ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Spikevax 0.2 mg/mL dispersion for injection
Spikevax 0.1 mg/mL dispersion for injection
Spikevax 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1. Qualitative and quantitative composition by strength and type of container

Strength	Container	Dose(s)	Composition per dose
Spikevax 0.2 mg/mL dispersion for injection	Multidose vial (red flip-off cap)	Maximum 10 doses of 0.5 mL each	One dose (0.5 mL) contains 100 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
		Maximum 20 doses of 0.25 mL each	One dose (0.25 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax 0.1 mg/mL dispersion for injection	Multidose vial (blue flip-off cap)	5 doses of 0.5 mL each	One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
		Maximum 10 doses of 0.25 mL each	One dose (0.25 mL) contains 25 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax 50 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only. Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.	One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (original).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection
White to off white dispersion (pH: 7.0 – 8.0).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Spikevax is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Refer to Table 2 for dosing across Spikevax strengths and vaccination type.

Table 2. Spikevax posology for primary series, a third dose in severely immunocompromised and booster doses

Strength	Vaccination type	Age(s)	Dose	Recommendations
Spikevax 0.2 mg/mL dispersion for injection	Primary series	Individuals 12 years of age and older	2 (two) doses (0.5 mL each, containing 100 micrograms mRNA)	It is recommended to administer the second dose 28 days after the first dose (see sections 4.4 and 5.1).
		Children 6 years through 11 years of age	2 (two) doses (0.25 mL each, containing 50 micrograms mRNA, which is half of the primary dose for individuals 12 years and older)	
	Third dose in severely immuno-compromised	Individuals 12 years of age and older	1 (one) dose of 0.5 mL, containing 100 micrograms mRNA	A third dose may be given at least

Strength	Vaccination type	Age(s)	Dose	Recommendations
		Children 6 years through 11 years of age	1 (one) dose of 0.25 mL, containing 50 micrograms mRNA	28 days after the second dose (see sections 4.8 and 5.1).
	Booster dose	Individuals 12 years of age and older	1 (one) dose of 0.25 mL, containing 50 micrograms mRNA	Spikevax may be used to boost individuals 12 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector vaccine at least 3 months after completion of the primary series (see section 5.1).
Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe*	Primary series†	Children 6 years through 11 years of age	2 (two) doses (0.5 mL each, containing 50 micrograms mRNA each)	It is recommended to administer the second dose 28 days after the first dose (see sections 4.4 and 5.1).
		Children 6 months through 5 years of age	2 (two) doses (0.25 mL each, containing 25 micrograms mRNA each, which is half of the primary dose for children 6 years through 11 years of age)*	
	Third dose in severely immuno-compromised‡	Children 6 years through 11 years of age	1 (one) dose of 0.5 mL, containing 50 micrograms mRNA	A third dose may be given at least 28 days after the second dose (see sections 4.8 and 5.1).
		Children 6 months through 5 years of age	1 (one) dose of 0.25 mL, containing 25 micrograms mRNA*	

Strength	Vaccination type	Age(s)	Dose	Recommendations
	Booster dose	Individuals 12 years of age and older	1 (one) dose of 0.5 mL, containing 50 micrograms mRNA	Spikevax may be used to boost individuals 6 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector vaccine at least 3 months after completion of the primary series (see section 5.1).
		Children 6 years through 11 years of age	1 (one) dose of 0.25 mL, containing 25 micrograms mRNA*	

* Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.
†For primary series for individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.
‡For the third dose in severely immunocompromised individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.

Paediatric population
The safety and efficacy of Spikevax in children less than 6 months of age have not yet been established (see section 5.1).

Elderly
No dose adjustment is required in elderly individuals ≥65 years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm or in infants and young children, the anterolateral aspect of the thigh.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Anaphylaxis has been reported in individuals who have received Spikevax. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. Subsequent doses of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of Spikevax.

Myocarditis and pericarditis

There is an increased risk for myocarditis and pericarditis following vaccination with Spikevax.

These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose (see section 4.8).

Available data indicate that most cases recover. Some cases required intensive care support and fatal cases have been observed.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Capillary leak syndrome flare-ups

A few cases of capillary leak syndrome (CLS) flare-ups have been reported in the first days after vaccination with Spikevax. Healthcare professionals should be aware of signs and symptoms of CLS to promptly recognise and treat the condition. In individuals with a medical history of CLS, planning of vaccination should be made in collaboration with appropriate medical experts.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical studies.

Limitations of vaccine effectiveness

Individuals may not be fully protected until 14 days after their second dose. As with all vaccines, vaccination with Spikevax may not protect all vaccine recipients.

Excipients with known effect

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

Different injectable vaccines should be given at different injection sites.

4.6 Fertility, pregnancy and lactation

Pregnancy

A large amount of observational data from pregnant women vaccinated with Spikevax during the second and third trimester has not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Spikevax can be used during pregnancy.

Breast-feeding

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to Spikevax is negligible. Observational data from women who were breastfeeding after vaccination have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax can be used during breastfeeding.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

Spikevax has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Adults
The safety of Spikevax was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30 351 participants 18 years of age and older who received at least one dose of Spikevax (n=15 185) or placebo (n=15 166)

(NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22 831 (75.2%) of participants were 18 to 64 years of age and 7 520 (24.8%) of participants were 65 years of age and older.

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Adolescents 12 through 17 years of age
Safety data for Spikevax in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study with multiple parts conducted in the United States. The first portion of the study involved 3 726 participants 12 through 17 years of age who received at least one dose of Spikevax (n=2 486) or placebo (n=1 240) (NCT04649151). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

The most frequent adverse reactions in adolescents 12 to 17 years of age were injection site pain (97%), headache (78%), fatigue (75%), myalgia (54%), chills (49%), axillary swelling/tenderness (35%), arthralgia (35%), nausea/vomiting (29%), injection site swelling (28%), injection site erythema (26%), and fever (14%).

This study transitioned to an open-label Phase 2/3 study in which 1 346 participants 12 years through 17 years of age received a booster dose of Spikevax at least 5 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 years through 11 years of age
Safety data for Spikevax in children were collected in an ongoing Phase 2/3 two-part randomised, observer-blind clinical study conducted in the United States and Canada (NCT04796896). Part 1 is an open-label phase of the study for safety, dose selection, and immunogenicity and included 380 participants 6 years through 11 years of age who received at least 1 dose (0.25 mL) of Spikevax. Part 2 is the placebo-controlled phase for safety and included 4 016 participants 6 years through 11 years of age who received at least one dose (0.25 mL) of Spikevax (n=3 012) or placebo (n=1 004). No participants in Part 1 participated in Part 2. Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

The most frequent adverse reactions in participants 6 years through 11 years of age following administration of the primary series (in Part 2) were injection site pain (98.4%), fatigue (73.1%), headache (62.1%), myalgia (35.3%), chills (34.6%), nausea/vomiting (29.3%), axillary swelling/tenderness (27.0%), fever (25.7%), injection site erythema (24.0%), injection site swelling (22.3%), and arthralgia (21.3%).

The study protocol was amended to include an open-label booster dose phase that included 1 294 participants 6 years through 11 years of age who received a booster dose of Spikevax at least 6 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 months through 5 years of age
An ongoing Phase 2/3 randomised, placebo-controlled, observer-blind study to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax was conducted in the United States and Canada.

This study involved 10 390 participants 6 months through 11 years of age who received at least one dose of Spikevax (n=7 798) or placebo (n=2 592).

The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months. This paediatric study involved 6 388 participants 6 months through 5 years of age who received at least one dose of Spikevax (n=4 791) or placebo (n=1 597). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

In this clinical study, the adverse reactions in participants 6 months through 23 months of age following administration of the primary series were irritability/crying (81.5%), pain at the injection site (56.2%), sleepiness (51.1%), loss of appetite (45.7%), fever (21.8%), swelling at the injection site (18.4%), erythema at the injection site (17.9%), and axillary swelling/tenderness (12.2%).

The adverse reactions in participants 24 through 36 months of age following administration of the primary series were pain at the injection site (76.8%), irritability/crying (71.0%), sleepiness (49.7%), loss of appetite (42.4%), fever (26.1%), erythema at the injection site (17.9%), swelling at the injection site (15.7%), and axillary swelling/tenderness (11.5%).

The adverse reactions in participants 37 months through 5 years of age following administration of the primary series were pain at the injection site (83.8%), fatigue (61.9%), headache (22.9%), myalgia (22.1%), fever (20.9%), chills (16.8%), nausea/vomiting (15.2%), axillary swelling/tenderness (14.3%), arthralgia (12.8%), erythema at the injection site (9.5%), and swelling at the injection site (8.2%).

