determine the next step what her next steps will be once they meet again as her last scheduled treatment today. Patient was still seeing acupuncture and it is helping. After the 5 PLEX treatments, the patient continues to note slowed cognition with persistent trouble with memory. There is no further treatment other to see what time does. Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This regulatory authority case was reported by an other health care professional and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), BALANCE DISORDER (Balance disorder), CONDITION AGGRAVATED (Condition aggravated), FACE INJURY (Face injury), FALL (Fall), FEEDING DISORDER (Feeding disorder), GAIT DISTURBANCE (Gait disturbance), ISCHAEMIA (Ischaemia), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities), MENTAL STATUS CHANGES (Mental status changes), MOVEMENT DISORDER (Movement disorder), MYELITIS TRANSVERSE (Myelitis transverse), SKIN ABRASION (Skin	0	Level 4	Level 4	0	conditional	This report is for a 62 years old male with medical history of schizophrenia, major cognitive disorder (no other explanation given), and tachycardia, and concomitant medications including clozapine, metoprolol and cholecalciferol, who 22 days after the 2nd dose of Spikevax according to the reporter suffered an unwitnessed fall, prior to this patient had been ambulating in the dayroom around midnight without difficulty at baseline and interacting with staff. During rounds, the staff found patient was in the bathroom face down, lost the balance but was not able to provide more information, was assisted up and had difficulty	

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	abrasion), SPINAL CORD DISORDER (Spinal cord disorder), SPINAL CORD INJURY CERVICAL (Spinal cord injury cervical), URINARY INCONTINENCE (Urinary incontinence), VERTEBRAL OSTEOPHYTE (Vertebral osteophyte) and WHITE MATTER LESION (White matter lesion) in a 62-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 035C21A) for COVID-19 vaccination. Concurrent medical conditions included Penicillin allergy, Drug allergy (allergy to memantine), Schizophrenia, Major neurocognitive disorder, Acute disseminated encephalomyelitis and Tachycardia (Tachycardia secondary to clozapine). Concomitant products included CLOZAPINE, METOPROLOL and CHOLECALCIFEROL for an unknown indication. On 01-Jun-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 23-Jun-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization and medically significant), BALANCE DISORDER (Balance disorder) (seriousness criterion hospitalization), CONDITION AGGRAVATED (Condition aggravated) (seriousness criterion hospitalization), FACE INJURY (Face injury) (seriousness criterion hospitalization), FALL (Fall) (seriousness criterion hospitalization), FEEDING DISORDER (Feeding disorder) (seriousness criterion hospitalization), GAIT DISTURBANCE (Gait disturbance) (seriousness criterion hospitalization), ISCHAEMIA (Ischaemia) (seriousness criterion hospitalization), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities) (seriousness criterion hospitalization), MENTAL STATUS CHANGES (Mental status changes) (seriousness criterion hospitalization), MOVEMENT DISORDER (Movement disorder) (seriousness criterion hospitalization), MYELITIS TRANSVERSE (Myelitis transverse) (seriousness criteria hospitalization and medically significant), SKIN ABRASION (Skin abrasion) (seriousness criterion hospitalization), SPINAL CORD DISORDER (Spinal cord disorder) (seriousness criteria hospitalization and medically significant), SPINAL CORD INJURY CERVICAL (Spinal cord injury cervical) (seriousness criteria hospitalization and medically significant), URINARY INCONTINENCE (Urinary incontinence) (seriousness criterion hospitalization).					walking. Staff noted three abrasions on his forehead and one on his chin and he was taking to the ER. It is not clear where was the patient living at the time or any other medical information related to his condition at the time of this event. It was reported that the patient suffered Balance disorder, face injury, Fall, feeding disorder, gait disturbance, Ischaemia, Loss of personal independence in daily activities, Mental status changes, Movement disorder, and was diagnosed with Myelitis transverse, and suspected ADEM. He had CT of the head and it was normal; MRI of the head and spine were abnormal. No other information was provided. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and accoring to the WHO causality assessment this case is considered conditional. There is very little information provided for the course of the patient's full medical history, including where and why he seems to b e living at a medical facility (maybe because of his schizophrenia?) as well as information missing regarding other laboratory tests conducted, treatment, medical course, etc.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	VERTEBRAL OSTEOPHYTE (Vertebral osteophyte) (seriousness criterion hospitalization) and WHITE MATTER LESION (White matter lesion) (seriousness criterion hospitalization). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), BALANCE DISORDER (Balance disorder), CONDITION AGGRAVATED (Condition aggravated), FACE INJURY (Face injury), FALL (Fall), FEEDING DISORDER (Feeding disorder), GAIT DISTURBANCE (Gait disturbance), ISCHAEMIA (Ischaemia), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities), MENTAL STATUS CHANGES (Mental status changes), MOVEMENT DISORDER (Movement disorder), MYELITIS TRANSVERSE (Myelitis transverse), SKIN ABRASION (Skin abrasion), SPINAL CORD DISORDER (Spinal cord disorder), SPINAL CORD INJURY CERVICAL (Spinal cord injury cervical), URINARY INCONTINENCE (Urinary incontinence), VERTEBRAL OSTEOPHYTE (Vertebral osteophyte) and WHITE MATTER LESION (White matter lesion) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In 2021, Blood pressure measurement: increased (High) 146/86. In 2021, Body temperature: normal (normal) 97.2. In 2021, Heart rate: normal (normal) 74. In 2021, Respiratory rate: increased (High) 20. On 23-Jun-2021, Computerised tomogram head: normal (normal) normal. On 23-Jun-2021, Magnetic resonance imaging head: abnormal (abnormal) abnormal. On 23-Jun-2021, Magnetic resonance imaging spinal: abnormal (abnormal) abnormal. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Treatment information was not provided. Patient suffered an unwitnessed fall, prior to this patient had been ambulating in the dayroom around midnight without difficulty at baseline and interacting with staff. During rounds, the staff found patient was in the bathroom face down, lost the balance but was not able to provide more information, was assisted up and had difficulty walking. Noted three abrasions on his forehead and one on his chin. Computerized tomogram spine was performed on 23 Jun 2021. Based on the current available information and temporal association between the use of the product							

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	and the start date of the events, a causal relationship cannot be excluded; however, concurrent conditions of the patient are confounding factors.							
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 04-Aug-2021. The most recent information was received on 04-Aug-2021 and was forwarded to Moderna on 11-Aug-2021. This regulatory authority case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Akute disseminierte Enzephalomyelitis) in a 34-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 006C21A) for Prophylactic vaccination. No Medical History information was reported. On 04-May-2021, the patient received dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 25-May-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Akute disseminierte Enzephalomyelitis) (seriousness criteria hospitalization and medically significant). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Akute disseminierte Enzephalomyelitis) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, CSF oligoclonal band: abnormal (abnormal) abnormal. On an unknown date, Magnetic resonance imaging: abnormal (abnormal) Showed 13 demyelinating lesions, verification of oligoclonal bands in cerebrospinal fluid. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. Concomitant medication use information was not provided by reporter. Treatment medication use information was not provided by reporter. The Differential diagnosis were ruled out that includes Encephalomyelitis disseminata. Company Comment: Very Limited information regarding the events has been provided at this time and a causal relationship cannot be excluded..	0	Level 4	Level 4	0	conditional	This report is for a 34 years old female with unknown medical history and concomitant medications, who 21 days after an unknown dose of Spikevax was diagnosed with ADEM. Test results included a lumbar puncture that showed CSF oligoclonal band abnormal, and a MRI that showed 13 demyelinating lesions, verification of oligoclonal bands in cerebrospinal fluid. The differential diagnosis of Encephalomyelitis disseminata was ruled out. No other information was provided. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and according to the WHO causality assessment this case is considered conditional. There is very little information provided for the course of the patient's full medical history, as well as information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

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	Most recent FOLLOW-UP information incorporated above includes: On 04-Aug-2021: Translation received on 11-AUG-2021 that contains updated sender comment (that include lab data). On 25-Aug-2021: Follow-up information included no new information.							
	This spontaneous case was reported by an other health care professional and describes the occurrence of NEUROPATHY PERIPHERAL (Peripheral nerve disorder NOS), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) and DYSAESTHESIA (Paresthesia (the entire body)) in a 48-year-old female patient who received mRNA-1273 (COVID 19 Vaccine Moderna) (batch no. 3003653) for COVID-19 vaccination. No Medical History information was reported. On 10-Jul-2021, the patient received first dose of mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular) 1 dosage form. In July 2021, the patient experienced NEUROPATHY PERIPHERAL (Peripheral nerve disorder NOS) (seriousness criterion medically significant) and DYSAESTHESIA (Paresthesia (the entire body)) (seriousness criterion medically significant). On an unknown date, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criterion medically significant) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) (seriousness criterion medically significant). At the time of the report, NEUROPATHY PERIPHERAL (Peripheral nerve disorder NOS), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) and DYSAESTHESIA (Paresthesia (the entire body)) had not resolved. The action taken with mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular) was unknown. For mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular), the reporter considered NEUROPATHY PERIPHERAL (Peripheral nerve disorder NOS), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) and DYSAESTHESIA (Paresthesia (the entire body)) to be possibly related.	Not done	Level 4	Level 4	Level4	Unaccessible	This is a spontaneous report in a 48-year-old female patient with no medical history reported and no information on concomitant medications, who received the first dose of Spikevax, and on an unknown date reported unspecified symptoms describing peripheral neuropathy, GBS, ADEM. No MRI or other lab panel was done. This case is classified as Brighton's level 4 diagnostic certainty (insufficient information to meet case definition) and considered WHO Unassessable. This case can not be judged because information is insufficient	

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	No concomitant medication details were reported. No treatment information details were reported. On an unknown date, at unknown time, body temperature before the vaccination was 36.2 degrees Celsius. Case/Sender's comment: Detailed examinations including MRI and electromyogram will be performed for suspected Guillain-Barre syndrome and ADEM. The events developed after the administration of COVID-19 vaccine mRNA (mRNA 1273) and there is temporal relationship. Company Comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 06-Aug-2021 and was forwarded to Moderna on 06-Aug-2021. This regulatory authority case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 55-year-old male patient who received mRNA-1273 (Spikevax) for Prophylactic vaccination. No Medical History information was reported. On 22-Jun-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 07-Jul-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization, medically significant and life threatening). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) outcome was unknown. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. Concomitant medication of the patient was not reported. No treatment information was provided by the reporter.	0	Level 4	Level 4	0	conditional	This report is for a 55 years old male with unknown medical history and concomitant medications, who 15 days after an unknown dose of Spikevax was diagnosed with ADEM. No other information was provided. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and according to the WHO causality assessment this case is considered conditional. There is very little information provided for the course of the patient's full medical history, as well as information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

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	Limited information regarding the event has been provided at this time and is insufficient for causality assessment. Most recent FOLLOW-UP information incorporated above includes: On 25-Aug-2021: Follow up information included no new information							
	This case was initially received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 16-Aug-2021. The most recent information was received on 15-Nov-2021 and was forwarded to Moderna on 25-Nov-2021. This case, initially reported to the [REDACTED] by a [REDACTED] pharmacist was received via the [REDACTED] (Ref, [REDACTED]). On 15-Nov-2021, follow-up information was received from a physician. On 06-Jul-2021, at 14:00, the patient received the 1st dose of the vaccine in the right arm. At 14:30, the patient experienced low back pain and pain in the joints of the left hand. At 15:00, pyrexia of 38.0 degrees Celsius developed. Around 18:00, periphery of vaccination site pain developed. On 07-Jul-2021, pain in the arm and low back and pyrexia persisted, and the patient took an over-the-counter aspirin. On 08-Jul-2021, at 12:00 body temperature went down to the low 37 degrees Celsius range, and the patient resumed usual activity to find gait disturbance. It was hard to put strength into the legs, and symptoms like knee buckling developed. Suspected spinal cord infarction and suspected acute disseminated encephalomyelitis developed. On 12-Jul-2021, although pain in the arm and low back improved, the patient had gait disturbance and visited a nearby hospital. Body temperature was 37.1 degrees Celsius and PCR testing was performed. The patient was then referred to another hospital. On 13-Jul-2021, the PCR test result was confirmed negative. The patient stated that the symptoms worsened toward evening, but that the patient was relatively well in the morning, and that the symptoms in the evening leveled off and did not worsen over time. The body temperature was 37.0 degrees Celsius, blood pressure: 146/90 mmHg, pulse: 129 times/minute. At 23:00, when the patient woke up, the weakness in the right leg worsened. Examination revealed marked increase in DTR,	0	Level 4	Level 4	0	conditional	This report is for a 33 years old male with unknown medical history and concomitant medications, who the same day after the 1st dose of Spikevax the patient experienced low back pain and pain in the joints of the left hand, pyrexia, vaccination site pain. Six days later the patient developed gait disturbance. During physical examination the patient was found to have marked increase in deep tendon reflexes and muscle weakness of lower limbs, with findings suggestive of disturbance of deep sensibility. The patient was hospitalized. Tests of spinal fluid was normal. Autoantibody tests conducted showed negative results for Anti-AQP4 antibody. According to the reporter no other abnormalities have been found in objective tests until now. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and according to the WHO causality assessment this case is considered conditional. There is no information provided on the patient's medical history and concomitant medications. Also, all test results conducted in the patient seems to be within normal values according to the reporter, and there is information missing regarding other laboratory tests conducted, treatment, medical course, etc.	

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	weakness of the lower extremities, and findings suggestive of deep sensory disturbance. The abnormal findings showed the disease which damaged lateral cord and posterior cord of the lumbar cord level from the thoracic spinal cord lower part, which was included in the differential diagnosis. On 14-Jul-2021, the patient was hospitalized. There was aggravation of the paralysis compared with at the time of the medical examination on the previous day. As paralysis progressed and gait disturbance occurred, steroid pulse therapy and oral DAPT were performed for three days. Ilio 3 +/4-, Quad 3/3 +, Ham 4/4, TA 4/5 -, GC3 +/3 +. There was worsened paralysis of the lower limbs. The upper extremities had no problems. The right knee buckled more frequently while walking. There was a feeling as if a piece of cloth was covering both palms and soles. The tactile sensation was 8/10 in hand and 7/10 in foot compared with the trunk. Thumb localizing test: the patient was able to localize the left thumb but was unsuccessful in localizing the right thumb three times, which showed that there was a clear aggravation. In the medical examination, there was desensitization of both palms and soles, and cervical cord lesion and peripheral neuropathy were also included in differential diagnosis. The myopathy was considered to be negative because the sensory disturbance could not be explained and the muscle enzyme had never been elevated on admission. The patient was aware of pain at the onset of symptoms, and a policy was adopted to exclude demyelinating diseases, tumors, DAVF, metabolic diseases, peripheral neuropathy, in addition to spinal cord infarction and acute disseminated encephalomyelitis. On 15-Jul-2021, BB 5/5 -, TB 5/5 -, WE 5/5 - WF 5/5 -. The patient had left upper limb paralysis. Ilio 3 +/4-, Quad 3/3 +, Ham 4-/4, TA4 +/5-, GC3 +/3 +. Subjectively, the right lower extremity was slightly improved, and abnormal sensations in the bilateral palms and soles tended to improve. Paralysis of the left upper extremity appeared. On 16-Jul-2021, BB 5/5 -, TB 5/5 -, Ilio 5 -/4 +, Quad 4 -/4 -, Ham 4/4, TA 5 -/5 -, GC 4/4. There was an overall improvement trend. Especially, the muscle force improvement of the right lower extremity was clear. The spinal cord infarction and ADEM were improved, and the dysesthesia of the palm disappeared. The dysesthesia of the sole remained. On 19-Jul-2021, BB 5/5, TB 5/5, Ilio 5-/5-, Quad 5-/5-, Ham 5-/5-, TA 5-/5-, GC 5-/5-. There was an overall improvement trend. Especially, the muscle force improvement of the right lower extremity was clear. The paresthesia of the palm disappeared, and							

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	the paresthesia of the sole remained. The hand was 10 and the sole was about 7/9 dull. On 26-Jul-2021, there was no problem on both sides in the manual muscle test. Hypoaesthesia of both soles was about 7-8/10. On 28-Jul-2021, a patient complained that abdominal muscles were losing their strength. On 01-Aug-2021, sensation improved in the sole of the right lower extremity. Only the top of the foot felt like it was covered with a piece of cloth. On 05-Aug-2021, the drug was switched to ASA alone. The patient's paralysis improved and he was able to walk alone. Deep sensory disturbance also improved. Paresthesia remained only in the lateral side of the right fifth finger. On 06-Aug-2021, Del 5/5, TPZ 5/5, BB 5/5, TB 5-/-5-, WE 5/5, WF 5/5, APB 5/5, Ilio 5/5-, Quad 5/5-, Ham 5-/-5-, TA 5/5, GC 5-/-5-. Only the dorsal five finger side of the right foot had paresthesia. Sensation also returned in both soles and palms. The patient's thumb localizing test was clearly improved, and both left and right thumbs were correctly localized. On 12-Aug-2021, MRI scan showed no abnormalities. The patient was placed on outpatient F/U and continued rehabilitation for a suspected spinal cord infarction with negative images. On 14-Aug-2021, the patient was discharged home. One tablet of aspirin 100 mg, 20 mg, and one Cp of esomeprazole magnesium hydrate were prescribed. The sequela of muscle force lowering of both lower extremities, knee buckling in walking, and dysesthesia of right lower extremity instep remained. • Grip strength (13-Jul-2021): 25/29 kg (about 40 kg when the patient was in [REDACTED]). • Manual muscle testing (13-Jul-2021): NF/E: 5/5, Deltoid: 5/5, BB: 5/5, TB: 5/5, WE: 5/5, WF: 5/5, APB: 5/5, Ilio: 4 +/4 +, Quad: 4 +/4 +, Ham: 4/4, TA: 4-/4-, GC: 3 +/3 +, adductor of thigh: 5-/5-, abducent of thigh: 4/4. • Walking (13-Jul-2021): the patient was able to walk independently, but left and right knee buckled frequently. No apparent convulsions. • Romberg test (13-Jul-2021): there was no problem, but the patient said that his trunk swayed and he felt like he was going to fall.							

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	Standing on one leg (13-Jul-2021): the patient was able to do so, but was quite swaying. • Squat (13-Jul-2021): the patient was unable to do so, lost the balance posteriorly and nearly collapsed. Tandem walking test (13-Jul-2021): there was a step out. the patient became difficult when the knee buckled. • Deep tendon reflexes (13-Jul-2021): BR: hyperactive/hyperactive, TR: hyperactive/hyperactive, BRR: elimination/elimination, PTR: very hyperactive/very hyperactive, ATR: very hyperactive/very hyperactive. Both sides of Wartenberg were positive. • Blood test (13-Jul-2021): there was high LDL-Cho blood disease and slight increase in FRN. • Blood test (14-Jul-2021) showed a slight elevation of lysozyme 5.3. • Nerve conduction velocity: rt5N (14-Jul-2021) medium: decreased incidence of F. Tivial: TL very slightly prolonged. Personal: normal range. Sural: SCV lower bound. • Lower extremity SEP (14-Jul-2021): All electrodes were repeatedly polished to 30 kilo-ohm or less, and N 18 could not be detected by right stimulation. Since the upper waveform appeared, it continued. CCT 16.8/17.6, normal range, each waveform latency normal range. • All spinal pMRI (14-Jul-2021): no apparent abnormal signal was noted in intramedullary T2/STIR. DWI also showed no apparent abnormality. Only mild disc herniation in L5/S1. • Total myelography MRI (15-Jul-2021): no obvious enhancement was observed. [Survey for acute disseminated encephalomyeli							
	This case was initially received via Takeda Pharmaceuticals (Reference number: [REDACTED] on 10-Aug-2021. The most recent information was received on 04-Sep-2021 and was forwarded to Moderna on 25-Nov-2021. This case was reported by a pharmacist via the Drug	0	Level 4	Level 4	0	conditional	This report is for a 48 years old female with unknown medical history and concomitant medications, who at an unknown time after an the 1st dose of Spikevax was diagnosed with ADEM. No other information was provided. This case	

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	Information Center. On 01-Sep-2021, follow-up information, reported by a physician, was received via the [REDACTED] (Ref, [REDACTED]). On 04-Sep-2021, follow-up information, reported by a physician, was received by Takeda via Moderna's adverse reaction reporting site [REDACTED]. On an unknown date, body temperature before the vaccination: 36.4 degrees Celsius. On 10-Jul-2021, at 17:10, the patient received the 1st dose of this vaccine. At 21:00, sensory abnormality in the right lower limb developed. The symptom then spread to the other limbs, trunk, and face in about 10 days, and headache, queasy, and strange feeling of vision also developed. On 19-Jul-2021, the patient visited the reporting hospital. Head MRI and cervical spine MRI showed findings suggestive of inflammatory demyelination in the cerebral white matter behind the right brain ventricle and in the medulla oblongata to the cervical cord (C1). Other diseases such as infectious diseases were negative in blood test and cerebrospinal fluid examination. The patient had no past history or family history of central nervous system disease or autoimmune disease, and based on the nerve conduction test results, cerebrospinal fluid test results, and the clinical course, the patient was diagnosed with acute disseminated encephalomyelitis (ADEM) after vaccination with this vaccine. On 04-Aug-2021, the patient was hospitalized. On 05-Aug-2021, high-dose steroid therapy (IVMP) was started. On 12-Aug-2021, sensory abnormality remained even after IVMP for 8 days was completed. The second IVMP was performed. On 15-Aug-2021, IVMP was terminated. On an unknown date, complex therapy with PSL 50 mg was performed. On 21-Aug-2021, the patient was discharged from the hospital with the dose of PSL tapered to 30 mg. The symptoms were resolving, but mild symptom remained only in the right lower limb. The outcome of acute disseminated encephalomyelitis was reported as resolving.					according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and according to the WHO causality assessment this case is considered conditional. There is no information provided for the patient's full medical history, including concomitant medications, as well as information missing regarding any laboratory tests conducted, treatment, medical course, etc.		