Tabulated list of adverse reactions

The safety profile presented below is based on data generated in several placebo-controlled clinical studies:

- 30 351 adults ≥ 18 years of age
- 3 726 adolescents 12 through 17 years of age
- 4 002 children 6 years through 11 years of age
- 6 388 children aged 6 months through 5 years of age
- and post-marketing experience.

Adverse reactions reported are listed according to the following frequency convention:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness (Table 3).

Table 3. Adverse reactions from Spikevax clinical studies and post authorisation experience in children and individuals 6 months of age and older

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Immune system disorders	Not known	Anaphylaxis
		Hypersensitivity
Metabolism and nutrition disorders	Very common	Decreased appetite†

MedDRA system organ class	Frequency	Adverse reactions
Psychiatric disorders	Very common	Irritability/crying†
Nervous system disorders	Very common	Headache Sleepiness†
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Common	Diarrhoea
	Uncommon	Abdominal pain§
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria¶
	Not known	Erythema multiforme Mechanical urticaria Chronic urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
Reproductive system and breast disorders	Not known	Heavy menstrual bleeding#
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills Pyrexia Injection site swelling Injection site erythema
	Common	Injection site urticaria Injection site rash Delayed injection site reaction♠
	Uncommon	Injection site pruritus
	Rare	Facial swelling♥
	Not known	Extensive swelling of vaccinated limb

*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site. Other lymph nodes (e.g., cervical, supraclavicular) were affected in some cases.

† Observed in the paediatric population (6 months to 5 years of age).

‡ Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the Spikevax group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.

§ Abdominal pain was observed in the paediatric population (6 to 11 years of age): 0.2% in the Spikevax group and 0% in the placebo group.

¶ Urticaria has been observed with either acute onset (within a few days after vaccination) or delayed onset (up to approximately two weeks after vaccination).

Most cases appeared to be non-serious and temporary in nature.

♠ Median time to onset was 9 days after the first injection, and 11 days after the second injection. Median duration was 4 days after the first injection, and 4 days after the second injection.

♥ There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

The reactogenicity and safety profile in 343 subjects receiving Spikevax, that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

Adults (booster dose)

The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in

participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax vaccine primary series. In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (0.25 mL, 50 micrograms) was similar to that after the second dose in the primary series.

Spikevax (original) in solid organ transplant recipients
The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose (fourth dose for mRNA vaccines and third dose for non-mRNA vaccines).

Reactogenicity was consistent with the known profile of Spikevax (original). There were no unexpected safety findings.

Description of selected adverse reactions

Myocarditis
The increased risk of myocarditis after vaccination with Spikevax is highest in younger males (see section 4.4).

Two large European pharmacoepidemiological studies have estimated the excess risk in younger males following the second dose of Spikevax. One study showed that in a period of 7 days after the second dose, there were about 1.316 (95% CI: 1.299, 1.333) extra cases of myocarditis in 12 to 29 year-old males per 10 000 compared to unexposed persons. In another study, in a period of 28 days after the second dose, there were 1.88 (95% CI: 0.956, 2.804) extra cases of myocarditis in 16 to 24 year-old males per 10 000 compared to unexposed persons.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, COVID-19 vaccines, ATC code: J07BN01

Mechanism of action

Spikevax (elasomeran) contains mRNA encapsulated in lipid nanoparticles. The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After

intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is non-replicating, and is expressed transiently mainly by dendritic cells and subcapsular sinus macrophages. The expressed, membrane-bound spike protein of SARS-CoV-2 is then recognised by immune cells as a foreign antigen. This elicits both T-cell and B-cell responses to generate neutralising antibodies, which may contribute to protection against COVID-19.

Clinical efficacy

Clinical efficacy in adults
The adult study was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or had received immunosuppressants within 6 months, as well as participants who were pregnant, or with a known history of SARS-CoV-2 infection. Participants with stable HIV disease were not excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of Spikevax. Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or Spikevax.

A total of 30 351 subjects were followed for a median of 92 days (range: 1-122) for the development of COVID-19 disease.

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28 207 subjects who received either Spikevax (n=14 134) or placebo (n=14 073) and had a negative baseline SARS-CoV-2 status. The PPS study population included 47.4% female, 52.6% male, 79.5% White, 9.7% African American, 4.6% Asian, and 6.2% other. 19.7% of participants identified as Hispanic or Latino. The median age of subjects was 53 years (range 18-94). A dosing window of -7 to +14 days for administration of the second dose (scheduled at day 29) was allowed for inclusion in the PPS. 98% of vaccine recipients received the second dose 25 days to 35 days after dose 1 (corresponding to -3 to +7 days around the interval of 28 days).

COVID-19 cases were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT PCR) and by a Clinical Adjudication Committee. Vaccine efficacy overall and by key age groups are presented in Table 4.

Table 4. Vaccine efficacy analysis: confirmed COVID-19[#] regardless of severity starting 14 days after the 2nd dose – PPS

Age group (years)	Spikevax			Placebo			
	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	% Vaccine efficacy (95% CI)*
Overall (≥18)	14 134	11	3.328	14 073	185	56.510	94.1 (89.3, 96.8)**
18 to <65	10 551	7	2.875	10 521	156	64.625	95.6 (90.6, 97.9)
≥65	3 583	4	4.595	3 552	29	33.728	86.4 (61.4, 95.2)
≥65 to <75	2 953	4	5.586	2 864	22	31.744	82.4% (48.9, 93.9)
≥75	630	0	0	688	7	41.968	100% (NE, 100)

[#]COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the 2nd dose.
*Vaccine efficacy and 95% confidence interval (CI) from the stratified Cox proportional hazard model

** CI not adjusted for multiplicity. Multiplicity adjusted statistical analyses were carried out in an interim analysis based on less COVID-19 cases, not reported here.

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 of 185 (16%) cases reported in the placebo group. Of the 30 participants with severe disease, 9 were hospitalised, 2 of which were admitted to an intensive care unit. The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO2) criterion for severe disease (≤ 93% on room air).

The vaccine efficacy of Spikevax to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% CI: 88.6, 96.5).

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Immunogenicity in adults – after booster dose (0.25 mL, 50 micrograms)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax vaccine as primary series. In an open label phase, 149 of those participants (Per Protocol Set) received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL, 50 micrograms) was shown to result in a geometric mean fold rise (GMFR) of 12.99 (95% CI: 11.04, 15.29) in neutralising antibodies from pre-booster compared to 28 days after the booster dose. The GMFR in neutralising antibodies was 1.53 (95% CI: 1.32, 1.77) when compared 28 days post dose 2 (primary series) to 28 days after the booster dose.

Immunogenicity of a booster dose following primary vaccination with another authorised COVID-19 vaccine in adults
Safety and immunogenicity of a heterologous booster with Spikevax were studied in an investigator-initiated study with 154 participants. The minimum time interval between primary series using a vector based or RNA-based COVID-19 vaccine and booster injection with Spikevax was 12 weeks (range: 12 weeks to 20.9 weeks). The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 1 prior to administration and at Day 15 and Day 29 after the booster dose. A booster response was demonstrated regardless of primary vaccination.

Only short-term immunogenicity data are available; long-term protection and immunological memory are currently unknown.

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) in the UK
COV-BOOST is a multicentre, randomised Phase 2 investigator-initiated study of third dose booster vaccination against COVID-19 with a subgroup to investigate detailed immunology. Participants were adults aged 30 years or older, in good physical health (mild to moderate well-controlled co-morbidities were permitted), who had received two doses of either Pfizer–BioNTech or Oxford–AstraZeneca (first dose in December 2020, January 2021 or February 2021), and were at least 84 days post second dose by the time of enrolment. Spikevax boosted antibody and neutralising responses and was well tolerated regardless of the prime series. The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 28 after the booster dose.

Pre-boost and post-boost neutralising antibody against the B.1.617.2 (Delta) variant in adults
Results of the pseudovirus neutralisation assay (PsVNA) against the B.1.617.2 (Delta) variant determined pre-booster and on Day 29 post booster showed that administration of a booster dose of

Spikevax (0.25 mL, 50 micrograms) in adults induced a 17-fold rise in neutralising antibodies against the Delta variant compared with pre-booster levels (GMFR = 17.28; 95% CI: 14.38, 20.77; n=295).

Clinical efficacy in adolescents 12 through 17 years of age
The adolescent study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study (NCT04649151) to evaluate the safety, reactogenicity, and efficacy of Spikevax in adolescents 12 to 17 years of age. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3 732 participants were randomised 2:1 to receive 2 doses of Spikevax or saline placebo 1 month apart.

A secondary efficacy analysis was performed in 3 181 participants who received 2 doses of either Spikevax (n=2 139) or placebo (n=1 042) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were zero symptomatic COVID-19 cases in the Spikevax group and 4 symptomatic COVID-19 cases in the placebo group.

Immunogenicity in adolescents 12 to 17 years of age – after Spikevax primary vaccination
A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in the per-protocol immunogenicity subsets of adolescents aged 12 through 17 (n=340) in the adolescent study and in participants aged 18 through 25 (n=296) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The geometric mean ratio (GMR) of the neutralising antibody titres in adolescents 12 to 17 years of age compared to the 18- to 25-year-olds was 1.08 (95% CI: 0.94, 1.24). The difference in seroresponse rate was 0.2% (95% CI: -1.8, 2.4). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in adolescents 12 years through 17 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study was to infer efficacy of the booster dose in participants 12 years through 17 years of age by comparing post-booster immune responses (Day 29) to those obtained post-dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in the adult study. Efficacy of the 50 microgram Spikevax booster dose is inferred if post-booster dose immune responses (nAb geometric mean concentration [GMC] and seroresponse rate [SRR]) meet prespecified noninferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy study.

In an open-label phase of this study, participants 12 years through 17 years of age received a single booster dose at least 5 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 257 booster dose participants in this study and a random subset of 295 participants from the young adult study (ages ≥18 to ≤25 years) who previously completed a primary vaccination series of two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

The GMR of the adolescent booster dose Day 29 GMC compared with young adults: Day 57 GMR was 5.1 (95% CI: 4.5, 5.8), meeting the noninferiority criteria (i.e., lower bound of the 95% CI >0.667 (1/1.5); point estimate ≥0.8); the SRR difference was 0.7% (95% CI: -0.8, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

In the 257 participants, pre-booster (booster dose-Day 1) nAb GMC was 400.4 (95% CI: 370.0, 433.4); on BD-Day 29, the GMC was 7 172.0 (95% CI: 6 610.4, 7 781.4). Post-booster booster dose-Day 29 GMC increased approximately 18-fold from pre-booster GMC, demonstrating the potency of the booster dose to adolescents. The SRR was 100 (95% CI: 98.6, 100.0).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of vaccine efficacy from the adult study.

Clinical efficacy in children 6 years through 11 years of age
The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study to evaluate the safety, reactogenicity, and efficacy of Spikevax in children aged 6 years through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 4 016 participants were randomised 3:1 to receive 2 doses of Spikevax or saline placebo 1 month apart.

A secondary efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 10 November 2021 was performed in 3 497 participants who received two doses (0.25 mL at 0 and 1 month) of either Spikevax (n=2 644) or placebo (n=853) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were three COVID-19 cases (0.1%) in the Spikevax group and four COVID-19 cases (0.5%) in the placebo group.

Immunogenicity in children 6 years through 11 years of age
An analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in a subset of children aged 6 years through 11 years (n=319) in the paediatric study and in participants aged 18 through 25 years (n=295) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titres in children 6 years through 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9, 2.1). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in children 6 years through 11 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study is to infer efficacy of the booster dose in participants 6 years through 11 years of age by comparing post-booster dose immune responses (Day 29) to those obtained post dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in that study, where 93% efficacy was demonstrated. Efficacy of the 25 microgram Spikevax booster dose is inferred if post-booster dose immune responses (neutralising antibody [nAb] geometric mean concentration [GMC] and seroresponse rate [SRR]) meet pre-specified non-inferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy trial.

In an open-label phase of this study, participants 6 years through 11 years of age received a single booster dose at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 95 booster dose participants in 6 years through 11-year-olds and a random subset of 295 participants from the young adult study who received two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

In the 95 participants, on booster dose-Day 29, the GMC was 5 847.5 (95% CI: 4 999.6, 6 839.1). The SRR was 100 (95% CI: 95.9, 100.0). Serum nAb levels for children 6 years through 11 years in the per-protocol immunogenicity subset with pre-booster SARS-CoV-2 negative status and the comparison with those from young adults (18 to 25 years of age) were studied. The GMR of booster dose Day 29 GMC compared to young adults Day 57 GMC was 4.2 (95% CI: 3.5, 5.0), meeting the noninferiority criteria (i.e., lower bound of the 95% CI > 0.667); the SRR difference was 0.7% (95% CI: -3.5, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of booster dose vaccine efficacy. The brisk recall response evident within 4 weeks of booster dosing is evidence of the robust priming induced by the Spikevax primary series.

Neutralising antibody against the B.1.617.2 (Delta) variant in children 6 years through 11 years of age
Serum samples of the per-protocol immunogenicity subset (n=134) of the ongoing paediatric study obtained at baseline and on Day 57 were tested in a PsVNA based on the B.1.617.2 (Delta) variant. In children 6 years through 11 years of age, the GMFR from baseline to D57 was 81.77 (95% CI: 70.38, 95.00) for the Delta variant (measured by PsVNA). Furthermore, 99.3% of children met the definition of seroresponse.

Clinical efficacy in children 6 months through 5 years of age
An ongoing Phase 2/3 study was conducted to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax in healthy children 6 months through 11 years of age. The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 21 February 2022 was performed in 5 476 participants 6 months through 5 years of age who received two doses (at 0 and 1 month) of either Spikevax (n=4 105) or placebo (n=1 371) and had a negative baseline SARS-CoV-2 status (referred to as the Per Protocol Set for Efficacy). Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics.

The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 years through 5 years of age and 68 days for participants 6 months through 23 months of age.

Vaccine efficacy in this study was observed during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

Vaccine efficacy (VE) in Part 2 for the Per Protocol Set for Efficacy for COVID-19 cases 14 days or more after dose 2 using the “COVID-19 P301 case definition” (i.e., the definition employed in the pivotal adult efficacy study) was 46.4% (95% CI: 19.8, 63.8) for children 2 years through 5 years of age and 31.5% (95% CI: -27.7, 62.0) for children 6 months through 23 months of age.

Immunogenicity in children 6 months through 5 years of age
For children aged 2 years through 5 years of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 264; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.014 (95% CI: 0.881, 1.167), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The geometric mean fold rise (GMFR) from baseline to Day 57 for these children was 183.3 (95% CI: 164.03, 204.91). The difference in seroresponse rates (SRR) between the children and young adults was -0.4% (95% CI: -2.7%, 1.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the SRR difference > -10%).

For infants and toddlers from 6 months through 23 months of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 230; 25 micrograms) to those of

young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.280 (95% CI: 1.115, 1.470), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in SRR rates between the infants/toddlers and young adults was 0.7% (95% CI: -1.0%, 2.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the seroresponse rate difference > -10%).

Accordingly, the prespecified success criteria for the primary immunogenicity objective were met for both age groups, allowing efficacy of 25 micrograms to be inferred in both children 2 years through 5 years and infants and toddlers aged 6 months through 23 months (Tables 5 and 6).

Table 5. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 6 months through 23 months of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		6 months through 23 months n=230	**18 years through 25 years n=291**	**6 months through 23 months/ 18 years through 25 years**	
Assay	**Time point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 780.7 (1 606.4, 1 973.8)	1 390.8 (1 269.1, 1 524.2)	1.3 (1.1, 1.5)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralising antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 6. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 2 years through 5 years of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		2 years through 5 years n=264	18 years through 25 years n=291	2 years through 5 years/ 18 years through 25 years	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 410.0 (1 273.8, 1 560.8)	1 390.8 (1 262.5, 1 532.1)	1.0 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

GMC = Geometric mean concentration

n = number of participants with non-missing data at baseline and at Day 57

* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.

[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.

[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.

[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.

[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Available data in children 12 weeks to 6 months of age

The safety and immunogenicity of Spikevax bivalent Original/Omicron BA.1 were evaluated in children 12 weeks to 6 months of age in Study P206. During the dose-finding part of the study, two dose levels (5 mcg and 10 mcg) evaluated as a two-dose regimen were generally well tolerated but did not lead to a substantial immune response.

Immunogenicity in solid organ transplant recipients

The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose.

Immunogenicity in the study was assessed by measurement of neutralising antibodies against pseudovirus expressing the ancestral SARS-CoV-2 (D614G) strain at 1 month after Dose 2, Dose 3, booster dose and up to 12 months from the last dose in Part A, and up to 6 months from booster dose in Part B.

Three doses of Spikevax (original) induced enhanced neutralising antibody titres compared to pre-dose 1 and post-dose 2. A higher proportion of SOT participants who had received three doses achieved seroresponse compared to participants who had received two doses. The neutralising antibody levels observed in SOT liver participants who had received three doses was comparable to the post-dose 2 responses observed in the immunocompetent, baseline SARS-CoV-2-negative adult participants. The neutralising antibody responses continued to be numerically lower post-dose 3 in SOT kidney participants compared to SOT liver participants. The neutralising levels observed one month after Dose 3 persisted through six months with antibody levels maintained at 26-fold higher and seroresponse rate at 67% compared to baseline.