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	No follow-up investigation will be made. [Clinical symptoms] The patient experienced this event for the first time. Central nervous system damage (event) which was clinically multifocal Encephalopathy unexplained by pyrexia (alteration of consciousness and behavior) The event was assumed to be caused by inflammatory demyelination. Encephalopathy, sensory abnormality (regarding sensory level, sensation was both present and absent), strange feeling of vision [Imaging test] (Date of test: 28-Jul-2021) Diffuse or multiple white matter lesions were found on T2-weighted/diffusion-weighted imaging (DWI) or FLAIR imaging (with or without gadolinium enhancement with T1-weighted imaging). The results did not meet both or one of the two criteria of MRI for multiple sclerosis. [Disease course] The observation period was not long enough to reveal that the disease had a single-phase pattern. Time from onset to last observation: 1 The observation period after the onset was within 3 months. [Cerebrospinal fluid examination] (Date of examination: 04-Aug-2021) Cell counts: 2, sugar: 59, and protein: 26 No elevation in IgG index [Autoantibody examination] (Date of examination: 04-Aug-2021) Anti-AQP4 antibody: negative in ELISA method and had not received the result of CBA method. Anti-MOG antibody: negative. Follow-up received on 04-SEP-2021 Updated: Reporter Information, Patient Information,							

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	Product Information, Event Information, Narrative The duplicate was identified on 15-SEP-2021 on review of data; all information from 2021TJP086961 has been merged into 2021TJP071927. No new information has been received on this case. Company Comment: The event developed after the administration of COVID-19 vaccine mRNA (mRNA 1273) and there is temporal relationship.							
	This case was received via [REDACTED] Reference number: [REDACTED] on 17-Aug-2021 and was forwarded to Moderna on 17-Aug-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of AUTOIMMUNE DEMYELINATING DISEASE (Autoimmune demyelinating disease), CONGENITAL CENTRAL NERVOUS SYSTEM ANOMALY (Congenital central nervous system anomaly), ENCEPHALOMALACIA (Encephalomalacia), ERECTILE DYSFUNCTION (Erectile dysfunction), CENTRAL NERVOUS SYSTEM LESION (Central nervous system lesion) and WHITE MATTER LESION (White matter lesion) in a 49-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Hypertension, Hypercholesterolemia and Obesity (BMI 28.7). On 30-Apr-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 28-May-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On 14-Jun-2021, the patient experienced AUTOIMMUNE DEMYELINATING DISEASE (Autoimmune demyelinating disease) (seriousness criterion medically significant), CONGENITAL CENTRAL NERVOUS SYSTEM ANOMALY (Congenital central nervous system anomaly) (seriousness criterion medically significant), ENCEPHALOMALACIA (Encephalomalacia) (seriousness criterion medically significant), ERECTILE DYSFUNCTION (Erectile dysfunction) (seriousness criterion medically significant), BALANCE DISORDER (Balance disorder), CENTRAL NERVOUS SYSTEM LESION (Central nervous system lesion) (seriousness criterion medically significant), DECREASED APPETITE (Decreased appetite), DISCOMFORT	MRI head: multiple dawson's fingers, active demyelination, involving supratentorial white matter and infratentorial brain, juxtacortical, subcortical, periventricular white matter, corpus callosum, cerebellar white matter, pons, medulla. Multiple lesions are associated with active demyelination, characteristic peripheral enhancement.	Level 2	Level 2	0	Possible	This report is for a 49 years old male with medical history of hypertension, hypercholesterolemia and obesity; concomitant medication information was not provided. 17 days after the 2nd dose of Spikevax patient went for a COVID-19 test because of intermittent low-grade fevers (up to 100-101 Fahrenheit) and body aches, fatigue, poor appetite. The test was negative. Around 2 weeks later, patient reported dizzy while walking and experiencing numbness and tingling in both hands, and associated weight loss, numbness of the perineum; erectile dysfunction; balance problem; and bilateral feet heaviness. MRI spine: multiple lesions in cervical cord at C2 centrally and right laterally and dorsally, C3 centrally, C6-7 dorsally, with associated enhancement. Lesions in the right lateral thoracic cord at T6, in the left hemicord at T9, dorsal cord at T9-10, right lateral cord at T12, with associated enhancement. MRI head showed multiple dawson's fingers, active demyelination, involving supratentorial white matter and infratentorial brain, juxtacortical, subcortical, periventricular white matter, corpus callosum, cerebellar white matter, pons, medulla. Multiple lesions are associated with active demyelination, characteristic peripheral enhancement. This case according to the Brighton collaboration case definition for ADEM is classified as Level 2A (case meets both level 2 ADEM & encephalitis). According WHO causality assessment this case is considered possible due to temporal association. But could also be explained by cofounders including hypertension, hypercholesterolemia and obesity. No report on infectious disease evaluation.	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Discomfort), DIZZINESS (Dizziness), DYSAESTHESIA (Dysaesthesia), HYPOAESTHESIA (Hypoaesthesia), PAIN (Pain), PARAESTHESIA (Paraesthesia), WEIGHT DECREASED (Weight decreased), WHITE MATTER LESION (White matter lesion) (seriousness criterion medically significant), PYREXIA (Pyrexia) and FATIGUE (Fatigue). At the time of the report, AUTOIMMUNE DEMYELINATING DISEASE (Autoimmune demyelinating disease), CONGENITAL CENTRAL NERVOUS SYSTEM ANOMALY (Congenital central nervous system anomaly), ENCEPHALOMALACIA (Encephalomalacia), ERECTILE DYSFUNCTION (Erectile dysfunction), BALANCE DISORDER (Balance disorder), CENTRAL NERVOUS SYSTEM LESION (Central nervous system lesion), DECREASED APPETITE (Decreased appetite), DISCOMFORT (Discomfott), DIZZINESS (Dizziness), DYSAESTHESIA (Dysaesthesia), HYPOAESTHESIA (Hypoaesthesia), PAIN (Pain), PARAESTHESIA (Paraesthesia), WEIGHT DECREASED (Weight decreased), WHITE MATTER LESION (White matter lesion), PYREXIA (Pyrexia) and FATIGUE (Fatigue) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 13-Jun-2021, Magnetic resonance imaging: multiple lesions in cervical code (abnormal) Lesions in the cervical cord at C2 centrally and right laterally and dorsally, C3 centrally, C6-7 dorsally, with associated enhancement. Lesions in the right lateral thoracic cord at T6, in the left hemicord at T9, dorsal cord at T9-10, right lateral cord at T12, with associated enhancement. On 13-Jun-2021, Magnetic resonance imaging head: multiple dawson's fingers, active demyelination (abnormal) Greater than 20 foci of signal abnormality involving supratentorial white matter and infratentorial brain, juxtacortical, subcortical, periventricular white matter, corpus callosum, cerebellar white matter, pons, medulla. Multiple lesions are associated with active demyelination, characteristic peripheral enhancement. Some are somewhat tumefactive. Multiple demonstrate developing cystic encephalomalacia/T1 black holes. -multiple Dawson's fingers -infratentorial lesion - multiple T1 black holes. On 14-Jun-2021, Body temperature: 100-101 (High) 100-101 Fahrenheit. On 14-Jun-2021, Magnetic resonance imaging head: abnormal (abnormal) abnormal. On 14-Jun-2021, SARS-CoV-2 test: negative (Negative) Negative. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any							

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	causality assessments. Relevant concomitant product usage were not reported by the reporter. The treatment information was not provided. On 14-JUN-2021, lab data included Magnetic resonance imaging neck. Result was not provided. Company comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. There seems to be a discrepancy in the event Congenital central nervous system anomaly since the vaccine was administered to a 49 year old male patient.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 19-Aug-2021 and was forwarded to Moderna on 19-Aug-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 59-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3002623) for COVID-19 vaccination. No Medical History information was reported. On 10-Jun-2021, the patient received second dose of mRNA-1273 (Spikevax) (Intramuscular) .5 milliliter. On 12-Jul-2021, after starting mRNA-1273 (Spikevax), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization, medically significant and life threatening). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) was resolving. mRNA-1273 (Spikevax) (Intramuscular) was withdrawn on 10-Jun-2021. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Company comment: Very limited information regarding this event has been provided at this time. No further follow-up information is expected. Most recent FOLLOW-UP information incorporated	0	Level 4	Level 4	0	conditional	This report is for a 59 years old female with unknown medical history and concomitant medications, who 32 days after the 2nd dose of Spikevax was diagnosed with ADEM. No other information was provided. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and according to the WHO causality assessment this case is considered conditional. There is no information provided for the patient's full medical history, including concomitant medications, as well as information missing regarding any laboratory tests conducted, treatment, medical course, etc.	[REDACTED]

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	above includes: On 19-Aug-2021: Translation received on 24-aug-2021, contain no new information.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 25-Aug-2021 and was forwarded to Moderna on 25-Aug-2021. This regulatory authority case was reported by a consumer and describes the occurrence of ENCEPHALOMYELITIS (DD Neuromyelitis optica [REDACTED]) in a 27-year-old male patient who received mRNA-1273 (Spikevax) (batch no. ABX5182) for Prophylactic vaccination. Previously administered products included for an unreported indication: TETANUS VACCINE (Lot Number: APAOH1B) on 25-May-2021. On 18-May-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 10-Jun-2021, the patient experienced ENCEPHALOMYELITIS (DD Neuromyelitis optica [REDACTED]) (seriousness criteria hospitalization and medically significant). At the time of the report, ENCEPHALOMYELITIS (DD Neuromyelitis optica [REDACTED]) outcome was unknown. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. No relevant concomitant medications were reported. No treatment information was provided. Most recent FOLLOW-UP information incorporated above includes: On 25-Aug-2021: Translated doc received on 27-Aug-2021 contains added information on patient's Historical Vaccine.	0	Level 4	Level 4	0	conditional	This report is for a 27 years old male with unknown medical history, and unknown concomitant medications. Patient had a tetanus vaccine 7 days after an unknown dose of Spikevax. Patient was diagnosed with neuromyelitis optica 23 days after an unknown dose of Spikevax. No other information was provided. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4, according to the Brighton classification for Encephalitis is classified as Level 4, and according to the WHO causality assessment this case is considered conditional. There is very little information provided for the course of the patient's full medical history, including where and why he seems to be living at a medical facility (maybe because of his schizophrenia?) as well as information missing regarding other laboratory tests conducted, treatment, medical course, etc.	
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 25-Aug-2021. The most recent information was received on 19-Oct-2021 and was forwarded to Moderna on 21-Oct-2021. This regulatory authority case was reported by a consumer and describes the occurrence of DEMYELINATING POLYNEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING), PERIPHERAL MOTOR NEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING) and PERIPHERAL SENSORY NEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING) in a 43-year-old male patient who received mRNA-1273 (Spikevax) (batch no.	0	Level 4	Level 4	Level 4	Unassessable	This report is for a 43 -year-old male with a medical history of intervertebral disc protrusion, who after receiving an unknown dose of Spikevax with an unknown time to onset, reported 'demyelinating polyneuropathy, peripheral motor neuropathy, peripheral sensory neuropathy'. No report of brain MRI. This case according to the Brighton collaboration case definition for ADEM is classified as Level 4 (Insufficient evidence to meet any level of case definition). This case is considered WHO 'Unassessable'. This case could not be assessed due to insufficient information, including the absence of MRI result.	

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	3004669) for COVID-19 vaccination. The patient's past medical history included Intervertebral disc bulging. On 29-Jul-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form in total. On 02-Aug-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING) (seriousness criterion medically significant), PERIPHERAL MOTOR NEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING) (seriousness criterion medically significant) and PERIPHERAL SENSORY NEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING) (seriousness criterion medically significant). At the time of the report, DEMYELINATING POLYNEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING), PERIPHERAL MOTOR NEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING) and PERIPHERAL SENSORY NEUROPATHY (SENSORIMOTOR polyneuropathy DEMYELINATING) was resolving. No concomitant medications was reported. No treatment drug details was reported. On 04-AUG-2021, patient had Electromyogram test, results were unknown. The patient had sensorimotor polyneuropathy demyelinating. Company Comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. This case involves a 43-year-old male subject with a medical history of intervertebral disc bulging who experienced the unlisted serious adverse events (medically significant) of demyelinating polyneuropathy, peripheral motor neuropathy and peripheral sensory neuropathy 3 days after his first vaccination with mRNA-1273. The benefit-risk relationship of mRNA-1273 is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 19-Oct-2021: Follow up document received on 19-OCT-2021 contains no new information.							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	On 19-Oct-2021: Translation document received on 21-Oct-2021 with Events verbatim translated and updated narrative.							
	This regulatory authority case was reported by a pharmacist and describes the occurrence of ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis), HERPES ZOSTER (Herpes zoster around left V1 area), SPEECH DISORDER (Incoherent speech), HYPOKINESIA (Dull response), DECREASED APPETITE (Poor intake) and SOMNOLENCE (Drowsiness) in a 73-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. No Medical History information was reported. On 15-Jul-2021, the patient received dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 17-Jul-2021, the patient experienced HERPES ZOSTER (Herpes zoster around left V1 area) (seriousness criterion hospitalization). On 19-Jul-2021, the patient experienced DECREASED APPETITE (Poor intake) (seriousness criterion hospitalization) and SOMNOLENCE (Drowsiness) (seriousness criterion hospitalization). On 21-Jul-2021, the patient experienced HYPOKINESIA (Dull response) (seriousness criterion hospitalization). On 22-Jul-2021, the patient experienced SPEECH DISORDER (Incoherent speech) (seriousness criterion hospitalization). On an unknown date, the patient experienced ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis) (seriousness criteria hospitalization and medically significant). The patient was treated with ACICLOVIR SODIUM (ACYCLOVIR [ACICLOVIR SODIUM]) for Herpes zoster, at an unspecified dose and frequency. At the time of the report, ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis), HERPES ZOSTER (Herpes zoster around left V1 area), SPEECH DISORDER (Incoherent speech), HYPOKINESIA (Dull response), DECREASED APPETITE (Poor intake) and SOMNOLENCE (Drowsiness) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 22-Jul-2021, Computerised tomogram head: normal (normal) CT showed no ICH, suspected to be Varicella Zoster Virus Encephalitis. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any	0	Level 5	Level 5	Level 5	Unlikely	This report is for a 73 year-old female, with no medical history information provided; who received an unknown dose of Spikevax vaccine and 2 days later reported the progressive occurrences of herpes zoster, decreased appetite, Encephalomyelitis, Hypokinesia (dull response), somnolence (drowsiness), and speech disorder (incoherent speech).CT head: normal, showed no intracranial hemorrhage (ICH). Suspected to be Varicella Zoster Virus Encephalitis. This case is more likely Varicella zoster encephalitis and not ADEM. CT brain normal. No MRI report. This case is considered WHO Unlikely. Herpes zoster infection provides plausible explanation.	

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	causality assessments. No concomitant medications were reported. On 17-Jul-2021, patient suffered from herpes zoster around left V1 area and had acyclovir injection at LMD, but vesicle and rash improved but still had pain. On 19-Jul-2021, patient had drowsiness and poor intake. On 21-Jul-2021, patient had dull response and on 22-Jul-2021 had incoherent speech. Patient came to our ER for help and at ER, CT of brain showed no ICH. It was suspected to be Varicella Zoster Virus Encephalitis. Age at time of onset of reaction was reported as 73.9. Company Comment: Based on the current available information and temporal association between the use of the product and the start date of the events, a causal relationship cannot be excluded. Most recent FOLLOW-UP information incorporated above includes: On 19-Aug-2021: Translation document received on 02 Sep 2021. Added seriousness criteria hospitalization and updated treatment information.							
	This spontaneous case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), URINARY RETENTION (urinary retention), BACK PAIN (back pain), NECK PAIN (neck pain), HEADACHE (headache), PYREXIA (fever), NAUSEA (nausea) and VOMITING (vomiting) in a 19-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. The patient's past medical history included Atopic dermatitis, Depression, Upper respiratory infection and Diarrhea. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On an unknown date, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization and medically significant), URINARY RETENTION (urinary retention) (seriousness criteria hospitalization and medically significant), BACK PAIN (back pain)	Distinctive for ADEM wide spread demyelinating lesions.	Level 2	Level 3	Level 3	Possible	This report is for a 19 year-old female, with medical history of atopic dermatitis, depression, upper respiratory tract infection, and diarrhoea. The patient received first dose of Spikevax vaccine and after an unknown time to onset, reported acute disseminated encephalomyelitis, back pain, headache, nausea, neck pain, fever, urinary retention, and vomiting. Confounders included past medical history of atopic dermatitis, depression, upper respiratory infection and diarrhea. MRI brain: abnormal, with distinct wide spread demyelinating lesions (ADEM). MRI spinal: abnormal, with distinct wide spread demyelinating lesions (ADEM). According to Brighton's case definition, this is Level 2 ADEM. This case is considered WHO Possible due to temporal association but confounders including upper respiratory tract infection, and diarrhoea provide a more plausible explanation for the occurrence of the event of ADEM. ADEM have been noted to precede symptoms of systemic viral illness.	

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	(seriousness criterion hospitalization), NECK PAIN (neck pain) (seriousness criterion hospitalization), HEADACHE (headache) (seriousness criterion hospitalization), PYREXIA (fever) (seriousness criterion hospitalization), NAUSEA (nausea) (seriousness criterion hospitalization) and VOMITING (vomiting) (seriousness criterion hospitalization). The patient was treated with METHYLPREDNISOLONE at an unspecified dose and frequency. At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), URINARY RETENTION (urinary retention), BACK PAIN (back pain), NECK PAIN (neck pain), HEADACHE (headache), PYREXIA (fever), NAUSEA (nausea) and VOMITING (vomiting) outcome was unknown. Not Provided DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Body temperature: high (High) Fever 37.5 degree Celsius. On an unknown date, Magnetic resonance imaging head: abnormal (abnormal) Showed distinctive for ADEM wide spread demyelinating lesions. On an unknown date, Magnetic resonance imaging spinal: abnormal (abnormal) Showed distinctive for ADEM wide spread demyelinating lesions. On an unknown date, Neurological examination: abnormal (abnormal) showed Nuchal rigidity, bilateral Babinski signs with out neurological deficit symptoms. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. No concomitant medical information were reported. Company Comment : Very limited information regarding this event has been provided at this time. Further information has been requested.							
	This literature-non-study case was reported in a literature article and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) and URINARY RETENTION (Urinary retention last 2 days) in a 19-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. LITERATURE REFERENCE: Kania K, Ambrosius W, Kupezyk ET, Kozubski W. Acute disseminated encephalomyelitis in a patient vaccinated against SARS-CoV-2. Ann Clin Transl Neurol. 2021 Concurrent medical conditions included Atopic	Widespread hyperintense area in T2-weighted and FLAIR images extended from medulla oblongata to Th11 segment with overlapping few contrast-enhancing lesions.	Level 2	Level 2	Level 2	Conditional	This literature-non-study case was reported in a literature article and described the occurrence of acute disseminated encephalomyelitis and urinary retention in a 19 year-old female who received the first dose of Spikevax on an unknown date. Concurrent medical conditions included atopic dermatitis and Depression. Concomitant medications were not provided. CSF pleocytosis (WBC: 294 × 106/l (High), infectious disease evaluation was negative, MRI brain and spine: abnormal showed multiple, poorly demarcated, hyperintense lesions in T2-weighted and fluid-attenuated inversion recovery (FLAIR) images located in both	

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	dermatitis and Depression. On an unknown date, the patient received first dose of mRNA-1273 (Spikevax) (unknown route) 1 dosage form. On 25-Apr-2021, after starting mRNA-1273 (Spikevax), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) (seriousness criteria hospitalization and medically significant). On an unknown date, the patient experienced URINARY RETENTION (Urinary retention last 2 days) (seriousness criteria hospitalization and medically significant). The patient was hospitalized on 28-Apr-2021 due to ACUTE DISSEMINATED ENCEPHALOMYELITIS. The patient was treated with CEFTRIAXONE for Empiric treatment, at an unspecified dose and frequency; ACYCLOVIR [ACICLOVIR] for Empiric treatment, at an unspecified dose and frequency and METHYLPREDNISOLONE for Acute disseminated encephalomyelitis, at an unspecified dose and frequency. On 12-May-2021, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) had resolved with sequelae. At the time of the report, URINARY RETENTION (Urinary retention last 2 days) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Antibody test: negative (Negative) upon hospitalization: including anti-aquaporin-4 and anti-myelin oligodendrocyte glycoprotein, were also negative. On an unknown date, Body temperature: 37.5°C 37.5°C- fever. On an unknown date, CSF culture: negative (Negative) negative for bacteria and fungi. On an unknown date, CSF lymphocyte count (40%-80%): 91% lymphocytes (reference range, 40%-80% (High) upon hospitalization: 91%. On an unknown date, CSF monocyte count (15%-45%): 8% monocytes (reference range 15%-45%) (Low) upon hospitalization: 8%. On an unknown date, CSF neutrophil count (0%-6%): 1% neutrophils (reference range 0%-6%) (normal) upon hospitalization: 1%. On an unknown date, CSF oligoclonal band: negative (Negative) upon hospitalization: negative. On an unknown date, CSF protein (200 mg/L-400 mg/L): 648 mg/L (High) upon hospitalization: 648 mg/L and 338 mg/L (normal) 338 mg/L (when the clinical status got improved after methylprednisolone). On an unknown date, CSF red blood cell count: 77/μl upon hospitalization: 77/μL. On an unknown date, CSF test: negative (Negative) upon hospitalization: negative for antibodies to						brain hemispheres, pons, the medulla oblongata, and cerebellum. According to Brighton's case definition, this case is ADEM Level 2A (case meets both level 2 ADEM and Myelitis). According to WHO causality assessment, this case is considered Conditional. The absence of information on time to onset, concomitant medications is a challenge to assessing for causality.	