A fourth (booster) dose of Spikevax (original) enhanced neutralising antibody response in SOT participants compared to post-dose 3, regardless of the previous vaccines received [mRNA-1273 (Moderna), BNT162b2 or any mRNA-containing combination]; however, SOT kidney participants had numerically lower neutralising antibody responses compared to SOT liver participants.

Elderly

Spikevax was assessed in individuals 6 months of age and older, including 3 768 subjects 65 years of age and older. The efficacy of Spikevax was consistent between elderly (≥65 years) and younger adult subjects (18-64 years).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with the Spikevax in one or more subsets of the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and reproductive and developmental toxicity.

General toxicity

General toxicity studies were conducted in rats (intramuscularly receiving up to 4 doses exceeding the human dose once every 2 weeks). Transient and reversible injection site oedema and erythema and transient and reversible changes in laboratory tests (including increases in eosinophils, activated partial thromboplastin time, and fibrinogen) were observed. Results suggests the toxicity potential to humans is low.

Genotoxicity/carcinogenicity

In vitro and *in vivo* genotoxicity studies were conducted with the novel lipid component SM-102 of the vaccine. Results suggests the genotoxicity potential to humans is very low. Carcinogenicity studies were not performed.

Reproductive toxicity

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 micrograms) and other ingredients included in a single human dose of Spikevax was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. SARS-CoV-2 antibody responses were present in maternal animals from prior to mating to the end of the study on lactation day 21 as well as in foetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryo foetal or offspring development or postnatal development. No data are available of Spikevax vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate)
Cholesterol
1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
Trometamol
Trometamol hydrochloride
Acetic acid
Sodium acetate trihydrate
Sucrose
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened multidose vial (Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, the unopened vaccine vial may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. Within this period, up to 12 hours may be used for transportation at 2°C to 8°C (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened vaccine vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the unopened vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

The unopened vaccine may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Punctured multidose vial (Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection)

Chemical and physical in-use stability has been demonstrated for 19 hours at 2°C to 25ºC after initial puncture (within the allowed use period of 30 days or 14 days, respectively, at 2°C to 8ºC and

including 24 hours at 8°C to 25ºC). From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

Spikevax 50 micrograms dispersion for injection in pre-filled syringe

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, pre-filled syringes may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened pre-filled syringes when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the pre-filled syringe will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

Pre-filled syringes may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

6.4 Special precautions for storage

Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection (multidose vials)

Store in a freezer at -50ºC to -15ºC.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.
For storage conditions of the multidose vial after first opening, see section 6.3.

Transportation of thawed multidose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 12 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax 50 micrograms dispersion for injection in pre-filled syringe

Store in a freezer at -50ºC to -15ºC.
Keep the pre-filled syringe in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use.

6.5 Nature and contents of container

Multidose vials

Spikevax 0.2 mg/mL dispersion for injection
5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a red flip-off plastic cap with seal (aluminium seal).

Pack size: 10 multidose vials. Each vial contains 5 mL.

Spikevax 0.1 mg/mL dispersion for injection
2.5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax 50 micrograms dispersion for injection in pre-filled syringe

0.5 mL dispersion in a pre-filled syringe (cyclic olefin polymer) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack size: 10 pre-filled syringes. Each pre-filled syringe contains 0.5 mL. Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.

6.6 Special precautions for disposal and other handling

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.

Store vials and pre-filled syringes in a freezer at -50ºC to -15ºC.

Keep the vial and pre-filled syringe in the outer carton in order to protect from light.

Multidose vial

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal.

Spikevax 0.2 mg/mL dispersion for injection
A maximum of ten (10) doses (of 0.5 mL each) or a maximum of twenty (20) doses (of 0.25 mL each) can be withdrawn from each vial (red flip-off cap).

Pierce the stopper preferably at a different site each time. Do not puncture the vial more than 20 times.

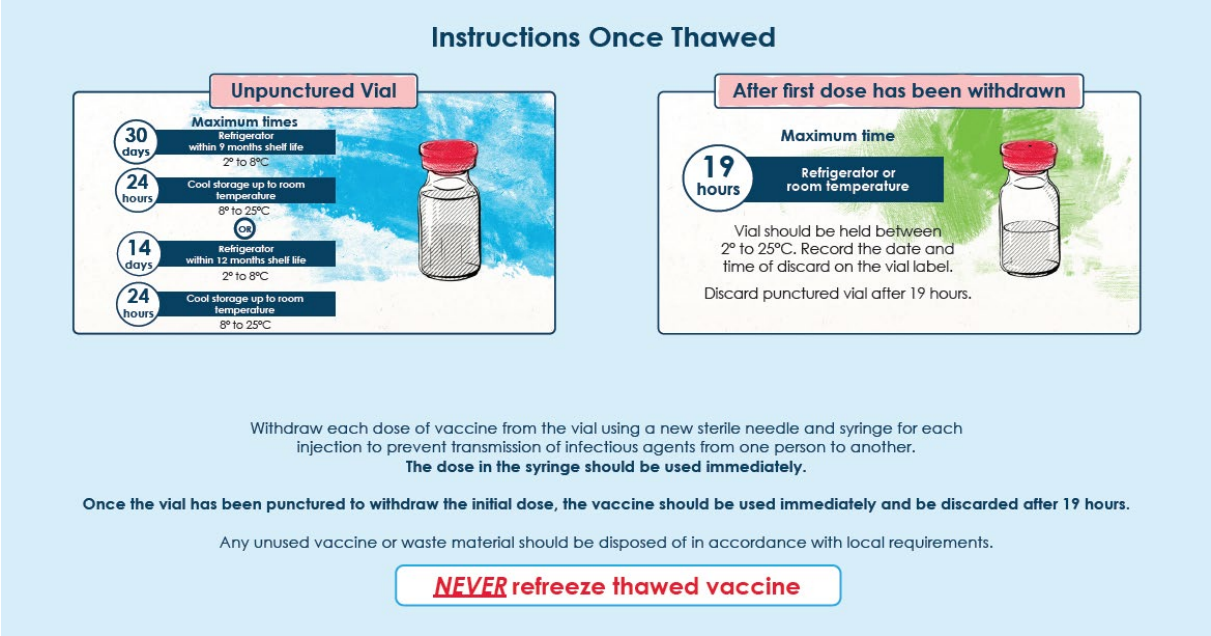
An additional overfill is included in each vial to ensure that a maximum of 10 doses of 0.5 mL or a maximum of 20 doses of 0.25 mL can be delivered.

Verify that the vial has a red flip-off cap and the product name is Spikevax 0.2 mg/mL. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each multidose vial before use following the instructions below (Table 7).

Table 7. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax 0.1 mg/mL dispersion for injection
Five (5) doses (of 0.5 mL each) or a maximum of ten (10) doses (of 0.25 mL each) can be withdrawn from each vial (blue flip-off cap).

Verify that the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

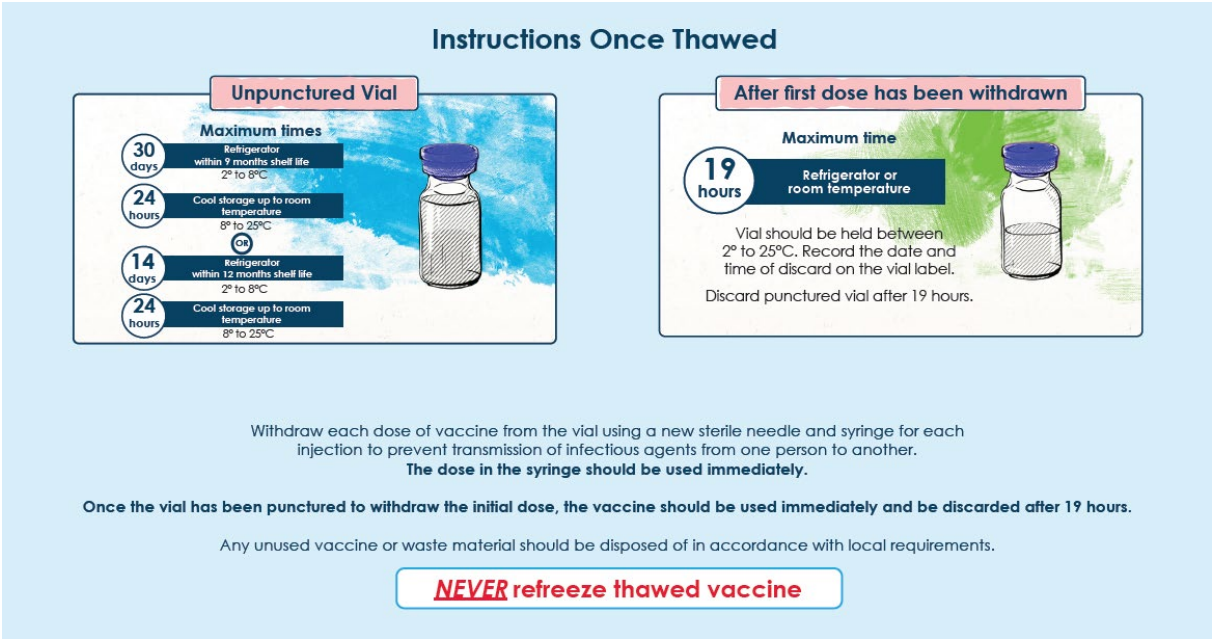
Pierce the stopper preferably at a different site each time.