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	major pathogens and cultures of bacteria and fungi; genome sequencing also revealed no pathogens (Neisseria meningitidis, Streptococcus pneumoniae, group B streptococcus, Haemophilus influenzae, Listeria monocytogenes, HSV1, HSV2, VZV, CMV, EBV, HHV6). On an unknown date, CSF white blood cell count: 294 × 106/l (High) Upon hospitalization, the cerebrospinal fluid (CSF) white blood cell (WBC) count was 294 9 106/L (reference range, 0–5 9 106/L) and 61 × 106/l (normal) 61 × 106/L (when the clinical status got improved after methylprednisolone). On an unknown date, Magnetic resonance imaging head: abnormal (abnormal) showed multiple, poorly demarcated, hyperintense lesions in T2-weighted and fluid-attenuated inversion recovery (FLAIR) images located in both brain hemispheres, pons, the medulla oblongata, and cerebellum. Few of them were contrast-enhanced lesions. On an unknown date, Magnetic resonance imaging thoracic: abnormal (abnormal) revealed a widespread hyperintense area in T2-weighted and FLAIR images extended from medulla oblongata to Th11 segment with overlapping few contrast-enhancing lesions. On an unknown date, Neurological examination: abnormal (abnormal) showed nuchal rigidity, bilateral Babinski signs without other neurological deficit symptoms. The action taken with mRNA-1273 (Spikevax) (Unknown) was unknown. For mRNA-1273 (Spikevax) (Unknown), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis (ADEM)) to be related and URINARY RETENTION (Urinary retention last 2 days) to be possibly related. Concomitant medications were not provided. Patient was admitted to the hospital with complaints of 3-day severe headache, fever (37.5°C), back and neck pain with nausea and vomiting. She also noticed urinary retention last 2 days. Patient had no significant medical history, upper respiratory infection, or diarrhea. Upon hospitalization, laboratory tests also included the reverse transcription real-time PCR (RT-PCR) and the antigen test were used to detect active SARS-CoV-2 infections with unknown results. Patient manifested a typical radiological pattern for ADEM with extensive, diffuse demyelinating							

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	lesions in the brain and along all cervical and thoracic spinal cord. The CSF examination results were specific for ADEM with pleocytosis and the absence of oligoclonal bands. However, clinical urinary retention without lower limbs motor or sensory deficits is quite rare. The therapeutic plasma exchange (TPE) was also initiated, but the procedure had been stopped because of allergic reactions. The clinical status improved after methylprednisolone. Control lumbar puncture was done 12 days after the first one. The patient was discharged from the hospital without any symptoms except a mild headache. On follow-up after 40 days, the patient complained of only mild headache. The patient recovered with residual effect of headache. Company Comment: This case concerns a 19-year-old female patient with no previous relevant medical history, who experienced the unexpected serious events of Acute disseminated encephalomyelitis and Urinary retention after Spikevax (mRNA- 1273 vaccine / Moderna COVID-19 Vaccine). The event occurred approximately 2 weeks after the first dose of Spikevax. The rechallenge is unknown since only information about the first dose was disclosed. The benefit-risk relationship of Spikevax vaccine is not affected by this report Most recent FOLLOW-UP information incorporated above includes: On 13-Sep-2021: Follow up received by safety on 14-Sep-2021 included an Email with abstract received from SARA team and does not contain any new information. On 14-Sep-2021: Follow up received by safety on 15-Sep-2021 included an Email with FTA received from SARA team and does not contain any new information. On 01-Oct-2021: Follow up received by safety on 04-Oct-2021 included a response from the author with no new information On 05-Oct-2021: Follow up received by safety on 05-Oct-2021 consists of an email with attached ADR form from the author, updated patient information, event start/end date, outcome, HCP causality and reporters qualification.							
	This case was received via [REDACTED] on 07-Sep-2021 and was forwarded to Moderna on 07-Sep-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) and IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy) in a 60-year-old female patient who	0	Level 5	Level 5	Level 5	Unlikely	This report of Immune-mediated neuropathy in 60 year-old female, occurred 14 days after receiving the second dose of Spikevax vaccine. Medical history of obesity and concurrent medical condition of allergy. Patient reported Arthralgia, Brachial plexopathy, Glucose tolerance impaired, Hypoaesthesia, Immune-mediated neuropathy, Injection site pain, Movement disorder, Neuralgic	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
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	received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 017C21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included Obesity. Concurrent medical conditions included Penicillin allergy since 09-Mar-2018, Drug allergy (Aspirin Reactions: Shortness of breath) since 09-Mar-2018, Drug allergy (Nsaids (Non-Steroidal Anti-Inflammatory Drug) Reactions:Shortness of breath) since 31-Jan-2021, Allergy to antibiotic (Amoxicillin Reactions:Rash) since 11-Apr-2012, Allergy (Cat/Feline Products Reactions: Other) since 09-Mar-2018 and Asthma. Concomitant products included ACETAMINOPHEN, CICLESONIDE (ALVESCO), FLUOXETINE, LEVONORGESTREL, LEVOTHYROXINE, LISINOPRIL and SALBUTAMOL SULFATE (VENTOLIN HFA) for an unknown indication. On 01-May-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On an unknown date, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 15-May-2021, the patient experienced GULLLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criterion medically significant), IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy) (seriousness criterion medically significant), BRACHIAL PLEXOPATHY (Brachial plexopathy), GLUCOSE TOLERANCE IMPAIRED (Glucose tolerance impaired), HYPOAESTHESIA (Hypoaesthesia), MOVEMENT DISORDER (Movement disorder), NEURALGIC AMYOTROPHY (Neuralgic amyotrophy), PARAESTHESIA (Paracesthesia), PAIN (Pain), ARTHRALGIA (Arthralgia) and INJECTION SITE PAIN (Injection site pain). The patient was treated with IMMUNOGLOBULIN HUMAN NORMAL (IVIGLOB-EX) at a dose of 0.4 g/ kg; ACETAMINOPHEN for Adverse event, at a dose of 1 dosage form and PREDNISONE for Adverse event, at a dose of 1 dosage form. At the time of the report, GULLLAIN-BARRE SYNDROME (Guillain-Barre syndrome), IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy), BRACHIAL PLEXOPATHY (Brachial plexopathy), GLUCOSE TOLERANCE IMPAIRED (Glucose tolerance impaired), HYPOAESTHESIA (Hypoaesthesia), MOVEMENT DISORDER (Movement disorder), NEURALGIC AMYOTROPHY (Neuralgic amyotrophy), PARAESTHESIA (Paracesthesia), PAIN (Pain), ARTHRALGIA (Arthralgia) and INJECTION SITE PAIN (Injection site pain) had not resolved.					amyotrophy, Pain, Paracesthesia. Anti-ganglioside antibody: positive (GBS), Galactosialidosis: positive asialo -GM1 and GD1a antibodies supporting immune-mediated neuropathy in the form of Parsonage-Turner syndrome (idiopathic brachial plexitis). MRI: abnormal Immune-mediated neuropathy (MA-HCC). Case of Guillain-Barre syndrome and Immune-mediated neuropathy. According to Brighton's case definition, this case is not ADEM, but rather GBS; and considered WHO Unlikely. Other disease provide plausible explanations.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 15-May-2021, Anti-ganglioside antibody: positive (Positive) Positive. On 15-May-2021, Blood glucose: abnormal (abnormal) IMPAIRED GLUCOSE TOLERANCE: 5.7%-6.4% DIAGNOSIS: 6.5 or greater (on 2 occasions) per KP Type 2 Diabetes Guideline.. On 15-May-2021, Blood immunoglobulin A: abnormal (abnormal) abnormal. On 15-May-2021, Glucose tolerance test: 5.7-6.4 (normal) 5.7%-6.4%. On 15-May-2021, Glycosylated haemoglobin: normal (normal) 5.9 % 4.5 to 5.6 %4.5 - 5.6 % H NORMAL. On 23-Aug-2021, Galactosialidosis: positive asialo (Positive) Positive asialo-GM1 and GD1a antibodies supporting immune-mediated neuropathy in the form of Parsonage-Turner syndrome (idiopathic brachial plexitis).. On 23-Aug-2021, Magnetic resonance imaging: abnormal (abnormal) Immune-mediated neuropathy (MA-HCC) (primary encounter diagnosis) (G54.0). For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Lab test done on 23-Aug-2021 for Immune-mediated neuropathy.Brachial plexopathy without trauma, Borderline diabetes mellitus, Metabolic function test, Blood immunoglobulin A , Full blood count, Platelet count with no results. Action taken was not applicable. This case concerns a 60 year-old, female subject, who experienced the unexpected events of GUILLAIN BARRE SYNDROME and IMMUNE MEDIATED NEUROPATHY. The event occurred approximately 14 days after the second dose of Spikevax. The rechallenge was unknown since there is no information about the first dose. The benefit-risk relationship of Spikevax in not affected by this report. Event terms, onset dates, and outcomes captured per Source Document from Regulatory Authority reporting. Even though events of Guillain Barre Syndrome and Immune Mediated neuropathy were reported as non serious, they were upgraded as per medical judgement and Important Medical Event list assessment.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 17-Sep-2021 and was forwarded to Moderna on 17-Sep-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACUTE	0	Level 4	Level 4	Level 4	Unassessable	This report is for a 19-year-old female, with no relevant medical history, who received the first dose of Spikevax and 13 days later reported acute disseminated encephalomyelitis. No report of MRI, CSF analysis and other labs. According to	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 19-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 prophylaxis. No Medical History information was reported. On 15-Apr-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 28-Apr-2021, after starting mRNA-1273 (Spikevax), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization and medically significant). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) was resolving. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant product information was provided. Treatment information was not provided. Company Comment : This case concerns a 19-year-old, female patient with no relevant medical history, who experienced the unexpected event of Acute disseminated encephalomyelitis. The event Acute disseminated encephalomyelitis occurred 13 days after the first dose of Moderna Covid-19 vaccine. The rechallenge was not applicable, as the event happened after the first dose. The event was considered related to the product per the reporter's assessment. The benefit-risk relationship of Moderna Covid-19 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 17-Sep-2021: Translation Received on 21-SEP-2021 and does not contain any new information.						Brighton's Collaboration case definition, this case is a Level 4 ADEM. Due to insufficient information this case can not be assessed and considered WHO Unassessable.	
	This case was received via [REDACTED] on 21-Sep-2021 and was forwarded to Moderna on 21-Sep-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of CERVICAL SPINAL STENOSIS (Cervical spinal stenosis), CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (Chronic inflammatory demyelinating polyradiculoneuropathy), DEMYELINATING	White matter lesions on brain.	Level 2	Level 5	Level 5	Possible	This report is for 47-year-old female with a medical history of peripheral venous disease and concurrent Bipolar disorder. Concomitant medications included bupropion, lorazepam, albuterol, and mometasone. 7 days after receiving the first dose of Spikevax vaccine, reported Arthralgia, Asthenia, Cervical spinal stenosis, Chronic inflammatory demyelinating polyradiculoneuropathy, Demyelinating polyneuropathy, Fine motor skill dysfunction, Impaired driving	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	POLYNEUROPATHY (Demyelinating polyneuropathy), FINE MOTOR SKILL DYSFUNCTION (Fine motor skill dysfunction), IMPAIRED DRIVING ABILITY (Impaired driving ability), MOBILITY DECREASED (Mobility decreased), ARTHRALGIA (Arthralgia), ASTHENIA (Asthenia), MUSCULAR WEAKNESS (Muscular weakness), MUSCULOSKELETAL DISORDER (Musculoskeletal disorder), MUSCULOSKELETAL STIFFNESS (Musculoskeletal stiffness), MYOCLONUS (Myoclonus), SPINAL OSTEOARTHRITIS (Spinal osteoarthritis), WALKING AID USER (Walking aid user), WHEELCHAIR USER (Wheelchair user) and WHITE MATTER LESION (White matter lesion) in a 47-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 025C21A) for COVID-19 vaccination. The patient's past medical history included Venous insufficiency. Concurrent medical conditions included Bipolar disorder. Concomitant products included BUPROPION HYDROCHLORIDE (WELLBUTRIN XL), LORAZEPAM, ALBUTEROL [SALBUTAMOL] and MOMETASONE FUROATE (ASMANEX) for an unknown indication. On 14-Apr-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 12-May-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On 21-Apr-2021, the patient experienced CERVICAL SPINAL STENOSIS (Cervical spinal stenosis) (seriousness criteria hospitalization, disability and medically significant), CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (Chronic inflammatory demyelinating polyradiculoneuropathy) (seriousness criteria hospitalization, disability and medically significant), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization, disability and medically significant), FINE MOTOR SKILL DYSFUNCTION (Fine motor skill dysfunction) (seriousness criteria hospitalization and disability), IMPAIRED DRIVING ABILITY (Impaired driving ability) (seriousness criteria hospitalization and disability), MOBILITY DECREASED (Mobility decreased) (seriousness criteria hospitalization and disability), ARTHRALGIA (Arthralgia) (seriousness criteria hospitalization and disability), ASTHENIA (Asthenia) (seriousness criteria hospitalization and disability), MUSCULAR WEAKNESS (Muscular weakness) (seriousness criteria hospitalization and disability).					ability, Mobility decreased, Muscular weakness, Musculoskeletal disorder, Musculoskeletal stiffness, Myoclonus, Spinal osteoarthritis. MRI head: white matter lesions on brain and abnormal white matter lesions. MRI Spine: moderate stenosis and abnormal degenerative changes. CT Spine & Brain: normal. According to Brighton's case definition, this case is a Level 2 ADEM (MRI brain showed white matter lesions). This case is considered WHO Possible due to temporal association, but could also be explained by concomitant medications that the patient was on, including bupropion.		

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	MUSCULOSKELETAL DISORDER (Musculoskeletal disorder) (seriousness criteria hospitalization and disability), MUSCULOSKELETAL STIFFNESS (Musculoskeletal stiffness) (seriousness criteria hospitalization and disability), MYOCLONUS (Myoclonus) (seriousness criteria hospitalization and disability), SPINAL OSTEOARTHRITIS (Spinal osteoarthritis) (seriousness criteria hospitalization and disability), WALKING AID USER (Walking aid user) (seriousness criteria hospitalization and disability), WHEELCHAIR USER (Wheelchair user) (seriousness criteria hospitalization and disability) and WHITE MATTER LESION (White matter lesion) (seriousness criteria hospitalization and disability). The patient was hospitalized on 25-May-2021 due to ARTHRALGIA, ASTHENIA, CERVICAL SPINAL STENOSIS, CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY, DEMYELINATING POLYNEUROPATHY, FINE MOTOR SKILL DYSFUNCTION, IMPAIRED DRIVING ABILITY, MOBILITY DECREASED, MUSCULAR WEAKNESS, MUSCULOSKELETAL DISORDER, MUSCULOSKELETAL STIFFNESS, MYOCLONUS, SPINAL OSTEOARTHRITIS, WALKING AID USER, WHEELCHAIR USER and WHITE MATTER LESION. At the time of the report, CERVICAL SPINAL STENOSIS (Cervical spinal stenosis), CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (Chronic inflammatory demyelinating polyradiculoneuropathy), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), FINE MOTOR SKILL DYSFUNCTION (Fine motor skill dysfunction), IMPAIRED DRIVING ABILITY (Impaired driving ability), MOBILITY DECREASED (Mobility decreased), ARTHRALGIA (Arthralgia), ASTHENIA (Asthenia), MUSCULAR WEAKNESS (Muscular weakness), MUSCULOSKELETAL DISORDER (Musculoskeletal disorder), MUSCULOSKELETAL STIFFNESS (Musculoskeletal stiffness), MYOCLONUS (Myoclonus), SPINAL OSTEOARTHRITIS (Spinal osteoarthritis), WALKING AID USER (Walking aid user), WHEELCHAIR USER (Wheelchair user) and WHITE MATTER LESION (White matter lesion) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 21-Apr-2021, Chest X-ray: normal (normal) normal. On 21-Apr-2021, Computerised tomogram head: normal (normal) No stroke normal. On 21-Apr-2021, Computerised tomogram spine:							

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	normal (normal) normal. On 21-Apr-2021, Electrocardiogram: normal (normal) normal. On 21-Apr-2021, Scan with contrast: abnormal (abnormal) abnormal. On 22-Apr-2021, Computerised tomogram thorax: normal (normal) normal. On 22-Apr-2021, Magnetic resonance imaging head: abnormal (abnormal) white matter lesions on brain. On 22-Apr-2021, Magnetic resonance imaging spinal: abnormal (abnormal) moderate stenosis and abnormal (abnormal) degenerative changes. On 22-Apr-2021, Ultrasound Doppler: normal (normal) normal. On 26-Apr-2021, Blood test: normal (normal) Normal No Auto Immune Disease. On 25-May-2021, Chest X-ray: normal (normal) normal. On 25-May-2021, Electrocardiogram: normal (normal) normal. On 26-May-2021, Computerised tomogram: normal (normal) normal. On 26-May-2021, Magnetic resonance imaging head: abnormal (abnormal) white matter lesions on brain and abnormal (abnormal) white matter lesions. On 28-May-2021, Lumbar puncture: normal (normal) Normal (no MS/Lyme). On 28-May-2021, Pulmonary function test: normal (normal) normal. On 14-Jun-2021, Electroencephalogram: normal (normal) normal. On 18-Jun-2021, Electroencephalogram: normal (normal) normal. On 15-Jul-2021, Electromyogram: abnormal (abnormal) CIDP diagnosis. On 02-Aug-2021, Magnetic resonance imaging thoracic: normal (normal) Normal no cord lesions. On an unknown date, Blood test: normal (normal) Multiple blood panels Various from hospital stays Normal. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Patient took PT/OT, speech therapy and IVIG infusion as treatment medication. Company Comment: This case concerns a 47-year-old, female patient with no relevant medical history, who experienced the unexpected events of demyelinating polyneuropathy, Chronic inflammatory demyelinating polyradiculoneuropathy, fine motor skill dysfunction and chronic inflammatory demyelinating polyradiculoneuropathy. The events occurred approximately 7 days after the second dose							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	of mRNA-1273. The rechallenge is not applicable, as the events happened after the second dose. The reporter assessed the events as related to the product. The benefit-risk relationship of mRNA-1273 in not affected by this report.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 23-Sep-2021 and was forwarded to Moderna on 23-Sep-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 43-year-old female patient who received mRNA-1273 (Spikevax) for COVID-19 vaccination. Concurrent medical conditions included Amblyopia. On 02-Jun-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 11-Jul-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization and medically significant). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) had not resolved. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Concomitant product use was not provided. Treatment information was not provided. Company Comment: This case concerns a 43 year old female with no relevant history who experienced the serious unexpected event of ACUTE DISSEMINATED ENCEPHALOMYELITIS. The event occurred approximately 40 days after the first dose of Spikevax. The rechallenge was not applicable (1st dose) The events were considered related to the study drug per the reporter's assessment. The benefit-risk relationship of the vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 23-Sep-2021: Translation received on 28-SEP-2021 contains No New Information.	0	Level 4	Level 5	level 5	Unassessable	This report is for a 43-year-old female , with a concurrent medical conditions of amblyopia, who received the first dose of Spikevax vaccine and 39 days later reported acute disseminated encephalomyelitis. No MRI report. According to the Brighton's case definition, this case is a has a level of certainty (LOC) 4 ADEM with insufficient data to meet any level of the case definition. Due to insufficient evidence, this case is considered WHO Unassessable.	
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 28-Sep-2021 and was forwarded to Moderna on 28-Sep-2021. This regulatory authority case was reported by an	0	Level 5	Level 4	Level 5	Unlikely	This report is for a 78-year-old male with past medical history of Spinal cord drainage, and concurrent medical conditions included: Sore throat, Toxic encephalopathy, Non-pyogenic	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	other health care professional and describes the occurrence of DEMENTIA (Dementia), ENCEPHALITIS (Encephalitis), ENCEPHALOMYELITIS (Encephalomyelitis viral), HERPES OESOPHAGITIS (Herpes oesophagitis), MENINGITIS ASEPTIC (Meningitis aseptic), MENINGOENCEPHALITIS HERPETIC (Meningoencephalitis herpetic), TOXIC ENCEPHALOPATHY (Toxic encephalopathy), APHASIA (Aphasia), CANDIDA INFECTION (Candida infection), DEHYDRATION (Dehydration), DISORIENTATION (Disorientation), DYSGEUSIA (Dysgeusia), PAIN (Pain), PHARYNGITIS STREPTOCOCCAL (Pharyngitis streptococcal), RETCHING (Retching), SPEECH DISORDER (Speech disorder), TYPE V HYPERLIPIDAEMIA (Type V hyperlipidaemia) and VOMITING (Vomiting) in a 78-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 020B21A) for COVID-19 vaccination. The patient's past medical history included Spinal cord drainage, Gastrostomy on 03-Apr-2021 and Central venous catheterisation on 03-Apr-2021. Concurrent medical conditions included Sore throat, Toxic encephalopathy, Non-pyogenic meningitis, Encephalomyelitis, Mixed hyperlipidemia, Candidiasis, Streptococcal pharyngitis and Dysphasia. Concomitant products included PARACETAMOL (TYLENOL), MELOXICAM, GABAPENTIN, FINASTERIDE, TAMSULOSIN and ALPRAZOLAM (ALPRAZ) for an unknown indication. On 01-Apr-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 03-Apr-2021, the patient experienced DEMENTIA (Dementia) (seriousness criteria hospitalization, medically significant and life threatening), ENCEPHALITIS (Encephalitis) (seriousness criteria hospitalization, medically significant and life threatening), ENCEPHALOMYELITIS (Encephalomyelitis viral) (seriousness criteria hospitalization, medically significant and life threatening), HERPES OESOPHAGITIS (Herpes oesophagitis) (seriousness criteria hospitalization, medically significant and life threatening), MENINGITIS ASEPTIC (Meningitis aseptic) (seriousness criteria hospitalization, medically significant and life threatening), MENINGOENCEPHALITIS HERPETIC (Meningoencephalitis herpetic) (seriousness criteria hospitalization, medically significant and life threatening), TOXIC ENCEPHALOPATHY (Toxic encephalopathy) (seriousness criteria hospitalization, medically significant and life threatening), APHASIA (Aphasia) (seriousness criteria hospitalization and					meningitis, Encephalomyelitis, Mixed hyperlipidemia, Candidiasis, Streptococcal pharyngitis and Dysphasia. Concomitant medications included paracetamol (tylenol), meloxicam, gabapentin, finasteride, tamsulosin, and alprazolam. On the second day of receiving Dose 2 of the Spikevax vaccine, reported Aphasia, Candida infection, Dehydration, Dementia, Disorientation, Dysgeusia, Encephalitis, Encephalomyelitis, Gastrostomy, Herpes oesophagitis, Meningitis aseptic, Meningoencephalitis herpetic, Pain, Pharyngitis streptococcal, Retching, Speech disorder, Spinal cord drainage, Toxic encephalopathy, Type V hyperlipidaemia, Vomiting, and Weight decreased. No MRI report. This case does not meet the criteria for case definition for ADEM, encephalitis and myelitis. This case is considered WHO Unlikely. The multiple confounding factors/concurrent medical conditions in this case provide plausible explanations.		

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	life threatening), CANDIDA INFECTION (Candida infection) (seriousness criteria hospitalization and life threatening), DEHYDRATION (Dehydration) (seriousness criteria hospitalization and life threatening), DISORIENTATION (Disorientation) (seriousness criteria hospitalization and life threatening), DYSGEUSIA (Dysgeusia) (seriousness criteria hospitalization and life threatening), PAIN (Pain) (seriousness criteria hospitalization and life threatening), PHARYNGITIS STREPTOCOCCAL (Pharyngitis streptococcal) (seriousness criteria hospitalization and life threatening), RETCHING (Retching) (seriousness criteria hospitalization and life threatening), SPEECH DISORDER (Speech disorder) (seriousness criteria hospitalization and life threatening), TYPE V HYPERLIPIDAEMIA (Type V hyperlipidaemia) (seriousness criteria hospitalization and life threatening) and VOMITING (Vomiting) (seriousness criteria hospitalization and life threatening). The patient was hospitalized from 09-Apr-2021 to 15-Apr-2021 due to APHASIA, CANDIDA INFECTION, DEMENTIA, DISORIENTATION, DYSGEUSIA, ENCEPHALITIS, ENCEPHALOMYELITIS, HERPES OESOPHAGITIS, MENINGITIS ASEPTIC, MENINGOENCEPHALITIS HERPETIC, PAIN, PHARYNGITIS STREPTOCOCCAL, RETCHING, SPEECH DISORDER, TOXIC ENCEPHALOPATHY, TYPE V HYPERLIPIDAEMIA and VOMITING, and then from 27-Apr-2021 to 10-May-2021 due to DEHYDRATION. At the time of the report, DEMENTIA (Dementia), ENCEPHALITIS (Encephalitis), ENCEPHALOMYELITIS (Encephalomyelitis viral), HERPES OESOPHAGITIS (Herpes oesophagitis), MENINGITIS ASEPTIC (Meningitis aseptic), MENINGOENCEPHALITIS HERPETIC (Meningoencephalitis herpetic), TOXIC ENCEPHALOPATHY (Toxic encephalopathy), APHASIA (Aphasia), CANDIDA INFECTION (Candida infection), DEHYDRATION (Dehydration), DISORIENTATION (Disorientation), DYSGEUSIA (Dysgeusia), PAIN (Pain), PHARYNGITIS STREPTOCOCCAL (Pharyngitis streptococcal), RETCHING (Retching), SPEECH DISORDER (Speech disorder), TYPE V HYPERLIPIDAEMIA (Type V hyperlipidaemia) and VOMITING (Vomiting) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 03-Apr-2021, Weight: decreased (Low) Lost 65 lbs. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments.							

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	Treatment included Pice Line w/Acylovir infusions. Patient did Central venous catheterization, Gastrostomy and Spinal cord drainage. It was reported that patient discharged with Bolus Feedings and on Aug.-Resumed regular diet. Company Comment: This case concerns a 78 year-old male patient with no reported medical history who experienced the unexpected events of dementia, encephalitis, encephalomyelitis, herpes oesophagitis, meningitis aseptic, meningoencephalitis herpetic, toxic encephalopathy, aphasia, candida infection, dehydration, disorientation, dysgeusia, pain, pharyngitis streptococcal, retching, speech disorder, type V hyperlipidemia, and vomiting. The events occurred approximately 2 days after the second dose of mRNA-1273. The rechallenge was not applicable as no additional dosing will be administered. The benefit-risk relationship of mRNA-1273 is not affected by this report.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 28-Sep-2021 and was forwarded to Moderna on 28-Sep-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) in a 67-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch nos. 013L20A and 039K20A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. Concurrent medical conditions included Drug allergy (Zocor Drug allergy causes Rash) and High cholesterol. On 15-Jan-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) 1 dosage form. On 12-Feb-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On 01-Feb-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criterion medically significant), BACK PAIN (Back pain), CHEST DISCOMFORT (Chest discomfort), GROIN PAIN (Groin pain), IMPAIRED DRIVING ABILITY (Impaired driving ability), INTERVERTEBRAL DISC PROTRUSION (Intervertebral disc protrusion), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities), MUSCULAR WEAKNESS (Muscular weakness), MUSCULOSKELETAL	Spine:abnormal. Cervical spine: small central disc herniation C3-4 and C4-5 moderate to marked right C5 nerve root compression	Not a case of ADEM	Level 5	Level 5	Unlikely	This is a case of a 67-year-old male with a medical history of hypercholesterolemia. 17 days after receiving the first dose of Spikevax, reported back pain, Chest discomfort, Demyelinating polyneuropathy, Groin pain, Impaired driving ability, Intervertebral disc protrusion, Loss of personal independence in daily activities, Muscular weakness, Musculoskeletal stiffness, Neck pain, Pain in extremity, Radiculopathy. MRI spine: abnormal, details of abnormality not provided. MRI cervical spine: small central disc herniation C3-4 and C4-5 moderate to marked right C5 nerve root compression. According to Brighton's classification case definition for ADEM, this case is NOT a case of ADEM but rather disc herniation with C5 nerve root compression. This case is confounded by the medical history of hypercholesterolemia. Logistic regression revealed that patients with hypercholesterolemia had a higher risk of disc herniation. This case is considered WHO Unlikely.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	STIFFNESS (Musculoskeletal stiffness), NECK PAIN (Neck pain), PAIN IN EXTREMITY (Pain in extremity) and RADICULOPATHY (Radiculopathy). The patient was treated with METHYLPREDNISOLONE (MEDROL DOSEPAK) on 03-Jun-2021 at an unspecified dose and frequency and IMMUNOGLOBULIN HUMAN NORMAL (IVIGLOB-EX) (intravenous) on 30-Jun-2021 at an unspecified dose and frequency. At the time of the report, DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), BACK PAIN (Back pain), CHEST DISCOMFORT (Chest discomfort), GROIN PAIN (Groin pain), IMPAIRED DRIVING ABILITY (Impaired driving ability), INTERVERTEBRAL DISC PROTRUSION (Intervertebral disc protrusion), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities), MUSCULAR WEAKNESS (Muscular weakness), MUSCULOSKELETAL STIFFNESS (Musculoskeletal stiffness), NECK PAIN (Neck pain), PAIN IN EXTREMITY (Pain in extremity) and RADICULOPATHY (Radiculopathy) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 01-Feb-2021, AST/ALT ratio: normal (normal) normal. On 01-Feb-2021, Aldolase: high (High) High. On 01-Feb-2021, Blood creatine: normal (normal) normal. On 01-Feb-2021, Blood creatine phosphokinase: normal (normal) normal. On 01-Feb-2021, Electromyogram: abnormal (abnormal) abnormal. On 01-Feb-2021, Magnetic resonance imaging spinal: abnormal (abnormal) abnormal. On 01-Feb-2021, Red blood cell sedimentation rate: high (High) high. On 23-Apr-2021, AST/ALT ratio: normal (normal) normal. On 23-Apr-2021, Aldolase: 2.2 (normal) normal. On 23-Apr-2021, Blood creatine: 0.95 (normal) normal. On 23-Apr-2021, Blood creatine phosphokinase: 67 (normal) normal. On 23-Apr-2021, C-reactive protein increased: 2.2 (normal) normal. On 23-Apr-2021, Red blood cell sedimentation rate increased: 36 (High) High. On 12-May-2021, Blood creatine phosphokinase: 73 (normal) normal. On 12-May-2021, C-reactive protein increased: 2.3 (normal) normal. On 12-May-2021, Red blood cell sedimentation rate increased: 21 (normal) normal. On 12-May-2021, Thyroid function test: normal							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	(normal) normal. On 24-May-2021, Electromyogram: abnormal (abnormal) EMG/NCS of upper extremities at facility: Left median sensory DL 4.4, CV 34 m/s normal amplitude Right median sensory absent Bilateral ulnar sensory absent Bilateral median motor DL prolonged Bilateral ulnar motor DL prolonged and in demyelinating range Right ulnar F responses 37.35 ms. On 11-Jun-2021, Electromyogram: normal (normal) EMG/NCS of lower extremities at facility: Bilateral peroneal and tibial motor responses normal Peroneal F responses 57.35. 57.35 Tibial F responses 52.07, 55.31 H reflexes 35, 35 MRI cervical spine WO 5/26/21: Small central disc herniation C3-4 and C4-5 Moderate to marked right C5 nerve root compression Normal cord signal. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medication reported. On 01 Feb 2021 patient went for C-reactive protein test with unknown results. Additional information added was that the patient was on Immunoglobulin therapy. Last week of May, patient physical condition dramatically deteriorated. Needed assistance to dress. Constant stiff neck, aching in legs with standing. Medrol pack started June 3rd - after patient felt immediately better. Symptoms increased again slowly since stopping it. June 2021: EMG/NCS consistent with demyelinating neuropathy June 30th: started IVIG, gradual improvement, no worsening since IVIG Company comment This case concerns a 67 year old male with history of high cholesterol who experienced serious unexpected event of demyelinating polyneuropathy 17 days after the first dose of the Moderna Covid 19 vaccine. Rechallenge was unknown. The benefit-risk relationship is not affected by this report.							
	This spontaneous case was reported by a consumer and describes the occurrence of PARAESTHESIA (second day after the numbness became bigger it became a tingling, and became hard, several times went to emergency), HYPOAESTHESIA (sensation in the face/hyposensitivity of the lower extremities/the second day after the numbness became bigger), PAIN (symptoms got worst and painful/was in pain and the pain got worse), CONDITION AGGRAVATED (numbness became bigger it became a tingling, and became hard, several times went to emergency), AUTOIMMUNE DISORDER (Its an autoimmune and the symptoms are still ongoing), MUSCLE TIGHTNESS	Chronic small lesions 13 by 7 by 5 mm. The lesion was located at P and eleven.5th MRA of the head --> another lesion in the PONS (part of the brain). a lesion in the amygdala	Not a case of ADEM	Level 4	Level 2	Conditional	This is a spontaneous report of a 35-year-old male patient with past medical history included nicotine dependence (seven pack-years, suspended since 2018), and concurrent medical conditions included nerve compression and allergies.; who received the second dose of Spikevax and on an unknown date, reported at various times, numbness, Muscle spasms, tightness, weakness, and pain in the lower limbs, Arthralgia, Asthenia, Ataxia, Autoimmune disorder, Back pain, cranial nerve disorder, Depression, Discomfort, unspecified	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	(tightness in leg), MUSCLE SPASMS (muscle spasm in leg/The patient also said that the leg problem got worst), MYELITIS TRANSVERSE (transverse myelitis), ENCEPHALOMYELITIS (encephalomyelitis), MULTIPLE SCLEROSIS (multiple sclerosis), ATAXIA (On both sides, right leg ataxia, progressive for 6 weeks), ANAEMIA FOLATE DEFICIENCY (slight macrocytic anemia/folic acid deficiency), CENTRAL NERVOUS SYSTEM LESION (The lesion its a chronic lesion,another small lesion of the same type,another lesion but this time in the amygdala/5th MRA of the head another lesion in the PONS (part of the brain)/3rd MRA was made in hospital lesion got bigger), DEPRESSION (Depressive episodes), GAIT DISTURBANCE (Difficult in gait movement), CRANIAL NERVE DISORDER (Intracranial lesion), ASTHENIA (reduction in strength of the bilateral hip flexion/slight reduction in strength of the bilateral hip flexion), INTERVERTEBRAL DISC PROTRUSION (medial disc protrusion/medial disc protrusion L5/S1), MUSCULAR WEAKNESS (Weakness in right leg), SPINAL CORD INJURY (Spinal cord lesion), TASTE DISORDER (Sensation of strange tase in mouth), VISION BLURRED (Blurred vision/Vision reduced), ANAMNESTIC REACTION (Anamnestic reaction), NEUROMYELITIS OPTICA SPECTRUM DISORDER (Neuromyelitis optica), SOMNOLENCE (Drowsiness), PAIN IN EXTREMITY (Pain in lower extremity), DISCOMFORT (Pressure in thoracic region that radiate to shoulder), HERNIA (1st MRA (magnetic resonance angiography) small hernia on the disc in the right leg), PYREXIA (fever), NAUSEA (Nausea) and NERVOUS SYSTEM DISORDER (Inflammatory CNS disease) in a 35-year-old male patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included Nicotine dependence (seven years back, suspended since 2018). Family history included Breast cancer (Mother had Breast cancer.). Concurrent medical conditions included Nerve compression, Allergy to animal dander (Cat epithelium), Allergy to animal dander (dog epithelium), Pollen allergy, Grass allergy (grass mixture) and Helicobacter gastritis since May 2021. On 16-Jun-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna) (unknown route) 1 dosage form. On 14-Jul-2021, received second dose of mRNA-1273 (COVID-19 Vaccine Moderna) (unknown route) dosage was changed to 1 dosage form. On 14-Jul-2021. the patient experienced					"Encephalomyelitis", Pain, Pain in extremity, Paraesthesia, Pyrexia, Sciatica, Sleep disorder, Somnolence, Spinal cord injury, Taste disorder, Vision blurred, Gait disturbance, Headache, Hernia, Hyperhidrosis, Hypoaesthesia, Inflammation, Intervertebral disc protrusion, Multiple sclerosis, Myelitis transverse, Nausea, Nerve compression, Nervous system disorder, Neuromyelitis optica spectrum disorder. There are incomplete descriptions of symptoms.		
							MRI: Chronic small lesions 13 by 7 by 5 mm. The lesion was located at P and eleven. 5th MRA of the head --> another lesion in the PONS (part of the brain). a lesion in the amygdala. 1st MRA: small hernia on the disc in the right leg.	
							Infectious diseases workup were all negative. (abnormal). MRI of the cervical and thoracic spine was performed, and an inflammatory lesion was found at the level of Th10 clinically corresponding to a picture of myelitis transversa . The patient was treated with oral corticosteroids and plasmapheresis.	
							According to Brighton's Collaboration case definition, this is NOT a case of ADEM, based on MRI findings of solitary lesions and inflammatory lesions. This case is considered WHO Conditional.	
							More information for proper assessment is needed.	

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	HYPERHIDROSIS (heavily sweating), BACK PAIN (pain in my back/Lumboradicular pain syndrome/pain in the lumbar musculature/Pain back) and HEADACHE (headache). In July 2021, the patient experienced PARAESTHESIA (second day after the numbness became bigger it became a tingling, and became hard, several times went to emergency) (seriousness criterion hospitalization), HYPOAESTHESIA (sensation in the face/hyposensitivity of the lower extremities/the second day after the numbness became bigger) (seriousness criterion hospitalization), PAIN (symptoms got worst and painful/was in pain and the pain got worse) (seriousness criterion hospitalization), CONDITION AGGRAVATED (numbness became bigger it became a tingling, and became hard, several times went to emergency) (seriousness criterion hospitalization) and NERVE COMPRESSION (disk problem or nerve compression). On 13-Aug-2021, the patient experienced MYELITIS TRANSVERSE (transverse myelitis) (seriousness criteria hospitalization and medically significant), ENCEPHALOMYELITIS (encephalomyelitis) (seriousness criteria hospitalization and medically significant) and NERVOUS SYSTEM DISORDER (Inflammatory CNS disease) (seriousness criterion hospitalization). In August 2021, the patient experienced ANAEMIA FOLATE DEFICIENCY (slight macrocytic anemia/folic acid deficiency) (seriousness criterion hospitalization). In September 2021, the patient experienced DEPRESSION (Depressive episodes) (seriousness criterion hospitalization). On an unknown date, the patient experienced AUTOIMMUNE DISORDER (Its an autoimmune and the symptoms are still ongoing) (seriousness criteria hospitalization and medically significant), MUSCLE TIGHTNESS (tightness in leg) (seriousness criterion hospitalization), MUSCLE SPASMS (muscle spasm in leg/The patient also said that the leg problem got worst) (seriousness criterion hospitalization), MULTIPLE SCLEROSIS (multiple sclerosis) (seriousness criteria hospitalization and medically significant), ATAXIA (On both sides, right leg ataxia, progressive for 6 weeks) (seriousness criterion hospitalization), CENTRAL NERVOUS SYSTEM LESION (The lesion its a chronic lesion,another small lesion of the same type,another lesion but this time in the amygdala/5th MRA of the head another lesion in the PONS (part of the brain)/3rd MRA was made in hospital lesion got bigger) (seriousness criterion hospitalization), GAIT DISTURBANCE (Difficult in gait movement) (seriousness criterion hospitalization), CRANIAL NERVE DISORDER (Intracranial lesion) (seriousness criterion hospitalization), ASTHENIA (reduction in strength of the bilateral hip flexion/slight reduction in strength of the bilateral hip flexion) (seriousness criterion hospitalization), INTERVERTEBRAL DISC PROTRUSION (medial disc protrusion/medial disc protrusion L5/S1)							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Caosality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(seriousness criterion hospitalization), MUSCULAR WEAKNESS (Weakness in right leg) (seriousness criterion hospitalization), SPINAL CORD INJURY (Spinal cord lesion) (seriousness criteria hospitalization and medically significant), TASTE DISORDER (Sensation of strange tase in mouth) (seriousness criterion hospitalization), VISION BLURRED (Blurred vision/Vision reduced) (seriousness criterion hospitalization), ANAMNESTIC REACTION (Anamnestic reaction) (seriousness criterion hospitalization), NEUROMYELITIS OPTICA SPECTRUM DISORDER (Neuromyelitis optica) (seriousness criteria hospitalization and medically significant), SOMNOLENCE (Drowsiness) (seriousness criterion hospitalization), PAIN IN EXTREMITY (Pain in lower extremity) (seriousness criterion hospitalization), DISCOMFORT (Pressure in thoracic region that radiate to shoulder) (seriousness criterion hospitalization), HERNIA (1st MRA (magnetic resonance angiography) small hernia on the disc in the right leg) (seriousness criterion hospitalization), PYREXIA (fever) (seriousness criterion hospitalization), NAUSEA (Nausea) (seriousness criterion hospitalization), SLEEP DISORDER (sometimes when is sleeping and wakes up around 2 to 5 feels like someone is watching me or/could not sleep), SCIATICA (Lumbar radicular pain syndrome), FEELING OF BODY TEMPERATURE CHANGE (I felt everything in the legs, it was constant,became bigger it/cold and hot feeling on the leg), INFLAMMATION (inflammation on the top of both foot) and ARTHRALGIA (Pain in joint in knees,ankles and wrist). The patient was hospitalized from 12-Aug-2021 to 25-Aug-2021 due to ANAEMIA FOLATE DEFICIENCY and ATAXIA, then from 12-Aug-2021 to 26-Aug-2021 due to MYELITIS TRANSVERSE, then from 03-Sep-2021 to 09-Sep-2021 due to CENTRAL NERVOUS SYSTEM LESION, DEPRESSION and NERVOUS SYSTEM DISORDER. The patient was treated with CORTISONE (intravenous) ongoing since an unknown date for Adverse event, at a dose of 2 days 1 gram, 3 days 2 grams; CORTISONE (oral) for Adverse event, at an unspecified dose and frequency; METHYLPREDNISOLONE SODIUM SUCCINATE (SOLUMEDROL) from 16-Aug-2021 to 18-Aug-2021 for Adverse event, at a dose of 1000 mg once a day; DEXLANSOPRAZOLE (DEXILANT) (oral) for Blister, at a dose of 60 mg; FOLIC ACID (oral) at a dose of 5 mg; METAMIZOLE SODIUM (NO							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 12-Oct-2021 and was forwarded to Moderna on 12-Oct-2021. This regulatory authority case was reported by a health care professional and describes the occurrence of BONE MARROW OEDEMA (Bone marrow oedema), DEMYELINATING	Marrow edema in the left T6 facet and transverse process (GBS)	Level 5	Level 5	Level 5	Unlikely	This is a case reported by a regulatory authority concerning a 61-year-old female with a past medical history included GERD, fatty liver, and immunoglobulin therapy, concurrent medical conditions included drug allergy (Methadone, trazodone), Anxiety, Depression, Schizoaffective disorder, and Guillain-Barre svndrome (acute inflammatory	

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	POLYNEUROPATHY (Demyelinating polyneuropathy), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), VERTEBRAL LESION (Vertebral lesion) and MUSCULAR WEAKNESS (Muscular weakness) in a 61-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 038B21A) for COVID-19 vaccination. The patient's past medical history included GERD, Fatty liver and Immunoglobulin therapy on 19-Apr-2021. Concurrent medical conditions included Drug allergy (Methadone), Drug allergy (Trazodone), Anxiety, Depression, Schizoaffective disorder and Guillain-Barre syndrome (acute inflammatory demyelinating polyradiculoneuropathy). Concomitant products included BREXPIRAZOLE (REXULTI) and PALIPERIDONE (INVEGA [PALIPERIDONE]) for an unknown indication. On 15-Apr-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On an unknown date, the patient received dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) at an unspecified dose. On 19-Apr-2021, the patient experienced BONE MARROW OEDEMA (Bone marrow oedema) (seriousness criteria hospitalization, disability and life threatening), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization, disability, medically significant and life threatening), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criteria hospitalization, disability, medically significant and life threatening) and VERTEBRAL LESION (Vertebral lesion) (seriousness criteria hospitalization, disability and life threatening). 19-Apr-2021, the patient experienced MUSCULAR WEAKNESS (Muscular weakness) (seriousness criteria hospitalization, disability and life threatening). The patient was hospitalized from 20-Apr-2021 to 08-May-2021 due to BONE MARROW OEDEMA, DEMYELINATING POLYNEUROPATHY, GUILLAIN-BARRE SYNDROME, MUSCULAR WEAKNESS and VERTEBRAL LESION. The patient was treated with IMMUNOGLOBULIN HUMAN NORMAL (IVIGLOB-EX) at an unspecified dose and frequency. At the time of the report, BONE MARROW OEDEMA (Bone marrow oedema), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), VERTEBRAL LESION (Vertebral lesion) and MUSCULAR WEAKNESS (Muscular weakness) had resolved.					demyelinating polyradiculoneuropathy) and concomitant medications included rexulti and paliperidone; who received the second dose of Spikevax and 4 days later reported Progressive lower extremity weakness, vertebral lesion, HCP described symptoms of GBS. Diagnostic reports included: CSF WBC count: increased, neutrophilia (greater than3000 CSF Culture: negative. Electromyogram: abnormal. Evidence of a length-dependent acquired demyelinating polyneuropathy with secondary axon loss which, given the patient's clinical history, is consistent with acute inflammatory demyelinating polyradiculoneuropathy (ie Guillain-Barre syndrome).. MR spinal: abnormal. Marrow edema in the left T6 facet and transverse process, 8 mm rounded lesion in the right lateral aspect of the central canal at T5. The patient recovered from the event. This case with concurrent GBS does not meet the case definition for ADEM. Hence, it is classified as ADEM level of certainty 5, and considered WHO Unlikely. The presence of cofounder, concurrent GBS, provides plausible explanations.		

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 19-Apr-2021, Blood glucose: decreased (Low) decreased. On 19-Apr-2021, CSF white blood cell count: increased (High) increased,LP- greater than3000 WBC predominantly neutrophils.. On 19-Apr-2021, Culture: negative (Negative) Negative. On 19-Apr-2021, Electromyogram: abnormal (abnormal) This study shows evidence of a length dependent acquired demyelinating polyneuropathy with secondary axon loss which, given the patient's clinical history, is consistent with acute inflammatory demyelinating polyradiculoneuropathy (ie Guillain-Barre syndrome).. On 19-Apr-2021, Lumbar puncture: abnormal (abnormal) abnormal. On 19-Apr-2021, Magnetic resonance imaging spinal: abnormal (abnormal) 1. Marrow edema in the left T6 facet and transverse process is of an unclear etiology. Further evaluation with bone scan and CT of the thoracic spine is recommended. 2. 8 mm rounded lesion in the right lateral aspect of the central canal at T5 is of an unclear etiology. It may represent a meningioma. Correlation with contrast enhanced MRI of the thoracic spine is recommended. 3. No fracture or joint dislocation is seen. 4. No significant central canal or neural foraminal stenosis.. On 19-Apr-2021, Protein total: increased (High) increased. For mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular), the reporter did not provide any causality assessments. Patient developed GBS- lumbar puncture proven- 4 days.Progressive lower extremity weakness requiring hospitalization. Hospitalized from 4/20/21-5/8/21 Company Comment: This case concerns a 61-year-old female subject, with no reported relevant medical history, who experienced the unexpected serious events of GUILLAIN-BARRE SYNDROME (AESI), DEMYELINATING POLYNEUROPATHY, BONE MARROW OEDEMA, VERTEBRAL LESION and MUSCULAR WEAKNESS. The events occurred 5 days after the administration of the second dose of Moderna COVID-19 Vaccine. The rechallenge was not applicable as no additional dosing will be given. The benefit-risk relationship of Moderna COVID-19 Vaccine is not affected by this report.							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 14-Oct-2021 and was forwarded to Moderna on 14-Oct-2021. This regulatory authority case was reported by a physician and describes the occurrence of ENCEPHALITIS (ENCEPHALITIS), HEADACHE (HEADACHE), FATIGUE (FATIGUE), EAR PAIN (EARACHE), PYREXIA (SUBJECTIVE FEVER) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (ACUTE DISSEMINATED ENCEPHALOMYELITIS) in a 57-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3002546) for Vaccination. The patient's past medical history included Meningitis (As a child.) and DVT (1997: DVT related to pregnancy. 2013: DVT related to knee injury.) in 2013. Concurrent medical conditions included Non-celiac gluten sensitivity, Genital herpes (Uses aciclovir (Zovirax) prophylactic during periods of stress.) and Osteopenia. Concomitant products included CALCIUM CARBONATE, COLECALCIFEROL (CALCIGRAN FORTE) for Osteopenia, CHLORTALIDONE (HIPREX [CHLORTALIDONE]) for Recurrent UTI. On 10-Jun-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. On 23-Jul-2021, the patient experienced ENCEPHALITIS (ENCEPHALITIS) (seriousness criteria hospitalization and medically significant), HEADACHE (HEADACHE) (seriousness criterion hospitalization), FATIGUE (FATIGUE) (seriousness criterion hospitalization), EAR PAIN (EARACHE) (seriousness criterion hospitalization), PYREXIA (SUBJECTIVE FEVER) (seriousness criterion hospitalization) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (ACUTE DISSEMINATED ENCEPHALOMYELITIS) (seriousness criteria hospitalization and medically significant). At the time of the report, ENCEPHALITIS (ENCEPHALITIS), FATIGUE (FATIGUE) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (ACUTE DISSEMINATED ENCEPHALOMYELITIS) was resolving and HEADACHE (HEADACHE), EAR PAIN (EARACHE) and PYREXIA (SUBJECTIVE FEVER) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): In July 2021, Coma scale: 11 (abnormal) 11 (score when admitted to hospital). In July 2021, Investigation: thrombosis (abnormal)	Symmetrically widespread high-signal changes in deep gray matter as well as in white matter (periventricular and parietooccipital). Findings compatible with ADEM	Level 2	Level 5	Level 5	Possible	This is a regulatory authority report concerning a 57-year-old female patient with a past medical history included meningitis (as a child.) and deep vein thrombosis (DVT), relevant concurrent medical conditions included genital herpes; concomitant medications included calcium supplements and chlortalidone; who received the first dose of Spikevax and 43 days later reported prodromal symptoms of headache, fatigue, ear pain, fever and pain in left groin and unspecified 'encephalitis' symptoms. Coma scale: 11 (score when admitted to hospital). . Diagnostic reports: CSF: Elevated protein levels and CSF albumin index (no pleocytosis). MRI head: abnormal, symmetrically widespread high-signal changes in deep gray matter as well as in white matter (periventricular and parietooccipital). Findings were compatible with acute disseminated encephalomyelitis. Examination revealed findings compatible with thrombosis in the left lower back (third occurrence). Other diagnostic tests with regard to underlying etiology, neuronal antibodies, and antibodies related to autoimmune encephalitis were negative. 4 weeks later, the repeat MRI head was normal with total regression of radiological findings. This case of ADEM with associated DVT is confounded by genital herpes, which is associated with HSV type 2, which can cause encephalomyelitis. This case is classified as ADEM level 2 diagnostic certainty, and considered WHO Possible due to temporal association, and event could also be explained by the confounding genital herpes, which can cause encephalomyelitis.	