An additional overfill is included in each vial to ensure that 5 doses of 0.5 mL or a maximum of 10 doses of 0.25 mL can be delivered.

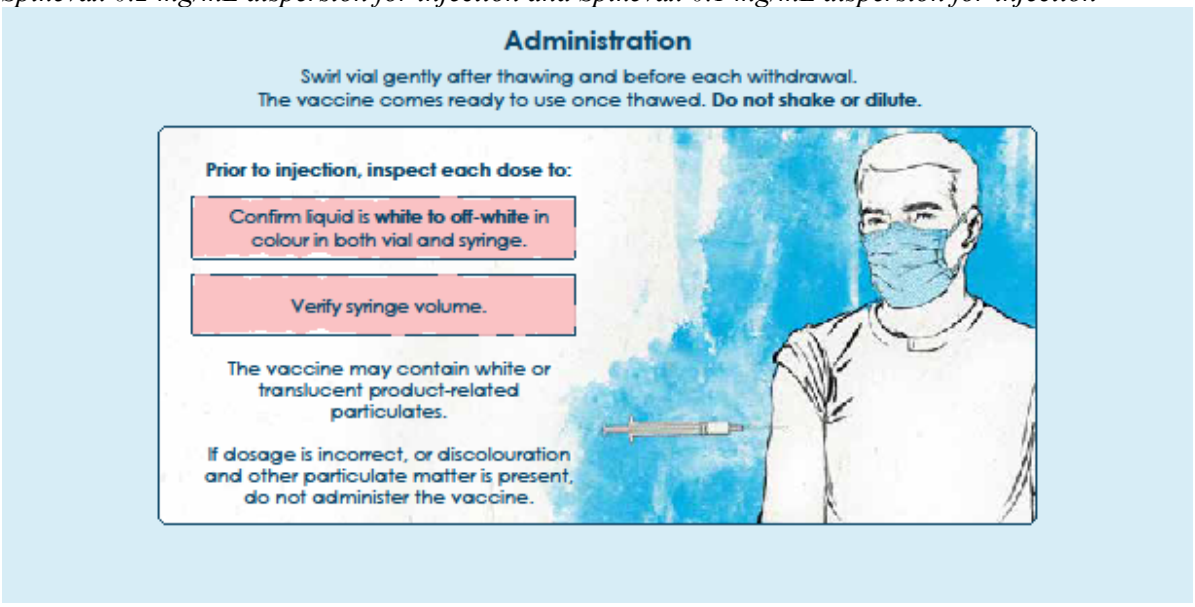
Thaw each multidose vial before use following the instructions below (Table 8).

Table 8. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection



Spikevax 50 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe. Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.

Spikevax is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (50 micrograms) mRNA and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 9).

Table 9. Thawing instructions for pre-filled syringes and cartons before use

Configuration	**Thaw instructions and duration**			
	Thaw temperature (in a refrigerator) (°C)	**Thaw duration (minutes)**	**Thaw temperature (at room temperature) (°C)**	**Thaw duration (minutes)**
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax 50 micrograms. If the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31

28037 Madrid
Spain

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/001
EU/1/20/1507/002
EU/1/20/1507/003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2021
Date of latest renewal: 03 October 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection
Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection
Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1. Spikevax bivalent Original/Omicron BA.1 qualitative and quantitative composition

Strength	**Container**	**Dose(s)**	**Composition per dose**
Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
	Multidose 5 mL vial (blue flip-off cap)	10 doses of 0.5 mL each or 20 doses of 0.25 mL each	
Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection	Single-dose 0.5 mL vial (blue flip-off cap)	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	

Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (original).

Imelasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron BA.1).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection
White to off white dispersion (pH: 7.0 – 8.0).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Spikevax bivalent Original/Omicron BA.1 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 years of age and older who have previously received at least a primary vaccination course against COVID-19 (see sections 4.2 and 5.1).

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 12 years of age and older
The dose of Spikevax bivalent Original/Omicron BA.1 is 0.5 mL given intramuscularly.

Children 6 years through 11 years of age
The dose of Spikevax bivalent Original/Omicron BA.1 is 0.25 mL given intramuscularly.

There should be an interval of at least 3 months between administration of Spikevax bivalent Original/Omicron BA.1 and the last prior dose of a COVID-19 vaccine.

Spikevax bivalent Original/Omicron BA.1 is only indicated for individuals who have previously received at least a primary vaccination course against COVID-19.

For details on the primary vaccination course for ages 6 and above, please refer to the Summary of Product Characteristics for Spikevax 0.2 mg/mL dispersion for injection.

Paediatric population
The safety and efficacy of Spikevax in children less than 6 months of age have not yet been established (see section 5.1).

Elderly
No dose adjustment is required in elderly individuals ≥65 years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Anaphylaxis has been reported in individuals who have received Spikevax (original). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. Subsequent doses of Spikevax bivalent Original/Omicron BA.1 should not be given to those who have experienced anaphylaxis to a prior dose of Spikevax (original).

Myocarditis and pericarditis

There is an increased risk for myocarditis and pericarditis following vaccination with Spikevax.

These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose (see section 4.8).

Available data indicate that most cases recover. Some cases required intensive care support and fatal cases have been observed.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Capillary leak syndrome flare-ups

A few cases of capillary leak syndrome (CLS) flare-ups have been reported in the first days after vaccination with Spikevax (original). Healthcare professionals should be aware of signs and symptoms of CLS to promptly recognise and treat the condition. In individuals with a medical history of CLS, planning of vaccination should be made in collaboration with appropriate medical experts.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical studies.

Limitations of vaccine effectiveness

As with all vaccines, vaccination with Spikevax bivalent Original/Omicron BA.1 may not protect all vaccine recipients.

Excipients with known effect

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say, essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

Different injectable vaccines should be given at different injection sites.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.1 during pregnancy.

However, a large amount of observational data from pregnant women vaccinated with Spikevax (original) during the second and third trimester has not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, Spikevax bivalent Original/ Omicron BA.1 can be used during pregnancy.

Breast-feeding

No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.1 during breastfeeding.

However, no effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to the vaccine is negligible. Observational data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax bivalent Original/Omicron BA.1 can be used during breastfeeding.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

Spikevax bivalent Original/Omicron BA.1 has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Adults
The safety of Spikevax (original) was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30 351 participants 18 years of age and older who received at least one dose of Spikevax (original) (n=15 185) or placebo (n=15 166) (NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22 831 (75.2%) of participants were 18 to 64 years of age and 7 520 (24.8%) of participants were 65 years of age and older.

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Adolescents 12 through 17 years of age
Safety data for Spikevax (original) in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study with multiple parts conducted in the United States. The first portion of the study involved 3 726 participants 12 through 17 years of age who received at least one dose of Spikevax (original) (n=2 486) or placebo (n=1 240) (NCT04649151). Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in adolescents 12 to 17 years of age were injection site pain (97%), headache (78%), fatigue (75%), myalgia (54%), chills (49%), axillary swelling/tenderness (35%), arthralgia (35%), nausea/vomiting (29%), injection site swelling (28%), injection site erythema (26%), and fever (14%).

This study transitioned to an open-label Phase 2/3 study in which 1 346 participants 12 years through 17 years of age received a booster dose of Spikevax at least 5 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 years through 11 years of age
Safety data for Spikevax (original) in children were collected in an ongoing Phase 2/3 two-part randomised, observer-blind clinical study conducted in the United States and Canada (NCT04796896). Part 1 is an open-label phase of the study for safety, dose selection, and immunogenicity and included 380 participants 6 years through 11 years of age who received at least 1 dose (0.25 mL) of Spikevax (original). Part 2 is the placebo-controlled phase for safety and included 4 016 participants 6 years through 11 years of age who received at least one dose (0.25 mL) of Spikevax (original) (n=3 012) or placebo (n=1 004). No participants in Part 1 participated in Part 2. Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in participants 6 years through 11 years of age following administration of the primary series (in Part 2) were injection site pain (98.4%), fatigue (73.1%), headache (62.1%), myalgia (35.3%), chills (34.6%), nausea/vomiting (29.3%), axillary swelling/tenderness (27.0%), fever (25.7%), injection site erythema (24.0%), injection site swelling (22.3%), and arthralgia (21.3%).