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	thrombosis in left lower back. In July 2021, Lumbar puncture: significant reduction in protein level. (abnormal) Control measurement 5 days into the disease course. Findings: significant reduction in protein level. and elevated protein levels (abnormal) Elevated protein levels and CSF albumin index (no pleocytosis).. In July 2021, Magnetic resonance imaging head: acute disseminated encephalomyelitis (abnormal) Symmetrically widespread high-signal changes in deep gray matter as well as in white matter (periventricular and parietooccipital). Findings compatible with ACUTE DISSEMINATED ENCEPHALOMYELITIS.. In August 2021, Magnetic resonance imaging head: normal (normal) Control measurement after 4 weeks. Result: total regression of radiological findings.. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the reporter considered ENCEPHALITIS (ENCEPHALITIS), HEADACHE (HEADACHE), FATIGUE (FATIGUE), EAR PAIN (EARACHE), PYREXIA (SUBJECTIVE FEVER) and ACUTE DISSEMINATED ENCEPHALOMYELITIS (ACUTE DISSEMINATED ENCEPHALOMYELITIS) to be possibly related. The patient was broadly examined with regard to underlying etiology, without significant findings CTA caput / collum without signs of vasculitis, CT full body without signs of malignancy, rheumatological tests, neuronal antibodies and antibodies related to Autoimmune encephalitis without significant findings, negative thrombophilia tests. Due to pain in left groin, examination was performed that revealed findings compatible with thrombosis in left lower back (third time this occurs in the patient). On Jul 2021 CT of Head was also done and had no significant findings. The concomitant drug Calcigran Forte contains A12AX-calcium combinations with vitamin D and other remedies No treatment information were provided. Company Comment: This case concerns a 57-year-old female patient, with relevant medical history of meningitis and deep vein thrombosis, who experienced the serious unexpected AESIs of ENCEPHALITIS and ACUTE DISSEMINATED ENCEPHALOMYELITIS and the non-serious unexpected AESI of THROMBOSIS. The events							

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	occurred approximately 1 months and 17 days after receiving the first dose of Spikevax. The rechallenge is not applicable since no information about the second dose is available. Findings in magnetic resonance imaging of the head were compatible with acute disseminated encephalomyelitis, and lumbar puncture showed elevated protein levels and CSF albumin index. It was also reported that examination revealed findings compatible with thrombosis in left lower back. Patient's medical history of meningitis and deep vein thrombosis remain as confounders. The benefit-risk relation of Spikevax is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 14-Oct-2021: Translation received on 18 Oct 2021 contain significant information. Dosage form of vaccine updated additional information on concomitant medication Caligran forte updated.							
	This regulatory authority case was reported by a consumer and describes the occurrence of ENCEPHALOMYELITIS (Encephalomyelitis) in a 60-year-old female patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for COVID-19 immunisation. The patient's past medical history included Elevated liver enzymes in 2019, Urothelial carcinoma in 2011 and Oesophageal carcinoma in 2019. Concomitant medical conditions included Drug allergy (Allergic to Dafalgan (Paracetamol)). On 01-Jul-2021, the patient received second dose of mRNA-1273 (COVID-19 Vaccine Moderna) (unknown route) 1 dosage form. On 10-Aug-2021, after starting mRNA-1273 (COVID-19 Vaccine Moderna), the patient experienced ENCEPHALOMYELITIS (Encephalomyelitis) (seriousness criteria hospitalization and medically significant). At the time of the report, ENCEPHALOMYELITIS (Encephalomyelitis) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On an unknown date, Albumin CSF: 0.8340 (High) 0.8340. On an unknown date, Blood creatine: 184 (High) 184 µmol/L. On an unknown date, CSF cell count: 128 (High) 128. On an unknown date, CSF immunoglobulin: increased (High) Increased (Intrathecal IgG synthesis (HSV1 plus 2 IgG (Li/Se-index): 3.59). On an unknown date, Magnetic resonance imaging head: abnormal (abnormal) MRI of the neurocranium revealed suspected multiple	No report	Not a case of ADEM	Level 5	level 5	Unlikely	This is a case of a 60-year-old female patient with past medical history included elevated liver enzymes, concurrent medical conditions included urothelial carcinoma since 2011 and oesophageal carcinoma in 2019. No report of concomitant medications; who received an unknown dose of Spikevax and 40 days later reported 'experienced encephalomyelitis'. No symptoms were specified. No imaging report. CSF cell count increased (128), albumin increased: 0.8340, immunoglobulin increased. This case is missing detailed clinical history, Brain MRI not done or no results available. According to Brighton's Collaboration case definition for ADEM, this case is NOT a case of ADEM, since it meets the exclusion criterion for ADEM due to confirmed diagnoses of cancers. This case is confounded by the medical history of elevated liver enzymes and cancers. Liver disease can cause metabolic encephalopathy, while urothelial/bladder cancer has been reported to metastasize to the brain hematogenously, causing paraneoplastic encephalomyelitis and esophageal adenocarcinoma has been associated with limbic encephalitis. This case is considered WHO Unlikely. The carcinomas provide plausible explanations.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	supratentorial demyelinating foci with a single active demyelinating foci in the frontal medullary camp right adjacent to the right lateral ventricle. There was no evidence of leptomeningeal enhancement.. On an unknown date, Magnetic resonance imaging spinal: abnormal (abnormal) An MRI of the lumbar spine showed multiple enhancing intramedullary lesions of the entire spinal axis with punctum maximum in the conus medullaris.. No concomitant medications were reported. Treatment medications provided Acyclovir 500 mg td. The 60-year-old female patient (body weight: 45 kg) received the second dose of COVID- 19 Vaccine Moderna/Spikevax (Elasomeran intramuscularly on 01-Jul-2021 for immunization against Covid-19, Lot. no. unknown). On 10-Aug-2021, the patient developed encephalomyelitis. This was interpreted as most likely infectious due to VZV myeloradiculitis. Differential diagnosis, reactivation by Covid-19 vaccination was also discussed. Clinically, the patient showed distal paraparesis and, in the course, hypesthesias of both legs, as well as a bladder dysfunction. Laboratory tests revealed lymphocytic pleocytosis (128/ml), moderate barrier disruption (0.8340 g/L albumin), and intrathecal IgG synthesis (HSV1 plus 2 IgG (Li/Se index): 3.59) in the CSF. Therapy was given with acyclovir 500 mg i.v. 1-1-1 for suspected VZV encephalomyelitis. At the time of the report, the patient had not recovered. It was not possible to obtain a medical history of any tobacco or alcohol consumption. Likewise, no kidney disease was known. The creatinine level was 184 µmol/L. Other relevant pre-existing conditions included liver enzyme elevation of unclear etiology since 2019. In addition, there was status post urothelial carcinoma in 2011 and esophageal carcinoma in 2019. Company Comment:This case concerns a 60 year-old, female patient with a history of Oesophageal carcinoma and Transitional cell carcinoma, who experienced the serious unexpected AESI event of Encephalomyelitis. The event occurred approximately 1 month and 10 days after the second dose of Moderna COVID-19 vaccine. The rechallenge was not applicable, as the event was reported exclusively after the second dose. The medical history, of Oesophageal carcinoma and Transitional cell carcinoma, remain as confounders. The benefit-risk relationship of Moderna COVID-19 vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 20-Oct-2021: Translation received on 22-Oct-							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	2021, lab data and innarrative updated.							
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED] on 15-Oct-2021 and was forwarded to Moderna on 22-Oct-2021. The license partner had received the report from [REDACTED] (Reference number: [REDACTED]). This case, initially reported to the [REDACTED] by a pharmacist, was received via the [REDACTED] (Ref, [REDACTED]). For the past year, the patient had sometimes experienced bilateral scleritis and received repeated eye-drop treatments with betamethasone sodium phosphate at the department of ophthalmology. On an unknown date, the patient received the 1st dose of the vaccine. On 10-Aug-2021, the patient received the 2nd dose of the vaccine. On 12-Aug-2021, the patient experienced pyrexia of 37.8 degrees Celsius. On 13-Aug-2021, pain in the left eye developed, and the patient visited an ophthalmologist. The visual acuity of the left eye was 1.2 with scleral hemorrhage in the left eye. No pain with eye movement was noted. CFF was slightly decreased, and left papilledema was noted. On 21-Aug-2021, at revisit, scleral congestion of the left eye had improved. On 23-Aug-2021, after waking up, the patient was aware of poor vision of the left eye. On 24-Aug-2021, the patient made a referral visit to the department of ophthalmology of another hospital for suspected optic neuritis. Contrast-enhanced head MRI was performed and showed suspected acute disseminated encephalomyelitis. On 26-Aug-2021, the patient visited a department of neurology and was hospitalized for detailed examinations and treatments. On 30-Aug-2021, spinal cord MRI showed multiple cerebral lesions and spinal cord lesion at the level of Th5. The patient had reduced visual acuity of the left eye and pain with eye movement. On 31-Aug-2021, steroid pulse therapy was started. On 02-Sep-2021, steroid pulse therapy was completed.	MRI head - suspected lesions of ADEM. MRI spine showed multiple cerebral lesions and spinal cord lesion at the level of Th5	Level 2	Level 3	Level 5	Possible	This case from regulatory authority is about a 52-year-old male patient with a medical history of bilateral scleritis and concomitant medication included betamethasone sodium phosphate eye drops; who received the second dose of Spikevax and 2 days later reported fever, day 3 reported pain in the left eye with scleral hemorrhage and left papilloedema, day 13 - poor vision left eye, day 14 - dx-optic neuritis, contrast-enhanced MRI head, - suspected acute disseminated encephalomyelitis. Day 20 - MRI spine showed multiple cerebral lesions and spinal cord lesion at the level of Th5. Treated with steroid and event resolving. Day 26 - repeat contrast-enhanced MRI : contrast effect disappeared in many areas, but some new lesions appeared. According to Brighton's Collaboration case definition, this case is classified as ADEM level of certainty 2, due to the presence of multiple cerebral lesions and spinal cord lesion; and considered WHO Possible, due to temporal relationship; but the event could also be explained by the concurrent optic scleritis.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On 06-Sep-2021, repeated contrast-enhanced MRI was performed. Contrast effect disappeared in many areas, but some new lesions appeared. On 10-Sep-2021, the visual acuity of the left eye improved from 0.6 to 0.9. On 15-Sep-2021, the 2nd course of the steroid pulse therapy was started. On 17-Sep-2021, the 2nd course of the steroid pulse therapy was completed. On 18-Sep-2021, oral administration of prednisolone 25 mg was started. On 24-Sep-2021, the patient was discharged from the hospital. As the symptoms had not resolved, the patient was to make outpatient visits hereafter. The outcome of scleral hemorrhage in the left eye was reported as resolving. The outcome of pyrexia, pain in the left eye, left papilledema, poor vision of the left eye, suspected optic neuritis, suspected acute disseminated encephalomyelitis, multiple cerebral lesions, spinal cord lesion at the level of Th5, reduced visual acuity of the left eye, and pain with eye movement was reported as ongoing and unchanged. Follow-up investigation will be made. Company Comment: The events developed after the administration of COVID-19 vaccine mRNA (mRNA 1273) and there is temporal relationship. Clinical symptoms: - Inflammatory demyelination is assumed to be the cause. - These are the first events with or without prior administration of this vaccine. - The events are clinically multifocal central nervous system (CNS) disorders (events). Localized or multiple findings attributable to the CNS (date of onset: 13-Aug-2021).							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	- Single or multiple cerebral nerve abnormalities, Single or multiple visual field defects, changes in deep tendon reflexes, and cerebellar dysfunction. Imaging test: MRI (date of inspection: 25-Aug-2021): - Diffuse or multiple white matter lesions were found on T2-weighted/diffusion-weighted imaging (DWI) or FLAIR images.							
	This regulatory authority case was reported by a pharmacist and describes the occurrence of HYPOAESTHESIA (Numbness of limbs), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), PAIN IN EXTREMITY (soreness and pain in both feet) and DEMYELINATING POLYNEUROPATHY (acute inflammatory demyelinating polyneuropathy) in a 40-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. No Medical History information was reported. On 08-Jul-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 19-Jul-2021, the patient experienced HYPOAESTHESIA (Numbness of limbs) (seriousness criterion hospitalization) and PAIN IN EXTREMITY (soreness and pain in both feet) (seriousness criterion hospitalization). On 12-Oct-2021, the patient experienced DEMYELINATING POLYNEUROPATHY (acute inflammatory demyelinating polyneuropathy) (seriousness criteria hospitalization and medically significant). On 13-Oct-2021, the patient experienced GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criteria hospitalization and medically significant). The patient was treated with TOCOPHERYL NICOTINATE (JUVELA N) on 19-Jul-2021 for Adverse event, at a dose of 200 mg; PREDNISOLONE (COMPESOLON) on 14-Aug-2021 for Adverse event, at a dose of 5 mg and HYDROXYCHLOROQUINE SULFATE (PLAQUENIL S) on 14-Aug-2021 for Adverse event, at a dose of 200 mg. At the time of the report, HYPOAESTHESIA (Numbness of limbs), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), PAIN IN EXTREMITY (soreness and pain in both feet) and DEMYELINATING POLYNEUROPATHY (acute inflammatory demyelinating polyneuropathy) outcome was unknown. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available):	Abnormal. Specific findings not described. Diagnosed with Guillain-Barre syndrome.	Level 4	Level 5	Level 4	Conditional	This case reported by a regulatory authority concerns a 40-year-old female, with no reported medical history and concomitant medications; who received the first dose of Spikevax and 11 days later reported " pain in extremity, numbness of limbs, weakness of both lower limbs, with tingling sensation, and muscle strength of scale 4. Day 66, reported unspecified symptoms describing demyelinating polyneuropathy, and Guillain-Barre syndrome. Diagnostic reports: MRI, CSF, electroneurography, all abnormal, but details not provided. Diagnosed with GBS. This case has insufficient information, it is classified as ADEM Level of certainty 4 and considered WHO Conditional. More data for proper assessment needed.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On an unknown date, Electroneurography: abnormal (abnormal) Diagnosed with Guillain-Barre syndrome. On an unknown date, Lumbar puncture: abnormal (abnormal) Diagnosed with Guillain-Barre syndrome. On an unknown date, Magnetic resonance imaging: abnormal (abnormal) Diagnosed with Guillain-Barre syndrome. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Concomitant product use was not provided by the reporter. Patient was found that both lower limbs were weak combined with tingling sensation, and the muscle strength of both lower limbs was scale 4. Company Comment This case concerns a 40-year-old female patient with no reported medical history who experienced the unexpected events of hypoesthesia, Guillain-Barre syndrome, Pain in the extremity, and demyelinating polyneuropathy. Pain in the extremity occurred 11 days after the first dose of mRNA-1273 (Moderna COVID-19 Vaccine and the other events occurred on an unspecified date later. The rechallenge was no details about a second dose was disclosed. Causality for the reported events was not provided by the reporter. The benefit-risk relationship of mRNA-1273 (Moderna COVID-19 Vaccine) is not affected by this report. The events were assessed as serious (hospitalization) per regulatory reporting. Guillain-Barre syndrome is an adverse event of special interest.							
	This case was received via [REDACTED] (Reference number: [REDACTED] on 02-Nov-2021 and was forwarded to Moderna on 02-Nov-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of AUTONOMIC NEUROPATHY (Autonomic neuropathy), IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy), ABDOMINAL PAIN UPPER (Abdominal pain upper), ANHIDROSIS (Anhidrosis), ARTHRALGIA (Arthralgia/ Joint pain), ASTHENIA (Asthenia/ Weakness), BURNING SENSATION (Burning sensation), CHEST PAIN (Chest pain/ Chest spasms), DECREASED APPETITE (Decreased appetite), ELECTRIC SHOCK SENSATION (Electric shock sensation), FRUSTRATION TOLERANCE DECREASED (Frustration tolerance decreased), GAIT DISTURBANCE (Gait disturbance),	Not provided	Level 5	Level 5	Level 4	Conditional	This case was reported by a regulatory authority concerned a 39-year-old female patient with a history of ventricular extrasystoles, vertigo, drug hypersensitivity, vitamin D deficiency, on vitamin D3, who received the first dose of Spikevax and from day 0 through day 9 reported "progressive experience muscular weakness, autonomic neuropathy, immune-mediated neuropathy, anhidrosis, arthralgia, gait disturbance, postural orthostatic tachycardia syndrome, hypoaesthesia, involuntary muscle contractions, paresthesia, urinary incontinence, petechiae, and tremor. No encephalopathy symptoms were reported. Diagnostic tests - MRI brain and CSF results were not reported. This case is classified as Brighton's level 5, NOT a case of ADEM,	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	HYPOAESTHESIA (Hypoaesthesia), IMPAIRED WORK ABILITY (Impaired work ability), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities), MUSCLE CONTRACTIONS INVOLUNTARY (Muscle contractions involuntary), MUSCLE SPASMS (Muscle spasms), MUSCLE TWITCHING (Muscle twitching), NASAL DISCOMFORT (Nasal discomfort), NERVE INJURY (Nerve injury), PARAESTHESIA (Paraesthesia), PETECHIAE (Petechiae on arms, legs and stomach), POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (Postural orthostatic tachycardia syndrome), SKIN BURNING SENSATION (Skin burning sensation/ Burning under skin), SMALL FIBRE NEUROPATHY (Small fibre neuropathy), TONGUE DISCOMFORT (Tongue discomfort), TREMOR (Tremor/ Internal tremors), URINARY INCONTINENCE (Urinary incontinence), NAUSEA (Nausea), FATIGUE (Fatigue), HEADACHE (Headache) and PAIN (Pain) in a 39-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 002B21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient's past medical history included Premature ventricular contractions (PVCs with occasional SVT.), Vertigo (Occasional vertigo from inner ear weakness) and Vitamin D low (Low side of normal vitamin D levels). Concurrent medical conditions included Penicillin allergy and Drug allergy (Allergy to Sulphur antibiotics.). Concomitant products included COLECALCIFEROL (VITAMIN D 3) for an unknown indication. On 10-Mar-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 10-Mar-2021, the patient experienced AUTONOMIC NEUROPATHY (Autonomic neuropathy) (seriousness criteria disability and medically significant), IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy) (seriousness criteria disability and medically significant), ANHIDROSIS (Anhidrosis) (seriousness criterion disability), BURNING SENSATION (Burning sensation) (seriousness criterion disability), FRUSTRATION TOLERANCE DECREASED (Frustration tolerance decreased) (seriousness criterion disability), GAIT DISTURBANCE (Gait disturbance) (seriousness criterion disability), HYPOAESTHESIA (Hypoaesthesia) (seriousness criterion disability), IMPAIRED WORK ABILITY (Impaired work ability) (seriousness criterion disability), LOSS OF					but rather transverse myelitis; This case is a Brighton's level 4 Myelitis based on limb weakness with upper motor neuron damage, autonomic and sensory dysfunction, but has insufficient evidence to meet levels 1, 2, or 3 of the case definition. This case is considered WHO-UMC Conditional. More data for proper assessment is needed. The medical history of ventricular extrasystoles, vertigo and decreased vitamin D are confounders for neuropathy and postural orthostatic tachycardia syndrome; and provide plausible explanations.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities) (seriousness criterion disability), MUSCLE CONTRACTIONS INVOLUNTARY (Muscle contractions involuntary) (seriousness criterion disability), NASAL DISCOMFORT (Nasal discomfort) (seriousness criterion disability), NERVE INJURY (Nerve injury) (seriousness criterion disability), POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (Postural orthostatic tachycardia syndrome) (seriousness criterion disability), SMALL FIBRE NEUROPATHY (Small fibre neuropathy) (seriousness criterion disability), TONGUE DISCOMFORT (Tongue discomfort) (seriousness criterion disability) and PAIN (Pain) (seriousness criterion disability). 10-Mar-2021, the patient experienced PRODUCT DOSE OMISSION ISSUE (Missed dose). On 11-Mar-2021, the patient experienced FATIGUE (Fatigue) (seriousness criterion disability). On 12-Mar-2021, the patient experienced ABDOMINAL PAIN UPPER (Abdominal pain upper) (seriousness criterion disability), ARTHRALGIA (Arthralgia/ Joint pain) (seriousness criterion disability), ASTHENIA (Asthenia/ Weakness) (seriousness criterion disability), DECREASED APPETITE (Decreased appetite) (seriousness criterion disability) and NAUSEA (Nausea) (seriousness criterion disability). On 13-Mar-2021, the patient experienced HEADACHE (Headache) (seriousness criterion disability). On 16-Mar-2021, the patient experienced ELECTRIC SHOCK SENSATION (Electric shock sensation) (seriousness criterion disability), MUSCLE TWITCHING (Muscle twitching) (seriousness criterion disability) and PARAESTHESIA (Paraesthesia) (seriousness criterion disability). 16-Mar-2021, the patient experienced MUSCLE SPASMS (Muscle spasms) (seriousness criterion disability), SKIN BURNING SENSATION (Skin burning sensation/ Burning under skin) (seriousness criterion disability) and TREMOR (Tremor/ Internal tremors) (seriousness criterion disability). On 17-Mar-2021, the patient experienced CHEST PAIN (Chest pain/ Chest spasms) (seriousness criterion disability). On 18-Mar-2021, the patient experienced URINARY INCONTINENCE (Urinary incontinence) (seriousness criterion disability). On 24-Apr-2021, the patient experienced PETECHIAE (Petechiae on arms, legs and stomach) (seriousness criterion disability). On 10-Mar-2021, PRODUCT DOSE OMISSION ISSUE (Missed dose) had resolved. At the time of the report, AUTONOMIC NEUROPATHY (Autonomic neuropathy), IMMUNE-MEDIATED NEUROPATHY (Immune-mediated neuropathy), ABDOMINAL PAIN UPPER (Abdominal pain upper), ANHIDROSIS (Anhidrosis), ARTHRALGIA (Arthralgia/ Joint pain), ASTHENIA (Asthenia/ Weakness), BURNING SENSATION (Burning sensation), CHEST PAIN (Chest pain/ Chest spasms),							

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	DECREASED APPETITE (Decreased appetite), ELECTRIC SHOCK SENSATION (Electric shock sensation), FRUSTRATION TOLERANCE DECREASED (Frustration tolerance decreased), GAIT DISTURBANCE (Gait disturbance), HYPOAESTHESIA (Hypoaesthesia), IMPAIRED WORK ABILITY (Impaired work ability), LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES (Loss of personal independence in daily activities), MUSCLE CONTRACTIONS INVOLUNTARY (Muscle contractions involuntary), MUSCLE SPASMS (Muscle spasms), MUSCLE TWITCHING (Muscle twitching), NASAL DISCOMFORT (Nasal discomfort), NERVE INJURY (Nerve injury), PARAESTHESIA (Paraesthesia), PETECHIAE (Petechiae on arms, legs and stomach), POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (Postural orthostatic tachycardia syndrome), SKIN BURNING SENSATION (Skin burning sensation/ Burning under skin), SMALL FIBRE NEUROPATHY (Small fibre neuropathy), TONGUE DISCOMFORT (Tongue discomfort), TREMOR (Tremor/ Internal tremors), URINARY INCONTINENCE (Urinary incontinence), NAUSEA (Nausea), FATIGUE (Fatigue), HEADACHE (Headache) and PAIN (Pain) had not resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 10-Mar-2021, Alpha tumour necrosis factor: increased (High) Increased. On 10-Mar-2021, Blood pressure measurement: increased (High) Increased. On 10-Mar-2021, C-reactive protein: increased (High) Increased. On 10-Mar-2021, Heart rate: increased (High) Increased. On 10-Mar-2021, Interleukin level: increased (High) Increased. On 10-Mar-2021, Quantitative sudomotor axon reflex test: abnormal (abnormal) Abnormal. On 10-Mar-2021, Tilt table test: positive (Positive) Positive. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Patient had spikes in heart rate and blood pressure even at rest. From 01-May-2021, Patient has increased burning, aching, pinching, stinging, throbbing, numbness and tingling. Patient feels a little better as of 20-Oct-2021 but							

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	symptoms reappear strong at unexpected times. Patient is able to walk for short distances and sometimes have severe pain and weakness. Patient tried walking short distance more and it ended up worsening the symptoms and was in bed for days again. Patient was tried to be treated with a high dose of steroid taper and patient was not able to tolerate. Company com							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 02-Nov-2021 and was forwarded to Moderna on 02-Nov-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of ASTHENIA (Asthenia), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), DIPLOPIA (Diplopia), EYELID PTOSIS (Eyelid ptosis), GAIT INABILITY (Gait inability), LIMB DISCOMFORT (Limb discomfort), PARAESTHESIA (Paraesthesia) and FACIAL PARALYSIS (Facial paralysis) in a 71-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for COVID-19 vaccination. Concurrent medical conditions included BPH, Hypertension, Hyperlipidemia and Allergy. Concomitant products included AMLODIPINE, BENAZEPRIL, ATORVASTATIN and COLECALCIFEROL (VITAMIN D [COLECALCIFEROL]) for an unknown indication. On 29-Jan-2021, the patient received dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 02-Feb-2021, the patient experienced ASTHENIA (Asthenia) (seriousness criterion hospitalization), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization and medically significant), DIPLOPIA (Diplopia) (seriousness criterion hospitalization), EYELID PTOSIS (Eyelid ptosis) (seriousness criterion hospitalization), GAIT INABILITY (Gait inability) (seriousness criterion hospitalization), LIMB DISCOMFORT (Limb discomfort) (seriousness criterion hospitalization), PARAESTHESIA (Paraesthesia) (seriousness criterion hospitalization) and FACIAL PARALYSIS (Facial paralysis) (seriousness criteria hospitalization and medically significant). At the time of the report, ASTHENIA (Asthenia), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), DIPLOPIA (Diplopia), EYELID PTOSIS (Eyelid ptosis), GAIT INABILITY (Gait inability), LIMB DISCOMFORT (Limb discomfort), PARAESTHESIA	MRI brain: normal.	Level 5	Level 5	Level 4	Conditional	This is a case reported by a regulatory authority concerning a 71-year-old male patient with concurrent medical conditions included benign prostatic hypertrophy (BPH), Hypertension, Hyperlipidemia and Allergy, and concomitant medications included AMLODIPINE, BENAZEPRIL, ATORVASTATIN and COLECALCIFEROL (VITAMIN D [COLECALCIFEROL]), who received an unknown dose of Spikevax and 4 days later reported "Asthenia, Demyelinating polyneuropathy, Diplopia, Eyelid ptosis, Facial paralysis, Gait inability, Limb discomfort, and Paraesthesia" No encephalopathy symptoms reported. Diagnostic results: Blood creatine phosphokinase: Increased. Electromyogram: abnormal (confirmed demyelinating Neuropathy), MRI head: normal. This case is classified as Brighton's level 5, NOT a case of ADEM. This case is a Brighton's level 4 Myelitis based on Demyelinating polyneuropathy but has insufficient evidence to meet levels 1, 2, or 3 of the case definition. This case is considered WHO-UMC Conditional. More data for proper assessment is needed. The concurrent medical conditions of benign prostatic hypertrophy (BPH), Hypertension, Hyperlipidemia, and concomitant medications of antihypertensives (amlodipine) and statins (atorvastatin) are confounders and provide plausible explanations to the occurrence of these events.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Paraesthesia) and FACIAL PARALYSIS (Facial paralysis) had resolved. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 02-Apr-2021, Blood creatine phosphokinase: increased (High) Increased. On 02-Apr-2021, Electromyogram: abnormal (abnormal) confirmed demyelinating Neuropathy. On 02-Apr-2021, Laboratory test: abnormal (abnormal) abnormal. On 02-Apr-2021, Magnetic resonance imaging head: normal (normal) MRI brain done on 2/4/21 at hospital was negative. The action taken with mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Treatment details includes: Started on IVIG with slow resolution of symptoms. Company Comment: This case concerns a 71-year-old, male patient with relevant medical history of ██████ exposure, Hypertension, Hyperlipidemia and Allergy, who experienced the unexpected serious events of Demyelinating polyneuropathy, Asthenia, Diplopia, Eyelid ptosis, Limb discomfort and Paraesthesia; and the expected serious event of Facial paralysis. The events occurred approximately 4 days after a dose of Moderna Covid-19 Vaccine which resulted in Hospitalization. The rechallenge was unknown since no information about another dose was disclosed. The patient's medical history of Agent orange exposure, Hypertension, Hyperlipidemia and Allergy, remain as confounders for the occurrence of the events. The benefit-risk relationship of Moderna Covid-19 Vaccine is not affected by this report.							
██████	This spontaneous case was reported by a consumer and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Diagnosed with ADEM/tingling in both arms, legs & hands/ unable to think straight/ sleeping less/ Left leg would stick out when walked/ Numbness inside of mouth/ Tingling inside of mouth/ Double vision / double vision of words & objects), VERTIGO (Head was spinning), VITREOUS FLOATERS (Black floaters in right eye), DECREASED APPETITE (loss of appetite), LOSS OF CONSCIOUSNESS (sensation of blacking out 3 different times prior to visit/Decreased level of consciousness), INCREASED UPPER AIRWAY SECRETION (Drainage in throat), THROAT TIGHTNESS (Pressure in throat), DIZZINESS	MRI done but no results available. CT head : normal	Level 3	Level 4	Level 5	Possible	This spontaneous reported case concerns a 21-year-old, female patient with a family history of Diabetes mellitus, Crohn's disease; who received the second dose of Spikevax and 25 days later reported "experienced progressive musculoskeletal stiffness, vertigo, decreased appetite, dizziness, loss of consciousness, ear infection, presyncope, blacking out, head discomfort, photophobia, headache, nausea, eye pain, ear pain, hypoaesthesia, asthenia, neck pain, dysesthesia, balance disorder, fatigue, muscular weakness, chest pain, vitreous floaters, skin irritation, dyspnoea, dyspnoea exertional and anxiety.	████████████████████

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Dizziness), EAR INFECTION (Ear infection/Ears felt like they had liquid in them/Ear pressure/still having issues with ears/inflammation in ears / inflammation in both ears), EYE PAIN (pain behind eyes), EAR PAIN (ear pain), MUSCULAR WEAKNESS (Muscle weakness), HYPOAESTHESIA (Numbness in both arms, legs & hands/Numbness in legs), SKIN IRRITATION (pinching feeling in the top of scalp), ANXIETY (Anxiety), ASTHENIA (Weakness of leg/I had a lack of energy), DYSPNOEA (difficulty breathing), NECK PAIN (neck pain/Soreness & pain in neck/pain in my neck), DYSSTASIA (Difficulty with standing for long periods of time/could stand for only 5-6 minutes), CHEST PAIN (Excruciating chest pain/had chest pain), BALANCE DISORDER (difficulty with balance/ off balance), PRESYNCOPE (Had the sensation of passing out/ felt like I was going to pass out), HEAD DISCOMFORT (Head pressure/ Feeling a lot of pressure in my head), PHOTOPHOBIA (Eyes were sensitive to light/had vision changes in the form of sensitivity to light, & saw halos/had sensitivity to brighter lights, like lightbulbs, & I saw streaks), HEADACHE (Head pain), NAUSEA (Nausea/ had a strong sense of smell to the point of nausea), FATIGUE (Tiredness/fatigue),DYSPNOEA EXERTIONAL (shortness of breath on exertion), MUSCULOSKELETAL STIFFNESS (Arm was really stiff), ABDOMINAL PAIN UPPER (Stomach pain), MUSCLE DISCOMFORT (Muscle issues), ASTHENOPIA (Eyes feel heavy/sleepy), Perfume sensitivity (sensitivity to sounds), PERFUME SENSITIVITY (sensitivity to scents/nose is overly sensitive to scents), CONFUSIONAL STATE (memory issues/confusion), DYSKINESIA (involuntary motor movements (legs start moving/shaking while laying in bed), VISION BLURRED (blurry at times with screens, double of words/letters on keyboard), OROPHARYNGEAL PAIN (Throat pain), DYSPHAGIA (Difficulty swallowing), PALPITATIONS (Irregular heart rate/palpitations), CHEST DISCOMFORT (Chest tightness), HYPOAESTHESIA (Numbness), PARAESTHESIA (Prickling/Tingling sensation), LIMB DISCOMFORT (plasticity issues in arms and legs), VACCINATION SITE PAIN (Arm was really sore at the injection site), CHILLS (Chills) and MYALGIA (muscle soreness over entire body) in a 21-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch nos. 001C21A and 030B21A) for COVID-19 vaccination. The occurrence of additional non-serious events is detailed below. The patient’s medical history, as provided by the reporter, included family history Diabetes mellitus, Crohn's disease. Past patient vaccination history includes , meningococcal B vaccine on 25-AUG-2021.					Diagnostic results: CT head: normal, MRI was done but result not provided. This case is classified as Brighton's level 3 and considered WHO-UMC Possible, based on the temporal association and the presence of alternative association including a family history of diabetes and Crohn's disease.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	meningococcal B vaccine 27-JUN-2016, HPV vaccine 10oct 2011 to 18-JUL-2012 , tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, adsorbed 17-MAY-2011 , meningococcal B vaccine on 17-MAY-2011, HPV vaccine on 17may2011, hepatitis A vaccine on 28-AUG-2008 , varicella virus vaccine on 26-JUN-2007, varicella virus vaccine on 26-JUN-2007 , measles, mumps and rubella virus vaccine on 17-JUN-2005, poliovirus vaccine, inactivated on 17-JUN-2005, diphtheria, tetanus toxoids and acellular pertussis vaccine no date capture , diphtheria, tetanus toxoids and acellular pertussis vaccine on 09-OCT-2009, hepatitis B vaccine, unspecified formulation on 09-OCT-2009, pneumococcal conjugate vaccine 06-JUL-2001, haemophilus influenzae type b vaccine, conjugate unspecified formulation on 06-JUL-2001, diphtheria, tetanus toxoids and acellular pertussis vaccine on 06-JUL-2001, varicella virus vaccine on 17-MAY-2001, measles, mumps and rubella virus vaccine 17may2001, pneumococcal conjugate vaccine, 13 valent on 15-JAN-2021, hepatitis B vaccine, unspecified formulation 15-JAN-2001, pneumococcal conjugate vaccine on 12-OCT-2001, haemophilus influenzae type b vaccine, conjugate unspecified formulation on 12-OCT-2001, hepatitis B vaccine on 12-OCT-2000, diphtheria, tetanus toxoids and acellular pertussis vaccine on 12-OCT-2000, pneumococcal conjugate vaccine on 10-AUG-2000, poliovirus vaccine on 10-AUG-2000, haemophilus influenzae type b vaccine, conjugate unspecified formulation on 10-AUG-2000, diphtheria, tetanus toxoids and acellular pertussis vaccine on 10-AUG-2000, poliovirus vaccine inactivated on 08-JUN-2000, haemophilus influenzae type b vaccine conjugate on 08-JUN-2000, diphtheria tetanus toxoids acellular pertussis vaccine 08-JUN-2000, product used for unknown indication. On 02-Apr-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 30-Apr-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (Intramuscular) dosage was changed to 1 dosage form. On 27 Apr 2021, the patient experienced DYSPHAGIA(Difficulty swallowing), PALPITATION(Irregular heart rate/palpitations), CHEST DISCOMFORT (Chest tightness), HYPOAESTHESIA (Numbness) and PARAESTHESIA (Prickling/Tingling sensation). On 30-Apr-2021, the patient experienced MUSCULOSKELETAL STIFFNESS (Arm was really stiff) and VACCINATION SITE PAIN (Arm was really sore at the injection site). On 06-May-2021, the patient experienced VERTIGO (Head was spinning) (seriousness criterion medically significant), DECREASED APPETITE (loss of appetite) (seriousness criterion medically significant), INCREASED UPPER AIRWAY							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	SECRETION (Drainage in throat) (seriousness criterion medically significant), THROAT TIGHTNESS (Pressure in throat) (seriousness criterion medically significant), DIZZINESS (Dizziness) (seriousness criterion medically significant), EAR INFECTION (Ear infection/Ears felt like they had liquid in them/Ear pressure/still having issues with ears/inflammation in ears / inflammation in both ears) (seriousness criterion medically significant), PRESYNCOPE (Had the sensation of passing out/ felt like I was going to pass out) (seriousness criterion medically significant), HEAD DISCOMFORT (Head pressure/ Feeling a lot of pressure in my head) (seriousness criterion medically significant), PHOTOPHOBIA (Eyes were sensitive to light/had vision changes in the form of sensitivity to light, & saw halos/had sensitivity to brighter lights, like lightbulbs, & I saw streaks) (seriousness criterion medically significant), HEADACHE (Head pain) (seriousness criterion medically significant), NAUSEA (Nausea/ had a strong sense of smell to the point of nausea) (seriousness criterion medically significant), ABDOMINAL PAIN UPPER (Stomach pain), MUSCLE DISCOMFORT (Muscle issues), ASTHENOPIA (Eyes feel heavy/sleepy) and CHILLS (Chills). On 15-May-2021, the patient experienced EYE PAIN (pain behind eyes) (seriousness criterion medically significant), EAR PAIN (ear pain) (seriousness criterion medically significant), HYPOAESTHESIA (Numbness in both arms, legs & hands/Numbness in legs) (seriousness criterion medically significant), ASTHENIA (Weakness of leg/I had a lack of energy) (seriousness criterion medically significant), NECK PAIN (neck pain/Soreness & pain in neck/pain in my neck) (seriousness criterion medically significant), DYSSTASIA (Difficulty with standing for long periods of time/could stand for only 5-6 minutes) (seriousness criterion medically significant), BALANCE DISORDER (difficulty with balance/ off balance) (seriousness criterion medically significant) and FATIGUE (Tiredness/fatigue) (seriousness criterion medically significant). 15-May-2021, the patient experienced MUSCULAR WEAKNESS (Muscle weakness) (seriousness criterion medically significant). On 01-Jul-2021, the patient experienced CHEST PAIN (Exc							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 09-Nov-2021 and was forwarded to Moderna on 09-Nov-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of ANGIOGRAM PULMONARY NORMAL (Angiogram pulmonary normal), AREFLEXIA (Areflexia), ARTHRALGIA (Arthralgia/joint soreness), ASTHENIA (Asthenia/generalized weakness), BACK PAIN	No MRI result	Level 5	Level 5	Level 2	Unlikely	This regulatory authority case in a 69-year-old male patient with concurrent medical conditions included Hypertension, Hyperlipidemia, GERD, Arthritis, Gout and Obesity; and concomitant medications included ALLOPURINOL, CELECOXIB (CELEBREX), VALSARTAN, SIMVASTATIN and BUDESONIDE, FORMOTEROL FUMARATE (SYMBICORT); who received the second dose of Spikevax and on the same day reported " progressive lower extremities	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Back pain), BLOOD CREATINE PHOSPHOKINASE INCREASED (Blood creatine phosphokinase increased), BLOOD IMMUNOGLOBULIN G NORMAL (Blood immunoglobulin G normal), BLOOD IMMUNOGLOBULIN M NORMAL (Blood immunoglobulin M normal), CSF GLUCOSE NORMAL (CSF glucose normal), CSF PROTEIN INCREASED (CSF protein increased), CSF TEST (CSF test), CSF WHITE BLOOD CELL COUNT INCREASED (CSF white blood cell count increased), CHEST X-RAY NORMAL (Chest X-ray normal), COMPUTERISED TOMOGRAM HEAD NORMAL (Computerised tomogram head normal), COMPUTERISED TOMOGRAM SPINE (Computerised tomogram spine), ELECTROCARDIOGRAM NORMAL (Electrocardiogram normal), FIBRIN D DIMER INCREASED (Fibrin D dimer increased), IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy), LUMBAR PUNCTURE (Lumbar puncture), NEUROLOGICAL EXAMINATION (Neurological examination), WEST NILE VIRUS TEST NEGATIVE (West Nile virus test negative), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome), HYPOAESTHESIA (Hypoaesthesia/numbness), MUSCULAR WEAKNESS (Muscular weakness/Progressive bilateral lower extremity weakness), NEUROPATHY PERIPHERAL (Neuropathy peripheral), PARAESTHESIA (Paraesthesia/tingling in his hands), POLLAKIURIA (Pollakiuria/urinary frequency), PRURITUS (Pruritus/itching), PYREXIA (Pyrexia/fever) and TRAUMATIC LUMBAR PUNCTURE (Traumatic lumbar puncture) in a 69-year-old male patient who received mRNA-1273 (Moderna COVID-19 Vaccine) (batch no. 039B21A) for COVID-19 vaccination. Concurrent medical conditions included Allergy to antibiotic (Rocephin), Hypertension, Hyperlipidemia, GERD, Arthritis, Gout and Obesity. Concomitant products included ALLOPURINOL, CELECOXIB (CELEBREX), VALSARTAN, SIMVASTATIN and BUDESONIDE, FORMOTEROL FUMARATE (SYMBICORT) for an unknown indication. On 29-May-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 29-May-2021, the patient experienced ANGIOGRAM PULMONARY NORMAL (Angiogram pulmonary normal) (seriousness criterion hospitalization), AREFLEXIA (Areflexia) (seriousness criterion hospitalization), ARTHRALGIA (Arthralgia/joint soreness) (seriousness criterion hospitalization).					weakness with areflexia, Arthralgia, Asthenia, Back pain, Paraesthesia, Hypoaesthesia, urinary frequency, Pruritus, Pyrexia, ". Diagnostic Labs: infectious disease panel: negative (West Nile virus IgG and IgM negative), blood creatine phosphokinase increased, CT head,& spine normal, CSF glucose normal, protein increased with pleocytosis, Demyelinating polyneuropathy, Fibrin D dimer increased, Guillain-Barre syndrome, Immunoglobulin therapy, The medical history of gout, obesity, arthritis, and hypertension remain confounders for paresthesia, peripheral neuropathy, arthralgia, and asthenia. This case is classified as Brighton's level 5, NOT a case of ADEM. This case is Brighton's level 2 Myelitis based on sensorimotor and autonomic dysfunctions and zero encephalopathy. This case is considered WHO-UMC Unlikely; with a time to onset of the same day as Spikevax vaccination that makes a relationship improbable (but not impossible). Concurrent medical conditions including Hypertension, Hyperlipidemia, GERD, Arthritis, Gout, and Obesity, and statins are strong confounders that provide plausible explanations.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	ASTHENIA (Asthenia/generalized weakness) (seriousness criterion hospitalization), BACK PAIN (Back pain) (seriousness criterion hospitalization), BLOOD CREATINE PHOSPHOKINASE INCREASED (Blood creatine phosphokinase increased) (seriousness criterion hospitalization), BLOOD IMMUNOGLOBULIN G NORMAL (Blood immunoglobulin G normal) (seriousness criterion hospitalization), BLOOD IMMUNOGLOBULIN M NORMAL (Blood immunoglobulin M normal) (seriousness criterion hospitalization), CSF GLUCOSE NORMAL (CSF glucose normal) (seriousness criterion hospitalization), CSF PROTEIN INCREASED (CSF protein increased) (seriousness criterion hospitalization), CSF TEST (CSF test) (seriousness criterion hospitalization), CSF WHITE BLOOD CELL COUNT INCREASED (CSF white blood cell count increased) (seriousness criterion hospitalization), CHEST X-RAY NORMAL (Chest X-ray normal) (seriousness criterion hospitalization), COMPUTERISED TOMOGRAM HEAD NORMAL (Computerised tomogram head normal) (seriousness criterion hospitalization), COMPUTERISED TOMOGRAM SPINE (Computerised tomogram spine) (seriousness criterion hospitalization), ELECTROCARDIOGRAM NORMAL (Electrocardiogram normal) (seriousness criterion hospitalization), FIBRIN D DIMER INCREASED (Fibrin D dimer increased) (seriousness criterion hospitalization), IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy) (seriousness criterion hospitalization), LUMBAR PUNCTURE (Lumbar puncture) (seriousness criterion hospitalization), NEUROLOGICAL EXAMINATION (Neurological examination) (seriousness criterion hospitalization), WEST NILE VIRUS TEST NEGATIVE (West Nile virus test negative) (seriousness criterion hospitalization), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy) (seriousness criteria hospitalization and medically significant), GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) (seriousness criteria hospitalization and medically significant), HYPOAESTHESIA (Hypoaesthesia/numbness) (seriousness criterion hospitalization), MUSCULAR WEAKNESS (Muscular weakness/Progressive bilateral lower extremity weakness) (seriousness criterion hospitalization), NEUROPATHY PERIPHERAL (Neuropathy peripheral) (seriousness criteria hospitalization and medically significant), PARAESTHESIA (Paraesthesia/tingling in his hands) (seriousness criterion hospitalization), POLLAKIURIA (Pollakiuria/urinary frequency) (seriousness criterion hospitalization), PRURITUS (Pruritus/itching) (seriousness criterion hospitalization) and PYREXIA (Pyrexia/fever) (seriousness criterion hospitalization). 29-May-2021, the patient experienced TRAUMATIC LUMBAR PUNCTURE (Traumatic lumbar							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	puncture) (seriousness criterion hospitalization). The patient was hospitalized from 29-May-2021 to 24-Jun-2021 due to MUSCULAR WEAKNESS and PARAESTHESIA, then from 31-May-2021 to 24-Jun-2021 due to ARTHRALGIA, ASTHENIA, POLLAKIURIA, PRURITUS and PYREXIA, then from 02-Jun-2021 to 24-Jun-2021 due to HYPOAESTHESIA, then from 04-Jun-2021 to 24-Jun-2021 due to BACK PAIN and GUILLAIN-BARRE SYNDROME, and then from 07-Jun-2021 to 24-Jun-2021 due to DEMYELINATING POLYNEUROPATHY. The patient was treated with DEXAMETHASONE ACETATE (DECADRON A) (oral) for Adverse event, at a dose of 8 milligram,IVP and po x 5 days; AZITHROMYCIN (Z-PAK) for Adverse event, at a dose of 1 dosage form; PREDNISONE (oral) for Adverse event, at a dose of 60 milligram; NAPROXEN (oral) for Adverse event, at a dose of 500 milligram; KCL (oral) for Adverse event, at a dose of 25 milligram; METHYLPREDNISOLONE (MEDROL [METHYLPREDNISOLONE]) for Adverse event, at a dose of 4 milligram and IMMUNOGLOBULIN HUMAN NORMAL (IVIGLOB-EX) for Guillain-Barre syndrome, at a dose of 1 dosage form. At the time of the report, AREFLEXIA (Areflexia), ARTHRALGIA (Arthralgia/joint soreness), ASTHENIA (Asthenia/generalized weakness), BACK PAIN (Back pain), DEMYELINATING POLYNEUROPATHY (Demyelinating polyneuropathy), HYPOAESTHESIA (Hypoaesthesia/numbness), MUSCULAR WEAKNESS (Muscular weakness/Progressive bilateral lower extremity weakness), NEUROPATHY PERIPHERAL (Neuropathy peripheral), PARAESTHESIA (Paraesthesia/tingling in his hands), POLLAKIURIA (Pollakiuria/urinary frequency), PRURITUS (Pruritus/itching), PYREXIA (Pyrexia/fever) and TRAUMATIC LUMBAR PUNCTURE (Traumatic lumbar puncture) outcome was unknown and GUILLAIN-BARRE SYNDROME (Guillain-Barre syndrome) was unknown. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. The patient also stated that he was transferred to a different hospital for neuro eval for suspected GBS Alternative Hospital course, Neuro A/P-Acute to subacute onset of progressive and ascending LE weakness with areflexia. Also stated that he had undergone lumbar puncture for multiple times. He was Unable to tolerate MRI, Also he had undergone immunotherapy. Lab data included Normal CXR, CTPA, ekg. Elevated CPK and d-dimer. Patient was also unable							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	to tolerate MRI. CSF results: traumatic tap, normal OP/glucose. Elevated WBC and protein. West Nile IgG+, IgM negative. Company comment: This case concerns a 69 year-old male patient with a history of gout, obesity, arthritis, hyperlipidemia, hypertension who experienced the unexpected serious events of Guillain-barre syndrome, an AESI, areflexia, pyrexia, pollakiuria, paresthesia, peripheral neuropathy, arthralgia, asthenia, demyelinating polyneuropathy and traumatic lumbar puncture. The events occurred approximately 1 day after the second dose of mRNA-1273 vaccine. The rechallenge was not applicable as no additional dosing							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 16-Nov-2021 and was forwarded to Moderna on 16-Nov-2021. This regulatory case was reported by a other health care professional and the occurrence of Abdominal pain upper (Abdominal pain upper), Acute disseminated encephalomyelitis (Acute disseminated encephalomyelitis), Asthenopia (Asthenopia), Balance disorder (Balance disorder), Chest pain (Chest pain), Chills (Chills), Computerised tomogram head normal (Computerised tomogram head normal), Confusional state (Confusional state), Costochondritis (Costochondritis), Decreased appetite (Decreased appetite), Diplopia (Diplopia), Discomfort (Discomfort), Dizziness (Dizziness), Dyspnoea (Dyspnoea), Dysstasia (Dysstasia), Ear discomfort (Ear discomfort), Ear inflammation (Ear inflammation), Ear pain (Ear pain), Eye pain (Eye pain), Fatigue (Fatigue), Gait disturbance (Gait disturbance), Head discomfort (Head discomfort), Headache (Headache), Hyperacusis (Hyperacusis), Hypoaesthesia (Hypoaesthesia), Hypoaesthesia oral (Hypoaesthesia oral), Hypoaesthesia teeth (Hypoaesthesia teeth), Magnetic resonance imaging abnormal (Magnetic resonance imaging abnormal), Memory impairment (Memory impairment), Muscle disorder (Muscle disorder), Muscular weakness (Muscular weakness), Myalgia (Myalgia), Nausea (Nausea), Neck pain (Neck pain), Oropharyngeal discomfort (Oropharyngeal discomfort), Pain of skin (Pain of skin), Paraesthesia (Paraesthesia), Paraesthesia oral (Paraesthesia oral), Parosmia (Parosmia), Photophobia (Photophobia) in a 20-year-old female patient, who received mRNA-1273 (Moderna COVID-19 Vaccine for COVID-19 vaccination. No medical history was provided. On 2-APR-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) batch no : 030B21A (unknown) to her left arm 1 dosage	MRI report: abnormal. No specifics provided	Level 3	Level 5	Level 4	Possible	This regulatory authority reported case concerns a 20-year-old female patient with no medical history provided, concomitant medications included antibiotics for ear infection; received the second dose of Spikevax and on an unknown time to onset reported motor, sensory and visual dysfunction, with a confusional state but no loss of consciousness. Diagnostic results: CT head: normal, MRI was performed, but the results are not available. Neurologist consultation was done, and the patient was diagnosed with Acute disseminated encephalomyelitis. Very limited information on treatment and events outcome. This case is classified as Brighton's level 3 and considered WHO Possible, based on temporal association and a causal relationship cannot be excluded due to the lack of information on medical history.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	form. On unknown date, patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) batch no : 001C21A (unknown) to her left arm,1 dosage form. On 27-APR-2021, patient experienced Abdominal pain upper, Acute disseminated encephalomyelitis, Asthenopia, Balance disorder, Chest pain, cCills, Computerised tomogram head normal, Confusional state , Costochondritis, Decreased appetite, Diplopia, Discomfort, Dizziness, Dyspnoea, Dysstasia, Ear discomfort, Ear inflammation, ear pain, eye pain, fatigue, Gait disturbance, Head discomfort, Headache, Hyperacusis, Hypoaesthesia , Hypoaesthesia oral, Hypoaesthesia teeth , Magnetic resonance imaging abnormal , Memory impairment, Muscle disorder , Muscular weakness, myalgia, nausea, Neck pain, Oropharyngeal discomfort, Pain of skin, Paraesthesia, Paraesthesia oral, Parosmia, Photophobia Events. The outcomes of the events Abdominal pain upper, Acute disseminated encephalomyelitis, Asthenopia, Balance disorder, Chest pain, cCills, Computerised tomogram head normal, Confusional state , Costochondritis, Decreased appetite, Diplopia, Discomfort, Dizziness, Dyspnoea, Dysstasia, Ear discomfort, Ear inflammation, ear pain, eye pain, fatigue, Gait disturbance, Head discomfort, Headache, Hyperacusis, Hypoaesthesia , Hypoaesthesia oral, Hypoaesthesia teeth , Magnetic resonance imaging abnormal , Memory impairment, Muscle disorder , Muscular weakness, myalgia, nausea, Neck pain, Oropharyngeal discomfort, Pain of skin, Paraesthesia, Paraesthesia oral, Parosmia, Photophobia were unknown. No concomitant medication details was given. Patient was taking Amoxicillin and Sudafed for Inflammation in both ears. More in the left ear than the right, , IC Meclizine 25 MG Tablet- Take 1 tablet by mouth three times a day for dizziness and IC Methylprednisolone 4 MG Tablet- Take 6 tablets on day 1 and decrease by 1 tab each day for a total of 6 days. Pain patches and IC Methocarbamol 750 MG Tablet- take 2 by mouth 4 times a day for Pressure/pain in head and extreme neck pain. Zyrtec, IC Naproxen 500 mg Tablet, IC Cyclobenzaprine 5 mg Tablet, and Flonase for Costochondritis and inflammation in ears. Few symptoms after COVID-19 were- loss of appetite, nausea, head pressure and pain, ears feel like they have liquid inside/pressure/sore, eyes sensitive to light, pressure/ liquid in throat, chest pain, stomach pain, chills, legs go numb/muscle issues. Tested for sinus, was normal. There is still inflammation in ears, prescribed to take -IC Prednisone 20 MG Tablet. double vision, sensitivity to light, checking for any potential sinus pressure issues, Tested for sinus pressure and looked at photos from April							