The study protocol was amended to include an open-label booster dose phase that included 1 294 participants 6 years through 11 years of age who received a booster dose of Spikevax (original) at least 6 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 months through 5 years of age
An ongoing Phase 2/3 randomised, placebo-controlled, observer-blind study to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax (original) was conducted in the United States and Canada. This study involved 10 390 participants 6 months through 11 years of age who received at least one dose of Spikevax (n=7 798) or placebo (n=2 592).

The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months. This paediatric study involved 6 388 participants 6 months through 5 years of age who received at least one dose of Spikevax (original) (n=4 791) or placebo (n=1 597). Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

In this clinical study, the adverse reactions in participants 6 months through 23 months of age following administration of the primary series were irritability/crying (81.5%), pain at the injection site (56.2%), sleepiness (51.1%), loss of appetite (45.7%), fever (21.8%), swelling at the injection site (18.4%), erythema at the injection site (17.9%), and axillary swelling/tenderness (12.2%).

The adverse reactions in participants 24 through 36 months of age following administration of the primary series were pain at the injection site (76.8%), irritability/crying (71.0%), sleepiness (49.7%), loss of appetite (42.4%), fever (26.1%), erythema at the injection site (17.9%), swelling at the injection site (15.7%), and axillary swelling/tenderness (11.5%).

The adverse reactions in participants 37 months through 5 years of age following administration of the primary series were pain at the injection site (83.8%), fatigue (61.9%), headache (22.9%), myalgia (22.1%), fever (20.9%), chills (16.8%), nausea/vomiting (15.2%), axillary swelling/tenderness (14.3%), arthralgia (12.8%), erythema at the injection site (9.5%), and swelling at the injection site (8.2%).

Tabulated list of adverse reactions

The safety profile presented below is based on data generated in several placebo-controlled clinical studies:
- 30 351 adults ≥ 18 years of age
- 3 726 adolescents 12 through 17 years of age
- 4 002 children 6 years through 11 years of age

- 6 388 children aged 6 months through 5 years of age
- and post-marketing experience.

Adverse reactions reported are listed according to the following frequency convention:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness (Table 2).

Table 2. Adverse reactions from Spikevax (original) clinical studies and post authorisation experience in children and individuals 6 months of age and older

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Immune system disorders	Not known	Anaphylaxis
		Hypersensitivity
Metabolism and nutrition disorders	Very common	Decreased appetite†
Psychiatric disorders	Very common	Irritability/crying†
Nervous system disorders	Very common	Headache Sleepiness†
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Common	Diarrhoea
	Uncommon	Abdominal pain§
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria¶
	Not known	Erythema multiforme Mechanical urticaria Chronic urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
Reproductive system and breast disorders	Not known	Heavy menstrual bleeding#
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills Pyrexia Injection site swelling Injection site erythema
	Common	Injection site urticaria Injection site rash Delayed injection site reaction♠
	Uncommon	Injection site pruritus

MedDRA system organ class	Frequency	Adverse reactions
	Rare	Facial swelling♥
	Not known	Extensive swelling of vaccinated limb

*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site. Other lymph nodes (e.g., cervical, supraclavicular) were affected in some cases.
† Observed in the paediatric population (6 months to 5 years of age).
‡ Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the Spikevax (original) group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.
§ Abdominal pain was observed in the paediatric population (6 to 11 years of age): 0.2% in the Spikevax (original) group and 0% in the placebo group.
¶ Urticaria has been observed with either acute onset (within a few days after vaccination) or delayed onset (up to approximately two weeks after vaccination).
# Most cases appeared to be non-serious and temporary in nature.
♠ Median time to onset was 9 days after the first injection, and 11 days after the second injection. Median duration was 4 days after the first injection, and 4 days after the second injection.
♥ There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

The reactogenicity and safety profile in 343 subjects receiving Spikevax (original), that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

Adults (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine primary series. In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (0.25 mL, 50 micrograms) was similar to that after the second dose in the primary series.

Spikevax bivalent Original/Omicron BA.1 (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax bivalent Original/Omicron BA.1 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Spikevax bivalent Original/Omicron BA.1 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose. The frequency of adverse reactions after immunisation with Spikevax bivalent Original/Omicron BA.1 was also similar or lower relative to that of a first booster dose of Spikevax (original) (50 micrograms) and relative to the second dose of the Spikevax (original) primary series (100 micrograms). The safety profile of Spikevax bivalent Original/Omicron BA.1 (median follow-up period of 113 days) was similar to the safety profile of Spikevax (original) (median follow up period of 127 days).

Spikevax (original) in solid organ transplant recipients
The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose (fourth dose for mRNA vaccines and third dose for non-mRNA vaccines).

Reactogenicity was consistent with the known profile of Spikevax (original). There were no unexpected safety findings.

Description of selected adverse reactions

Myocarditis
The increased risk of myocarditis after vaccination with Spikevax (original) is highest in younger males (see section 4.4).

Two large European pharmacoepidemiological studies have estimated the excess risk in younger males following the second dose of Spikevax (original). One study showed that in a period of 7 days after the second dose, there were about 1.316 (95% CI: 1.299, 1.333) extra cases of myocarditis in 12 to 29 year-old males per 10 000 compared to unexposed persons. In another study, in a period of 28 days after the second dose, there were 1.88 (95% CI: 0.956, 2.804) extra cases of myocarditis in 16 to 24 year-old males per 10 000 compared to unexposed persons.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, COVID-19 vaccines, ATC code: J07BN01

Mechanism of action

Spikevax (elasomeran) and Spikevax bivalent Original/Omicron BA.1 (elasomeran/imelasomeran) both contain mRNA encapsulated in lipid nanoparticles. The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is non-replicating, and is expressed transiently mainly by dendritic cells and subcapsular sinus macrophages. The expressed, membrane-bound spike protein of SARS-CoV-2 is then recognised by immune cells as a foreign antigen. This elicits both T-cell and B-cell responses to generate neutralising antibodies, which may contribute to protection against COVID-19.

Clinical efficacy

Immunogenicity in adults – after Spikevax bivalent Original/Omicron BA.1 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.1 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent

Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part G evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.1 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a booster dose of Spikevax (original) (50 micrograms) at least 3 months prior to enrolment. In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part F group serves as the within-study, non-contemporaneous comparator group for Part G in the comparison between the two booster vaccines, Spikevax bivalent Original/Omicron BA.1 and Spikevax (original), when administered as second booster doses.

In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the original SARS-CoV-2 estimated neutralising antibody geometric mean titre (GMT) and corresponding 95% CI was 6 422.3 (5 990.1, 6 885.7) and 5 286.6 (4 887.1, 5 718.9) 28 days after the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster doses, respectively. These GMTs represent the ratio between response of Spikevax bivalent Original/Omicron BA.1 versus Spikevax (original) against the ancestral SARS-CoV-2 (D614G) strain. The GMR (97.5% CI) was 1.22 (1.08, 1.37) meeting the pre-specified criterion for non-inferiority (lower bound of 97.5% CI ≥0.67).

The estimated Day 29 neutralising antibody GMTs against Omicron, BA.1 were 2 479.9 (2 264.5, 2 715.8) and 1 421.2 (1 283.0, 1 574.4) in the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster groups, respectively, and the GMR (97.5% CI) was 1.75 (1.49, 2.04), which met the pre-specified superiority criterion (lower bound of CI >1).

Three-month antibody persistence of Spikevax bivalent Original/Omicron BA.1 booster vaccine against COVID-19
Participants in Study P205 Part G were sequentially enrolled to receive 50 micrograms of Spikevax (original) (n = 376) or Spikevax bivalent Original/Omicron BA.1 (n = 437) as second booster doses. In participants with no pre-booster incidence of SARS-CoV-2, Spikevax bivalent Original/Omicron BA.1 elicited Omicron-BA.1-neutralising antibody titres (observed GMT) that were significantly higher (964.4 [834.4, 1 114.7]) than those of Spikevax (original) (624.2 [533.1, 730.9]) and similar between boosters against ancestral SARS-CoV-2 at three months.