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	appointment, both of which look normal. Numb/tingling inside of mouth, hands, arms, and legs; legs feel weak/not able to walk or stand for long periods of time, off balance, upper neck pain, muscle sore ness over entire body, vision changes: seeing double, sensitivity to light, Pinching feeling on scalp, memory issues/confusion, still inflammation in ears, having IC Prednisone 20 MG Tablet. difficulty breathing, shortness of breath, and chest pains, Oxygen level was normal. On 14 Sep checked lungs and heart-both normal Sep. Online call-given an inhaler and Covid test came back negative.G iven IC Sertraline HCL 50 MG Tablet. On October 10/5-8, diagnosed with ADEM and Started IV treatments and given steroids on 7 OCT- Primary care and Follow up about MRI results and how other medication is going on 24 OCT. Follow up appointment 11/30: Follow up after 2nd MRI. Company comment: This regulatory authority case concerns a 20-year-old female patient with no relevant medical history, who experienced the unexpected event of Acute disseminated encephalomyelitis (AESI) and other non serious events after mRNA- 1273 Moderna vaccine. The onset of the events occurred approximately 25 days after the second dose of mRNA- 1273 vaccine. Clinical manifestations included loss of appetite, nausea, headache, neck pain, chest pain, ears discomfort, asthenopia, photophobia, phonophobia and gait disturbance. Initially, ear inflammation and costochondritis were diagnosed. Treatment with amoxicillin, meclizine, methylprednisolone and naproxen was prescribed. Computerised tomography of the head was unremarkable. Subsequently, the patient developed hypoacsthesia, weakness in legs, diplopia, confusion and dyspnoea. MRI was performed, but the results are not available. Neurologist consultation was done, and the patient was diagnosed with Acute disseminated encephalomyelitis. Very limited information regarding this event was reported. Unspecified intravenous treatment and steroids were given. Information regarding outcome is not available. The rechallenge is not applicable, since the event was reported exclusively after the second dose. The benefit-risk relationship of mRNA- 1273 vaccine is not affected by this report.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 17-Nov-2021 and was forwarded to Moderna on 17-Nov-2021. This regulatory authority case was reported by a physician and describes the occurrence of the first episode of ASTHENIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID	No MRI result	Level 4	Level 5	Level 5	Conditional	This regulatory authority reported case concerns a 54-year-old female patient with past medical history included upper respiratory tract infection (Laryngotracheobronchitis) and no concomitant medication information; who received an unknown dose of Spikevax and 2 days later reported Asthenia, Demyelinating polyneuropathy, Myalgia. Limited information provided. No information about diagnostic results, and	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	EXAMINATION), DEMYELINATING POLYNEUROPATHY (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION), MYALGIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) and the second episode of ASTHENIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) in a 54-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 023F21) for COVID-19 vaccination. The patient's past medical history included Infection respiratory (Upper respiratory tract infection (Laryngotracheobronchitis) from 14-OCT-2021 TO 29-OCT-2021.) from 14-Oct-2021 to 29-Oct-2021. On 29-Oct-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) .5 milliliter in total. On 31-Oct-2021, the patient experienced the first episode of ASTHENIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) (seriousness criterion hospitalization), DEMYELINATING POLYNEUROPATHY (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) (seriousness criteria hospitalization and medically significant), MYALGIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) (seriousness criterion hospitalization) and the second episode of ASTHENIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) (seriousness criterion hospitalization). At the time of the report, DEMYELINATING POLYNEUROPATHY (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE					treatment. Events were resolving at the time of the report. This case is classified as Brighton level 4, based on insufficient information, and considered WHO Conditional. More information needed for proper assessment.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION), MYALGIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) and the last episode of ASTHENIA (DIAGNOSIS OF MILD DEMYELINATING SENSORIMOTOR POLYNEUROPATHY IN THE ABSENCE OF ALBUMINOCYTOLOGICAL DISSOCIATION UPON CEREBROSPINAL FLUID EXAMINATION) was resolving. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medications reported by reporter. No treatment medications provided by the reporter. Company comment: This case concerns a 54-year-old female patient with no relevant medical history, who experienced the unexpected adverse events of special interest Demyelinating Polyneuropathy, and unexpected events of Myalgia and Asthenia. The event occurred 2 days after receiving an undisclosed dose number of mRNA-1273 Vaccine with outcome of hospitalization. The rechallenge was not applicable since dose number was not disclosed. The benefit-risk relationship of mRNA-1273 Vaccine is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 17-Nov-2021: Translation document received on 18-Nov-2021: Medical history comments were updated.							
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 16-Nov-2021 and was forwarded to Moderna on 22-Nov-2021. This case, initially reported to the [REDACTED] by a [REDACTED] physician, was received via the [REDACTED] (Ref, [REDACTED]). On an unknown date, the patient received the 1st dose of this vaccine. On 30-Jul-2021, the patient received the 2nd dose of this vaccine. Around 20-Aug-2021, acute disseminated encephalomyelitis (ADEM) developed. The patient	MRI showed contrast enhancement effect of the brain surface in multiple locations, while some abnormal FLAIR signals	Level 2	Level 5	Level 5	Conditional	This regulatory authority reported case concerns a 54-year-old male patient with no medical history and concomitant medications reported; who received the second dose of Spikevax and 21 days later reported "headache, dysesthesia and acute disseminated encephalomyelitis" Diagnostic results: contrast-enhanced MRI showed contrast enhancement effect of the brain surface in multiple locations, while some abnormal FLAIR signal. Lab tests were negative for infectious encephalitis, inflammatory diseases, and tumors, and the events were resolved. This case is classified as Brighton's level 2 and considered WHO Possible, based on temporal association and a causal relationship cannot be excluded due to the lack of information on medical history.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	was aware of headache. On an unknown date, the dysesthesia of the precordia appeared. On 07-Oct-2021, since the symptoms did not improve, the patient visited the reporting department. On 12-Oct-2021, the abnormal signal mainly on the right temporal lobe was recognized in the head MRI. On 14-Oct-2021, the patient was admitted to the reporting department for detailed examination and treatment purposes. On 15-Oct-2021, increased cell number was recognized in the cerebrospinal fluid. On 18-Oct-2021, contrast-enhanced MRI showed contrast enhancement effect of the brain surface in multiple locations, while some abnormal FLAIR signals tended to be reduced. Other tests were negative for infectious encephalitis, inflammatory diseases, and tumors, and the symptoms showed a tendency toward improvement. Therefore, the patient was followed up without treatment. On 11-Nov-2021, contrast-enhanced MRI showed that the contrast enhancement effect disappeared and the abnormal signal on FLAIR was greatly reduced. The patient's symptoms were confirmed to improve. The outcome of acute disseminated encephalomyelitis was reported as resolving. Follow-up investigation will be made. Company Comment: The event developed after the administration of COVID-19 vaccine mRNA (mRNA 1273) and there is temporal relationship.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 24-Nov-2021 and was forwarded to Moderna on 24-Nov-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) in a 27-year-old male patient who received mRNA-1273 (COVID 19 Vaccine Moderna) for COVID-19 vaccination. No Medical History information was reported.	No MRI result	Level 4	Level 4	Level 4	Conditional	This regulatory authority reported case concerns a 27-year-old male patient with no medical history and concomitant medications information; who received the second dose of Spikevax and 21 days later reported "acute disseminated encephalomyelitis". No diagnostic reports. At the time of the report, Acute disseminated encephalomyelitis had resolved. This case is classified as Brighton level 4, based on insufficient information and considered WHO Conditional. More data for proper assessment is needed.	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	On 13-Aug-2021, the patient received dose of mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 10-Sep-2021, after starting mRNA-1273 (COVID 19 Vaccine Moderna), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criterion hospitalization). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) had resolved. For mRNA-1273 (COVID 19 Vaccine Moderna) (Intramuscular), the reporter did not provide any causality assessments. No concomitant medication was reported. Treatment medication was not provided by the reporter. Company comment This case concerns a 27-year-old male patient with no relevant medical history provided, who experienced the unexpected serious event of Acute disseminated encephalomyelitis (AESI). The event occurred nearly a month after the patient received an unspecified dose of the mRNA-1273 vaccine. At the time of this report, the event had resolved, however, no further information regarding the clinical course of the event was provided. Action taken with the suspect drug and re-challenge were retained in line with source document, as not applicable. The benefit-risk relationship of the mRNA-1273 vaccine is not affected by this report. Event seriousness assessed as per Regulatory Authority reporting. Most recent FOLLOW-UP information incorporated above includes: On 24-Nov-2021: Translated received on 25-Nov-2021: Event verbatim was translated.							
	This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) and HERPES ZOSTER REACTIVATION (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) in a 60-year-old female patient who received mRNA-1273 (COVID-19 Vaccine Moderna) for an unknown indication. The patient's past medical history included Urothelial carcinoma bladder in 2011. Concurrent medical conditions included Carcinoma	MRI of the lumbar spine normal	Level 4	Level 5	Level 5	Unlikely	This regulatory authority reported case concerns a 60-year-old female patient with past medical history included urothelial carcinoma bladder in 2011. Concurrent medical conditions included Carcinoma of the esophagus (Patient has been in remission from esophageal cancer that was treated with radiation in 2019.) since 2019, Hearing loss, Irritable bowel, Drug allergy (Dafalgan), and Arthrosis. Concomitant medication included HARPAGOMED; HEPA-S; CONDROSULF; MAGNESIUM DIASPORAL [MAGNESIUM CITRATE]; VITAMIN D3	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	of esophagus (Patient is in remission from esophageal cancer that was treated with radiation in 2019.) since 2019, Hearing loss, Irritable bowel, Drug allergy (Dafalgan) and Arthrosis. Concomitant products included HARPAGOPHYTUM PROCUMBENS ROOT (HARPAGOMED), CYNARA CARDUNCULUS (HEPA-S), CHONDROITIN SULFATE SODIUM (CONDROSULF), MAGNESIUM CITRATE (MAGNESIUM DIASPORAL [MAGNESIUM CITRATE]) and COLECALCIFEROL (VITAMIN D3 [REDACTED]) for an unknown indication. On 01-Jun-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) 1 dosage form. On 01-Jul-2021, received second dose of mRNA-1273 (COVID-19 Vaccine Moderna) (Intramuscular) dosage was changed to 1 dosage form. On 13-Jul-2021, the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) (seriousness criteria hospitalization, disability and medically significant) and HERPES ZOSTER REACTIVATION (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) (seriousness criteria hospitalization, disability and medically significant). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) and HERPES ZOSTER REACTIVATION (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) was resolving. DIAGNOSTIC RESULTS (normal ranges are provided in parenthesis if available): On 29-Jul-2021, Magnetic resonance imaging: normal (normal) MRI of the lumbar spine on was unremarkable. In August 2021, Electromyogram: abnormal (abnormal) Motor evoked potentials (MEPs) and pathological electromyography. In August 2021, Immunology test: abnormal (abnormal) VZV IgG (Li/Se index) markedly elevated, HSV 1/2 IgG (Li/Se index) elevated, HSV 1/2 IgG (serum) > 30.0. In August 2021, Lumbar puncture: abnormal (abnormal) CSF: 128/ ul cell count, protein 1.23 g/l, albumin 0.8 g/l, type II oligoclonal bands, moderate blood-brain barrier dysfunction, intrathecal synthesis of IgG-class immunoglobulins, and suspected IgM. In August 2021, Microbiology test: abnormal (abnormal) VZV PCR weakly positive in 1 of the 3 measurements.. For mRNA-1273 (COVID-19 Vaccine Moderna)					She received the second dose of Spikevax and 12 days later reported " Herpes zoster reactivation and Acute disseminated encephalomyelitis, and " Diagnostic results: MRI spine normal, Immunology test: abnormal, VZV IgG (Li/Se index) markedly elevated, HSV 1/2 IgG (Li/Se index) elevated, HSV 1/2 IgG (serum) > 30.0. CSF: pleocytosis-128/ ul cell count, protein 1.23 g/l, albumin 0.8 g/l, type II oligoclonal bands. At the time of the report, Acute disseminated encephalomyelitis was resolving. This case is classified as Brighton level 4, based on insufficient information and considered WHO Unlikely. Based on the patient's concurrent reactivation of herpes zoster and prior medical conditions, this case is heavily confounded that making a causal relationship with Spikevax improbable (but not impossible). These confounders provide plausible explanations.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Intramuscular), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) and HERPES ZOSTER REACTIVATION (Encephalomyelitis disseminata as a consequence of Varicella zoster virus) to be possibly related. It was reported that the patient previously had osteoarthritis. On 27 Jul patient visited hospital and prescribed analgesic therapy that did not relieved symptoms. The patient manifested subsequent distal paraparesis (difficulty walking alone) with sensory disturbances (difficulty feeling the genital area and sensing proper bladder emptying). On 10 Aug the patient was admitted and diagnosed with acute disseminated encephalomyelitis (ADEM) with probable (DD) reactivation from herpes zoster virus (or Varicella zoster virus or VZV). The patient had varicella in the past. The main diagnostic tests performed and the results were for CSF its 128 per ul cell count, protein it was 1.23 gram per litre, albumin result was 0.8 gram per litre, type II oligoclonal bands, moderate blood-brain barrier dysfunction, intrathecal synthesis of immunoglobulin class IgG and suspected IgM. Company comment: This case concerns a 60-year-old female patient, with relevant history of varicella, Urothelial carcinoma bladder and Carcinoma of esophagus treated with radiation in 2019, who experienced the serious unexpected events of ACUTE DISSEMINATED ENCEPHALOMYELITIS and HERPES ZOSTER REACTIVATION. The events occurred twelve days after receiving the second dose of the mRNA-1273 vaccine. The rechallenge is not applicable since no information about further dosing has been disclosed. She had pain in the lumbar area with a normal magnetic resonance imaging of the lumbar spine, but she was admitted after adding to her symptoms distal paraparesis and sensory disturbances. A electromyography with signs of demyelination, a lumbar puncture, microbiology test and immunology test were performed with pathological results. Patient's medical history of varicella remains as a confounder. The benefit-risk relationship of the mRNA-1273 is not affected by this report. Most recent FOLLOW-UP information incorporated above includes: On 24-Nov-2021: Translation document received on 26 Nov 2021 contains, medical history comment were translated, laboratory investigation and I narrative was updated.							
	This case was received via [REDACTED] (Reference number: [REDACTED]) on 30-Nov-2021 and was forwarded to Moderna on 30-Nov-2021. This regulatory authority case was reported by an other health care professional and describes the	No MRI result	Level 4	Level 5	Level 5	Unlikely	This case was reported by an HCP and described the occurrence of stroke in a female patient (age unknown), who received the second dose of Spikevax and 7 weeks later received the Herpes zoster (Shingrix) vaccine. Co-suspect products	