Clinical efficacy in adults
The adult study was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or had received immunosuppressants within 6 months, as well as participants who were pregnant, or with a known history of SARS-CoV-2 infection. Participants with stable HIV disease were not excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of Spikevax (original). Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or Spikevax (original).

A total of 30 351 subjects were followed for a median of 92 days (range: 1-122) for the development of COVID-19 disease.

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28 207 subjects who received either Spikevax (original) (n=14 134) or placebo (n=14 073) and had a negative baseline SARS-CoV-2 status. The PPS study population included 47.4% female, 52.6% male, 79.5% White, 9.7% African American, 4.6% Asian, and 6.2% other. 19.7% of participants identified as Hispanic or Latino. The median age of subjects was 53 years (range 18-94). A dosing window of –7 to +14 days for administration of the second dose (scheduled at day 29) was allowed for inclusion in the PPS. 98% of vaccine recipients received the second dose 25 days to 35 days after dose 1 (corresponding to -3 to +7 days around the interval of 28 days).

COVID-19 cases were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT PCR) and by a Clinical Adjudication Committee. Vaccine efficacy overall and by key age groups are presented in Table 3.

Table 3. Vaccine efficacy analysis: confirmed COVID-19[#] regardless of severity starting 14 days after the 2nd dose – PPS

Age group (years)	Spikevax (original)			Placebo			
	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	% Vaccine efficacy (95% CI)*
Overall (≥18)	14 134	11	3.328	14 073	185	56.510	94.1 (89.3, 96.8)**
18 to <65	10 551	7	2.875	10 521	156	64.625	95.6 (90.6, 97.9)
≥65	3 583	4	4.595	3 552	29	33.728	86.4 (61.4, 95.2)
≥65 to <75	2 953	4	5.586	2 864	22	31.744	82.4% (48.9, 93.9)
≥75	630	0	0	688	7	41.968	100% (NE, 100)

[#]COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the 2nd dose.
*Vaccine efficacy and 95% confidence interval (CI) from the stratified Cox proportional hazard model
** CI not adjusted for multiplicity. Multiplicity adjusted statistical analyses were carried out in an interim analysis based on less COVID-19 cases, not reported here.

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 of 185 (16%) cases reported in the placebo group. Of the 30 participants with severe disease, 9 were hospitalised, 2 of which were admitted to an intensive care unit. The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO2) criterion for severe disease (≤ 93% on room air).

The vaccine efficacy of Spikevax (original) to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% CI: 88.6, 96.5).

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Immunogenicity in adults – after booster dose (0.25 mL, 50 micrograms)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine as primary series. In an open-label phase, 149 of those participants (Per Protocol Set) received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL, 50 micrograms) was shown to result in a geometric mean fold rise (GMFR) of 12.99 (95% CI: 11.04, 15.29) in neutralising antibodies from pre-booster compared to

28 days after the booster dose. The GMFR in neutralising antibodies was 1.53 (95% CI: 1.32, 1.77) when compared 28 days post dose 2 (primary series) to 28 days after the booster dose.

Immunogenicity of a booster dose following primary vaccination with another authorised COVID-19 vaccine in adults
Safety and immunogenicity of a heterologous booster with Spikevax (original) were studied in an investigator-initiated study with 154 participants. The minimum time interval between primary series using a vector-based or RNA-based COVID-19 vaccine and booster injection with Spikevax (original) was 12 weeks (range: 12 weeks to 20.9 weeks). The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 1 prior to administration and at Day 15 and Day 29 after the booster dose. A booster response was demonstrated regardless of primary vaccination.

Only short-term immunogenicity data are available; long-term protection and immunological memory are currently unknown.

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) in the UK
COV-BOOST is a multicentre, randomised Phase 2 investigator-initiated study of third dose booster vaccination against COVID-19 with a subgroup to investigate detailed immunology. Participants were adults aged 30 years or older, in good physical health (mild to moderate well-controlled co-morbidities were permitted), who had received two doses of either Pfizer–BioNTech or Oxford–AstraZeneca (first dose in December 2020, January 2021 or February 2021), and were at least 84 days post second dose by the time of enrolment. Spikevax (original) boosted antibody and neutralising responses and was well tolerated regardless of the prime series. The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 28 after the booster dose.

Pre-boost and post-boost neutralising antibody against the B.1.617.2 (Delta) variant in adults
Results of the pseudovirus neutralisation assay (PsVNA) against the B.1.617.2 (Delta) variant determined pre-booster and on Day 29 post-booster showed that administration of a booster dose of Spikevax (original) (0.25 mL, 50 micrograms) in adults induced a 17-fold rise in neutralising antibodies against the Delta variant compared with pre-booster levels (GMFR = 17.28; 95% CI: 14.38, 20.77; n=295).

Clinical efficacy in adolescents 12 through 17 years of age
The adolescent study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study (NCT04649151) to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in adolescents 12 to 17 years of age. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3 732 participants were randomised 2:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis was performed in 3 181 participants who received 2 doses of either Spikevax (original) (n=2 139) or placebo (n=1 042) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were zero symptomatic COVID-19 cases in the Spikevax (original) group and 4 symptomatic COVID-19 cases in the placebo group.

Immunogenicity in adolescents 12 to 17 years of age – after Spikevax primary vaccination
A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in the per-protocol immunogenicity subsets of adolescents aged 12 through 17 (n=340) in the adolescent study and in participants aged 18 through 25 (n=296) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at

baseline. The geometric mean ratio (GMR) of the neutralising antibody titres in adolescents 12 to 17 years of age compared to the 18- to 25-year-olds was 1.08 (95% CI: 0.94, 1.24). The difference in seroresponse rate was 0.2% (95% CI: -1.8, 2.4). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in adolescents 12 years through 17 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study was to infer efficacy of the booster dose in participants 12 years through 17 years of age by comparing post-booster immune responses (Day 29) to those obtained post-dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in the adult study. Efficacy of the 50 microgram Spikevax booster dose is inferred if post-booster dose immune responses (nAb geometric mean concentration [GMC] and seroresponse rate [SRR]) meet prespecified noninferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy study.

In an open-label phase of this study, participants 12 years through 17 years of age received a single booster dose at least 5 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 257 booster dose participants in this study and a random subset of 295 participants from the young adult study (ages ≥18 to ≤25 years) who previously completed a primary vaccination series of two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

The GMR of the adolescent booster dose Day 29 GMC compared with young adults: Day 57 GMR was 5.1 (95% CI: 4.5, 5.8), meeting the noninferiority criteria (i.e., lower bound of the 95% CI >0.667 (1/1.5); point estimate ≥0.8); the SRR difference was 0.7% (95% CI: -0.8, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

In the 257 participants, pre-booster (booster dose-Day 1) nAb GMC was 400.4 (95% CI: 370.0, 433.4); on BD-Day 29, the GMC was 7 172.0 (95% CI: 6 610.4, 7 781.4). Post-booster booster dose-Day 29 GMC increased approximately 18-fold from pre-booster GMC, demonstrating the potency of the booster dose to adolescents. The SRR was 100 (95% CI: 98.6, 100.0).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of vaccine efficacy from the adult study.

Clinical efficacy in children 6 years through 11 years of age
The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in children aged 6 years through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 4 016 participants were randomised 3:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 10 November 2021 was performed in 3 497 participants who received two doses (0.25 mL at 0 and 1 month) of either Spikevax (original) (n=2 644) or placebo (n=853) and had a negative baseline

SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were three COVID-19 cases (0.1%) in the Spikevax (original) group and four COVID-19 cases (0.5%) in the placebo group.

Immunogenicity in children 6 years through 11 years of age
An analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in a subset of children aged 6 years through 11 years (n=319) in the paediatric study and in participants aged 18 through 25 years (n=295) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titres in children 6 years through 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9, 2.1). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in children 6 years through 11 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study is to infer efficacy of the booster dose in participants 6 years through 11 years of age by comparing post-booster dose immune responses (Day 29) to those obtained post dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in that study, where 93% efficacy was demonstrated. Efficacy of the 25 microgram Spikevax booster dose is inferred if post-booster dose immune responses (neutralising antibody [nAb] geometric mean concentration [GMC] and seroresponse rate [SRR]) meet pre-specified non-inferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy trial.

In an open-label phase of this study, participants 6 years through 11 years of age received a single booster dose at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 95 booster dose participants in 6 years through 11 years and a random subset of 295 participants from the young adult study who received two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

In the 95 participants, on booster dose-Day 29, the GMC was 5847.5 (95% CI: 4999.6, 6839.1). The SRR was 100 (95% CI: 95.9, 100.0). Serum nAb levels for children 6 years through 11 years in the per-protocol immunogenicity subset with pre-booster SARS-CoV-2 negative status and the comparison with those from young adults (18 to 25 years of age) were studied. The GMR of booster dose Day 29 GMC compared to young adults Day 57 GMC was 4.2 (95% CI: 3.5, 5.0), meeting the noninferiority criteria (i.e., lower bound of the 95% CI > 0.667); the SRR difference was 0.7% (95% CI: -3.5, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of booster dose vaccine efficacy. The brisk recall response evident within 4 weeks of booster dosing is evidence of the robust priming induced by the Spikevax primary series.