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infectious Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	occurrence of CEREBROVASCULAR ACCIDENT (Cerebrovascular accident), DEMYELINATION (Demyelination), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), LYMPHOMA (Lymphoma) and BEDRIDDEN (Bedridden) in a female patient of an unknown age who received mRNA-1273 (Moderna COVID-19 Vaccine) for an unknown indication. The occurrence of additional non-serious events is detailed below. Co-suspect products included non-company products DIPHTHERIA VACCINE TOXOID, PERTUSSIS VACCINE ACELLULAR, TETANUS VACCINE TOXOID (TDAP) for an unknown indication and VARICELLA ZOSTER VACCINE RGE (CHO) (SHINGRIX) for an unknown indication. No Medical History information was reported. On 15-Mar-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form, dose of DIPHTHERIA VACCINE TOXOID, PERTUSSIS VACCINE ACELLULAR, TETANUS VACCINE TOXOID (TDAP) (unknown route) 1 dosage form and first dose of VARICELLA ZOSTER VACCINE RGE (CHO) (SHINGRIX) (unknown route) 1 dosage form. On 01-May-2021, the patient experienced CEREBROVASCULAR ACCIDENT (Cerebrovascular accident), DEMYELINATION (Demyelination), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), LYMPHOMA (Lymphoma), BEDRIDDEN (Bedridden), GAIT DISTURBANCE (Gait disturbance), HYPOKINESIA (Hypokinesia) and NEUROLOGICAL SYMPTOM (Neurological symptom). At the time of the report, CEREBROVASCULAR ACCIDENT (Cerebrovascular accident), DEMYELINATION (Demyelination), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), LYMPHOMA (Lymphoma), BEDRIDDEN (Bedridden), GAIT DISTURBANCE (Gait disturbance), HYPOKINESIA (Hypokinesia) and NEUROLOGICAL SYMPTOM (Neurological symptom) had not resolved. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. No concomitant medications were reported. Company Comment: This case concerns a female patient with no relevant medical history and co-suspect products of diphtheria vaccine tetanus vaccine and varicella zoster vaccine, who					included Tdap Vaccine and Spikevax. About 3 weeks after receiving Shingrix and Tdap Vaccine, the patient reported " experienced stroke, acute disseminated encephalomyelitis, lymphoma Acute disseminated encephalomyelitis, Bedridden, Cerebrovascular accident, Demyelination, Gait disturbance, Hypokinesia, Lymphoma, Neurological symptom.No diagnostic results. This case is classified as Brighton level 4, based on insufficient information and considered WHO Unlikely. With a time to onset of over 80 days that makes a relationship with Spikevax improbable (but not impossible). The Herpes zoster (Shingrix) vaccine or other medical conditions not reported provide plausible explanations.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	experienced the unexpected events of CEREBROVASCULAR ACCIDENT (Cerebrovascular accident), DEMYELINATION (Demyelination), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) and LYMPHOMA (Lymphoma) The events occurred approximately a month and a half after the second dose of the mRNA-1273 . Rechallenge was not applicable since the event occurred after the second dose so, no rechallenge was done and recurrence was not applicable. The benefit-risk relationship of mRNA-1273 is not affected by this report. It was reported that patient developed Stroke, Lymphoma, Lymphoma; Severe demyelination of brain; Neurological disease; Minimal movement in left arm ad left leg; Can't get out of bed or walk without help; Can't get out of bed or walk without help. It was reported that stroke in a female patient who received Herpes zoster (Shingrix) for prophylaxis. Co-suspect products included DTPa (Reduced antigen) (Tdap Vaccine) for prophylaxis and COVID 19 MRNA VACCINE MODERNA for prophylaxis. Previously administered products included Moderna vaccine (received 1st dose on 15th February 2021). On 5th May 2021, the patient received the 1st dose of Shingrix and Tdap Vaccine. On 15th March 2021, the patient received the 2nd dose of COVID 19 MRNA VACCINE MODERNA. In May 2021, less than 3 weeks after receiving Shingrix and Tdap Vaccine, the patient experienced stroke (serious criteria GSK medically significant), acute disseminated encephalomyelitis (serious criteria GSK medically significant), lymphoma (serious criteria GSK medically significant), demyelination (serious criteria GSK medically significant), neurological symptom, movements reduced, bedridden and walking difficulty. On an unknown date, the outcome of the stroke, acute disseminated encephalomyelitis, lymphoma, demyelination, neurological symptom, movements reduced, bedridden and walking difficulty were not recovered/not resolved. It was unknown if the reporter considered the stroke, acute disseminated encephalomyelitis, lymphoma, demyelination, neurological symptom, movements reduced, bedridden and walking difficulty to be related to Shingrix and Tdap Vaccine. Additional details were provided as follows: The reporter was an epidemiology lead. The age at vaccination was not reported. The reporter knew someone whose mother (patient) received the Moderna and Shingrix vaccines and in May 2021, less than 3 weeks after receiving Shingrix and Tdap Vaccine This case was linked to [REDACTED] Linked Report).							
	This case was received via [REDACTED]	No MRI result. Claimed to be abnormal	Level 5	Level 5	Level 5	Conditional	This case concerns an 18-year-old female,	[REDACTED]

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	(Reference number: on 30-Nov-2021 and was forwarded to Moderna on 30-Nov-2021. This regulatory authority case was reported by an other health care professional and describes the occurrence of MULTIPLE SCLEROSIS (Multiple sclerosis), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), VISUAL IMPAIRMENT (Visual impairment), MAGNETIC RESONANCE IMAGING ABNORMAL (Magnetic resonance imaging abnormal) and IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy) in an 18-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for an unknown indication. No Medical History information was reported. On 12-Jun-2021, the patient received first dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 12-Jun-2021, received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) dosage was changed to 1 dosage form. On 01-Oct-2021, the patient experienced MULTIPLE SCLEROSIS (Multiple sclerosis) (seriousness criteria hospitalization and medically significant), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization and medically significant), VISUAL IMPAIRMENT (Visual impairment) (seriousness criterion hospitalization), MAGNETIC RESONANCE IMAGING ABNORMAL (Magnetic resonance imaging abnormal) (seriousness criterion hospitalization) and IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy) (seriousness criterion hospitalization). At the time of the report, MULTIPLE SCLEROSIS (Multiple sclerosis), ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), VISUAL IMPAIRMENT (Visual impairment), MAGNETIC RESONANCE IMAGING ABNORMAL (Magnetic resonance imaging abnormal) and IMMUNOGLOBULIN THERAPY (Immunoglobulin therapy) had not resolved. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Concomitant products were not provided. Patient was diagnosed with acute disseminated encephalomyelitis, and treated over the course of stay with high dose steroids, and IVIG. Through additional work-up, patient has been diagnosed with					with no medical history or concomitant medication information provided. She received an unknown dose of Spikevax and after an unknown time to onset reported: " Acute disseminated encephalomyelitis, Visual impairment". MRI abnormal, Immunoglobulin therapy. Through additional work-up, patient has been diagnosed with MS.		

Case ID	Narrative (Complete)	Diagnostic Results (MRI, Infections Disease panels)	Brighton Collaboration Case Definition			WHO-UMC Causality Assessment	MAH comment	WW Identifier
			ADEM	Encephalitis	Acute Transverse Myelitis			
	Multiple sclerosis. Causality was difficult to determine, but patient history was overall unremarkable, except for admission with vision changes, and abnormal Magnetic resonance imaging a few months after vaccination from Moderna COVID-19 vaccine.							
	This case was received via Takeda Pharmaceuticals (Reference number: [REDACTED]) on 06-Dec-2021 and was forwarded to Moderna on 10-Dec-2021. This regulatory authority case was reported by a physician and describes the occurrence of ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), SEPSIS (Sepsis), DISSEMINATED INTRAVASCULAR COAGULATION (Disseminated intravascular coagulation), RENAL FAILURE (Renal failure) and PNEUMONIA ASPIRATION (Aspiration pneumonia) in a 48-year-old male patient who received mRNA-1273 (COVID-19 Vaccine Moderna Intramuscular Injection) for COVID-19 vaccination. No Medical History information was reported. On 15-Aug-2021, the patient received first dose of mRNA-1273 (COVID-19 Vaccine Moderna Intramuscular Injection) (Intramuscular) 1 dosage form. On 01-Sep-2021, after starting mRNA-1273 (COVID-19 Vaccine Moderna Intramuscular Injection), the patient experienced ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis) (seriousness criteria hospitalization, disability, medically significant and life threatening). On 25-Sep-2021, the patient experienced SEPSIS (Sepsis) (seriousness criteria hospitalization, disability, medically significant and life threatening) and DISSEMINATED INTRAVASCULAR COAGULATION (Disseminated intravascular coagulation) (seriousness criteria hospitalization, disability, medically significant and life threatening). On 27-Sep-2021, the patient experienced RENAL FAILURE (Renal failure) (seriousness criteria hospitalization, disability, medically significant and life threatening). On an unknown date, the patient experienced PNEUMONIA ASPIRATION (Aspiration pneumonia) (seriousness criteria hospitalization, disability, medically significant and life threatening). At the time of the report, ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), SEPSIS (Sepsis), DISSEMINATED INTRAVASCULAR COAGULATION (Disseminated intravascular coagulation) and RENAL FAILURE (Renal failure) had not resolved and PNEUMONIA ASPIRATION (Aspiration pneumonia) had resolved. DIAGNOSTIC RESULTS (normal ranges are	Magnetic resonance imaging: abnormal. Diffuse/ multiple white matter lesions were shown on T2-weighted/diffusion-weighted imaging (DWI)	Level 2	Level 4	Level 4	Conditional	This case was reported by a regulatory authority, concerning a 48-year-old male patient with no medical history information and concomitant medications reported, who received the first dose of Spikevax vaccine and 17 days later, reported "the occurrence of Acute disseminated encephalomyelitis". On days 41 through 43, patient was reported to have developed sepsis, disseminated intravascular coagulation, renal failure and pneumonia aspiration. Diagnostic results for infective causes were negative, Magnetic resonance imaging head showed diffuse/multiple white matter lesions on T2-weighted /diffusion-weighted imaging (DWI) This case is classified as Brighton's level 2 ADEM based on MRI report, and considered WHO Conditional. More information about the medical history and concomitant medications are needed for proper assessment.	

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			ADEM	Encephalitis	Acute Transverse Myelitis			
	provided in parenthesis if available): On 09-Sep-2021, CSF cell count: 27 (Inconclusive) 27 per microlitre. On 09-Sep-2021, CSF glucose: 53 (Inconclusive) 53 milligram per decilitre. On 09-Sep-2021, CSF immunoglobulin G index: normal (normal) Nonc. On 09-Sep-2021, CSF oligoclonal band: normal (normal) None. On 09-Sep-2021, CSF pressure: 300 (Inconclusive) 300 or higher mm (H2O). On 09-Sep-2021, CSF protein: 247 mg/dl (Inconclusive) 247 milligram per decilitre. On 25-Oct-2021, Magnetic resonance imaging: abnormal (abnormal) Diffuse or multiple white matter lesions were shown on T2-weighted/diffusion-weighted imaging (DWI) or FLAIR imaging (with or without gadolinium enhancement on T1-weighted imaging), Diffuse, ill-defined, and large (larger than 1-2 cm) lesions were found predominantly in the cerebral white matter, Lesions with low T1 signal intensities were not found in white matter., Deep gray matter lesion was found, Both or either of the following MRI criteria for multiple sclerosis were not met: (Demonstration of spatially multiple occurrence by MRI), One or more T2 lesions are seen in at least two of the four CNS areas (periventricular, subcortical, infratentorial, and spinal cord). (It need not be a contrast-enhanced lesion. In patients with brain stem or spinal cord symptoms, the responsible lesions of these symptoms are excluded.) (Demonstration of temporally multiple occurrence by MRI), Asymptomatic gadolinium-enhanced lesions coexist with asymptomatic nonenhanced lesions (at any time). Or symptomatic or asymptomatic T2 lesions and/or gadolinium-enhanced lesions newly developed later (at any time) compared to the baseline MRI. On an unknown date, Magnetic resonance imaging: abnormal (abnormal) Disseminated lesions with high T2 signal intensities which was mild in the cervical spinal cord and was marked in the whole thoracic spinal cord. For mRNA-1273 (COVID-19 Vaccine Moderna Intramuscular Injection) (Intramuscular), the reporter considered ACUTE DISSEMINATED ENCEPHALOMYELITIS (Acute disseminated encephalomyelitis), SEPSIS (Sepsis), DISSEMINATED INTRAVASCULAR COAGULATION (Disseminated intravascular coagulation), RENAL FAILURE (Renal failure) and PNEUMONIA ASPIRATION (Aspiration pneumonia) to be possibly related. Company comment: This RA case concerns a 48 male patient with no reported medical history , who experienced Serious (Life threatening, medically							

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	significant, Disability , hospitalization,AESI), unexpected events of Acute disseminated encephalomyelitis (ADEM) which occurred 18 days after vaccination with the 1st dose mRNA-1273 vaccine (Moderna Covid 19 Vaccine) , After 1 month and 11 days he experienced Serious , Unexpected events of Disseminated Intravascular Coagulation and Sepsis . Serious , unexpected , AESI event of renal failure after 1 month and 13 days of vaccination with the 1st dose. Pneumonia Aspiration occurred on an unknown time. The patient was intubated (later on weaned) , underwent hemodialysis , blood purification therapy and steroid pulse therapy . All mentioned events remains unchanged except for the Aspiration Pneumonia which has resolved. The events were reported as possibly related by the reporter. The re-challenge for this case is not applicable. The benefit -risk relationship of mRNA -1273 (Moderna Covid 19 Vaccine) is not affected by this report.. The progression to acute disseminated encephalomyelitis and septic DIC, which has been under follow-up, are all considered to be caused by immune abnormalities triggered by vaccination with the vaccine.							
	This regulatory authority case was reported by an other health care professional and describes the occurrence of ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis) and ENCEPHALITIS (Encephalitis/Encephalomyelitis) in a 71-year-old female patient who received mRNA-1273 (Moderna COVID-19 Vaccine) for an unknown indication. Concurrent medical conditions included Type II diabetes mellitus (under control with metformin.) and Dyslipidemia (under control with rosuvastatin). On 30-Sep-2021, the patient received second dose of mRNA-1273 (Moderna COVID-19 Vaccine) (unknown route) 1 dosage form. On 14-Oct-2021, the patient experienced ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis) (seriousness criterion hospitalization) and ENCEPHALITIS (Encephalitis/Encephalomyelitis) (seriousness criterion hospitalization). At the time of the report, ENCEPHALOMYELITIS (Encephalitis/Encephalomyelitis) and ENCEPHALITIS (Encephalitis/Encephalomyelitis) had not resolved. For mRNA-1273 (Moderna COVID-19 Vaccine) (Unknown), the reporter did not provide any causality assessments. Concomitant drug includes: Metformin, rosuvastatin. No medical history was reported.	Brain MRI: no acute infarction. No other report stated	Level 3	Level 4	Level 4	Conditional	This is a case of a 71-year-old female patient with concurrent medical conditions including Type II diabetes mellitus and Dyslipidemia; and concomitant medications included metformin and rosuvastatin; who received the second dose of Spikevax and 14 days later was reported "to have experienced sudden consciousness disturbance, bizarre behavior - slow and dull response, sat in the toilet in a daze, wore her clothes inside out), dizziness and fever". Diagnostic results: Infection panels, autoimmune and tumor marker all negative. Brain CT: no ICH but ventriculomegaly. Brain MRI: no acute infarction. EEG: focal cortical dysfunction with epileptiform discharge at left hemisphere. This case is classified as Brighton's level 3 ADEM based clinical features of encephalopathy, and EEG findings; and considered WHO Conditional. More information about the medical history and detailed report of MRI Brain that was done are needed for proper assessment.	

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	10/14/2021 suffered from sudden consciousness disturbance with bizarre [sic: bizarre] behaviors (slow response, sat in the toilet in a daze, wore her clothes inside out), dizziness since 10/14. NE was negative. Brain CT on 10/14: no ICH but ventriculomegaly. Seizure or stroke was impressed. She was admitted on 10/14. Bokey was prescribed. 10/15 Brain MRI, TCC on 10/18: no acute infarction. EEG: focal cortical dysfunction at l't hemisphere with epileptiform discharge at left hemisphere. AED was used. However, persistent [sic:persistent] dull response was noted. Repeat EEG on 10/18, 10/20 and brain CTA on 10/19, which showed less blood volume [sic: volume], flow, more MTT in right F-P-O-T lobe. Adjust AED to keppra 750 mg Q12H + depakin 400 mg Q8H. Then fever was developed. Empiric antibiotic with ceftriaxone (10/15-20), Vancomycin for r/o pneumonia, r/o CNS infection. Lumbar puncture on 10/19, which showed CSF routine, meningitis panel PCR all negative. Japanese encephalitis was reported. Autoimmune and tumor marker all negative. Antibiotic was DC by INF. Due to consciousness drowsy, was transferred to for 2nd opinion on 10/25/2021. Received 1st Moderna COVID-19 vaccination on 07/08/2021, 09/30; E2-3V2M5; pupil 2+/2+; MP >3 Under the impression of probable encephalitis, with seizure, etiology to be determined, was admitted to ward for further survey & treatment. After exclude INF, malignancy & autoimmune associated, Vaccine cannot be excluded. 12/01/2021 collapsed after receiving the vaccination for over 10 days and was hospitalized. It yet to recover, and that has applied for adverse reaction remedies. Intracranial hemorrhage and cerebral infarction not found in brain CT. Stroke suspected and patient hospitalized. EEG: focal cortical dysfunction with epileptiform discharge at left hemisphere. Antibiotics administered (10/15-20). No abnormalities found in CSF test (10/19). Company Comment : This case concerns a 71 year old female patient, with no relevant medical history, who was hospitalized due to serious unexpected events of encephalomyelitis and encephalitis. The events started 14 days after the second mRNA 1273 vaccine when patient suffered from vertigo, confusion and bizarre behaviors. Patient went to the hospital and was admitted, initial impression was a stroke, however a Brain CT scan did not reveal intracranial hemorrhage or infarction, EEG showed focal cortical dysfunction with epileptiform discharge at left hemisphere. Patient received drug therapy during her stay. Patient developed a fever and Meningitis was suspected, hence antibiotics were started. Lumbar puncture was done, which showed CSF test no abnormalities, meningitis panel PCR all negative. Japanese encephalitis was reported 14 days after the vaccine. Autoimmune and tumor marker all negative. Antibiotic was discontinued and patient was transferred to a different institution for second opinion. Patient has yet to recover from the events. The events were							

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	considered related to the product per the reporter's assessment. The patient's age remains as a confounder to the events. The benefit-risk relationship of mRNA 1273 vaccine is not affected by this report.							
	This case was initially received via European Medicines Agency (Reference number: [REDACTED]) on 22-Dec-2021. The most recent information was received on 23-Dec-2021 and was forwarded to Moderna on 23-Dec-2021. This regulatory authority case was reported by a pharmacist and describes the occurrence of DYSAESTHESIA (dysaesthesia to the feet, to demyelinating psychic polyneuropathy) and DEMYELINATING POLYNEUROPATHY (dysaesthesia to the feet, to demyelinating psychic polyneuropathy) in a 77-year-old female patient who received mRNA-1273 (Spikevax) (batch no. 3001941) for COVID-19 vaccination. No Medical History information was reported. On 24-Apr-2021, the patient received first dose of mRNA-1273 (Spikevax) (Intramuscular) .5 milliliter. On 24-Apr-2021, the patient experienced DYSAESTHESIA (dysaesthesia to the feet, to demyelinating psychic polyneuropathy) (seriousness criterion medically significant) and DEMYELINATING POLYNEUROPATHY (dysaesthesia to the feet, to demyelinating psychic polyneuropathy) (seriousness criterion medically significant). At the time of the report, DYSAESTHESIA (dysaesthesia to the feet, to demyelinating psychic polyneuropathy) and DEMYELINATING POLYNEUROPATHY (dysaesthesia to the feet, to demyelinating psychic polyneuropathy) was resolving. The action taken with mRNA-1273 (Spikevax) (Intramuscular) was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. No relevant concomitant and treatment medications were reported Patient not performed second dose Company comment: This case concerns a 77-year-old female patient, with no reported medical history, who experienced the serious, unexpected AESI of Demyelinating polyneuropathy and the serious, unexpected event of Dysaesthesia. The events occurred the same day after the first dose of mRNA-1273 vaccine. The benefit-risk relationship of mRNA-1273 vaccine is not affected by this report. Event seriousness	No MRI result	Not a case of ADEM	Level 5	Level 5	Unlikely	This regulatory authority reported case concerns a 77-year-old female patient with no reported medical history and concomitant medications, who received an unknown dose of Spikevax and on the same day, reported experiencing "foot disesthesia, and demyelinating sensory polyneuropathy". No diagnostic report was provided. This case is classified as Brighton's level 5-NOT a case of ADEM, based on the absence of symptoms of encephalopathy; and case is considered WHO Unlikely, with a time to onset that makes a relationship improbable. Other disease or medications not reported, could provide plausible explanations.	

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	assessed as per Regulatory Authority reporting as medically significant and retained for consistency with the RA report. Most recent FOLLOW-UP information incorporated above includes: On 23-Dec-2021: Updated outcome for events and event verbatim. On 06-Jan-2022: Follow up received that contains No New Information. On 06-Jan-2022: Follow up received that contains Non significant information.							
	This case was received via European Medicines Agency (Reference number: [REDACTED]) on 23-Dec-2021 and was forwarded to Moderna on 23-Dec-2021. This regulatory authority case was reported by a physician and describes the occurrence of DEMYELINATING POLYNEUROPATHY (Neuropathy demyelinisante) in a 64-year-old male patient who received mRNA-1273 (Spikevax) (batch no. 214018) for COVID-19 vaccination. The patient's past medical history included Monoclonal gammopathy. On 14-Aug-2021, the patient received dose of mRNA-1273 (Spikevax) (Intramuscular) 1 dosage form. In August 2021, the patient experienced DEMYELINATING POLYNEUROPATHY (Neuropathy demyelinisante) (seriousness criterion medically significant). At the time of the report, DEMYELINATING POLYNEUROPATHY (Neuropathy demyelinisante) outcome was unknown. For mRNA-1273 (Spikevax) (Intramuscular), the reporter did not provide any causality assessments. Concomitant product use was not provided by the reporter. No treatment information was provided. This is a regulatory case concerning a 64-year-old male patient with a medical history of monoclonal gammopathy, who experienced the unexpected serious event of demyelinating polyneuropathy. The event occurred on the same month of receiving a dose of mRNA – 1273 vaccine. At the time of report the outcome of the event was unknown. The rechallenge is not applicable since no information about the other dose was disclosed. The reporter's assessment was not provided. The benefit-risk relationship of the vaccine is not affected by this report.	No MRI report	Level 4	Level 5	Level 4	Unassessable	This case of a 64-year-old male patient with medical history of monoclonal gammopathy but no concomitant medications reported; who received an unknown dose of Spikevax and after an unknown time to onset reported demyelinating polyneuropathy". No diagnostic results reported. This case is classified as Brighton's level 5, NOT a case of ADEM based on absence of encephalopathy; and considered WHO Unassessable. This case can not be assessed due to insufficient information.	