Neutralising antibody against the B.1.617.2 (Delta) variant in children 6 years through 11 years of age
Serum samples of the per-protocol immunogenicity subset (n=134) of the ongoing paediatric study obtained at baseline and on Day 57 were tested in a PsVNA based on the B.1.617.2 (Delta) variant.

In children 6 years through 11 years of age, the GMFR from baseline to D57 was 81.77 (95% CI: 70.38, 95.00) for the Delta variant (measured by PsVNA). Furthermore, 99.3% of children met the definition of seroresponse.

Clinical efficacy in children 6 months through 5 years of age
An ongoing Phase 2/3 study was conducted to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax in healthy children 6 months through 11 years of age. The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 21 February 2022 was performed in 5 476 participants 6 months through 5 years of age who received two doses (at 0 and 1 month) of either Spikevax (n=4 105) or placebo (n=1 371) and had a negative baseline SARS-CoV-2 status (referred to as the Per Protocol Set for Efficacy). Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics.

The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 years through 5 years of age and 68 days for participants 6 months through 23 months of age.

Vaccine efficacy in this study was observed during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

Vaccine efficacy (VE) in Part 2 for the Per Protocol Set for Efficacy for COVID-19 cases 14 days or more after dose 2 using the "COVID-19 P301 case definition" (i.e., the definition employed in the pivotal adult efficacy study) was 46.4% (95% CI: 19.8, 63.8) for children 2 years through 5 years of age and 31.5% (95% CI: -27.7, 62.0) for children 6 months through 23 months of age.

Immunogenicity in children 6 months through 5 years of age
For children aged 2 years through 5 years of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 264; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.014 (95% CI: 0.881, 1.167), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The geometric mean fold rise (GMFR) from baseline to Day 57 for these children was 183.3 (95% CI: 164.03, 204.91). The difference in seroresponse rates (SRR) between the children and young adults was -0.4% (95% CI: -2.7%, 1.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the SRR difference > -10%).

For infants and toddlers from 6 months through 23 months of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 230; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.280 (95% CI: 1.115, 1.470), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in SRR rates between the infants/toddlers and young adults was 0.7% (95% CI: -1.0%, 2.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the seroresponse rate difference > -10%).

Accordingly, the prespecified success criteria for the primary immunogenicity objective were met for both age groups, allowing efficacy of 25 micrograms to be inferred in both children 2 years through 5 years and infants and toddlers aged 6 months through 23 months (Tables 4 and 5).

Table 4. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 6 months through 23 months of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

	6 months through 23 months n=230	**18 years through 25 years n=291**	**6 months through 23 months/ 18 years through 25 years**

Assay	Time point	GMC (95% CI)*	GMC (95% CI)*	GMC ratio (95% CI)[a]	Met noninferiority objective (Y/N)[b]
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 780.7 (1 606.4, 1 973.8)	1 390.8 (1 269.1, 1 524.2)	1.3 (1.1, 1.5)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralising antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 5. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 2 years through 5 years of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		2 years through 5 years n=264	18 years through 25 years n=291	2 years through 5 years/ 18 years through 25 years	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 410.0 (1 273.8, 1 560.8)	1 390.8 (1 262.5, 1 532.1)	1.0 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.

[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Available data in children 12 weeks to 6 months of age
The safety and immunogenicity of Spikevax bivalent Original/Omicron BA.1 were evaluated in children 12 weeks to 6 months of age in Study P206. During the dose-finding part of the study, two dose levels (5 mcg and 10 mcg) evaluated as a two-dose regimen were generally well tolerated but did not lead to a substantial immune response.

Immunogenicity in solid organ transplant recipients
The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose.

Immunogenicity in the study was assessed by measurement of neutralising antibodies against pseudovirus expressing the ancestral SARS-CoV-2 (D614G) strain at 1 month after Dose 2, Dose 3, booster dose and up to 12 months from the last dose in Part A, and up to 6 months from booster dose in Part B.

Three doses of Spikevax (original) induced enhanced neutralising antibody titres compared to pre-dose 1 and post-dose 2. A higher proportion of SOT participants who had received three doses achieved seroresponse compared to participants who had received two doses. The neutralising antibody levels observed in SOT liver participants who had received three doses was comparable to the post-dose 2 responses observed in the immunocompetent, baseline SARS-CoV-2-negative adult participants. The neutralising antibody responses continued to be numerically lower post-dose 3 in SOT kidney participants compared to SOT liver participants. The neutralising levels observed one month after Dose 3 persisted through six months with antibody levels maintained at 26-fold higher and seroresponse rate at 67% compared to baseline.

A fourth (booster) dose of Spikevax (original) enhanced neutralising antibody response in SOT participants compared to post-dose 3, regardless of the previous vaccines received [mRNA-1273 (Moderna), BNT162b2 or any mRNA-containing combination]; however, SOT kidney participants had numerically lower neutralising antibody responses compared to SOT liver participants.

Elderly

Spikevax (original) was assessed in individuals 6 months of age and older, including 3 768 subjects 65 years of age and older. The efficacy of Spikevax (original) was consistent between elderly (≥65 years) and younger adult subjects (18-64 years).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with the Spikevax (original) in one or more subsets of the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and reproductive and developmental toxicity.

General toxicity

General toxicity studies were conducted in rats (intramuscularly receiving up to 4 doses exceeding the human dose once every 2 weeks). Transient and reversible injection site oedema and erythema and transient and reversible changes in laboratory tests (including increases in eosinophils, activated partial thromboplastin time, and fibrinogen) were observed. Results suggests the toxicity potential to humans is low.

Genotoxicity/carcinogenicity

In vitro and *in vivo* genotoxicity studies were conducted with the novel lipid component SM-102 of the vaccine. Results suggests the genotoxicity potential to humans is very low. Carcinogenicity studies were not performed.

Reproductive toxicity

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 micrograms) and other ingredients included in a single human dose of Spikevax (original) was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. SARS-CoV-2 antibody responses were present in maternal animals from prior to mating to the end of the study on lactation day 21 as well as in foetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryo foetal or offspring development or postnatal development. No data are available of Spikevax (original) vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate)
Cholesterol
1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
Trometamol

Trometamol hydrochloride
Acetic acid
Sodium acetate trihydrate
Sucrose
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened multidose vial (Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, the unopened vaccine vial may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. Within this period, up to 12 hours may be used for transportation at 2°C to 8°C (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened vaccine vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the unopened vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

The unopened vaccine may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Punctured multidose vials (Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection)

Chemical and physical in-use stability has been demonstrated for 19 hours at 2°C to 25ºC after initial puncture (within the allowed use period of 30 days or 14 days, respectively, at 2°C to 8ºC and including 24 hours at 8°C to 25ºC). From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

Unopened single-dose vial (Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, single-dose vials may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. Within this period, single-dose vials may be transported up to 12 hours at 2°C to 8°C (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened single-dose vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the single-dose vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

Single-dose vials may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, pre-filled syringes may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened pre-filled syringes when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the pre-filled syringe will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

Pre-filled syringes may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

6.4 Special precautions for storage

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials)

Store in a freezer at -50ºC to -15ºC.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.
For storage conditions of the multidose vial after first opening, see section 6.3.

Transportation of thawed multidose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 12 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection (single-dose vials)

Store in a freezer at -50ºC to -15ºC.
Keep the single-dose vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of single-dose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed single-dose vials in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, single-dose vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Store in a freezer at -50ºC to -15ºC.
Keep the pre-filled syringe in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use.

6.5 Nature and contents of container

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials)

2.5 mL or 5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size:
10 multidose vials. Each vial contains 2.5 mL.
10 multidose vials. Each vial contains 5 mL.

Not all pack sizes may be marketed.

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection (single-dose vials)

0.5 mL dispersion in a (type 1 glass or type 1 equivalent glass) single-dose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size: 10 single-dose vials. Each vial contains 0.5 mL.

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

0.5 mL dispersion in a pre-filled syringe (cyclic olefin polymer) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack size: 10 pre-filled syringes. Each pre-filled syringe contains 0.5 mL.

6.6 Special precautions for disposal and other handling

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.

Store vials and pre-filled syringes in a freezer at -50ºC to -15ºC.

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of

Product Characteristics for that formulation.

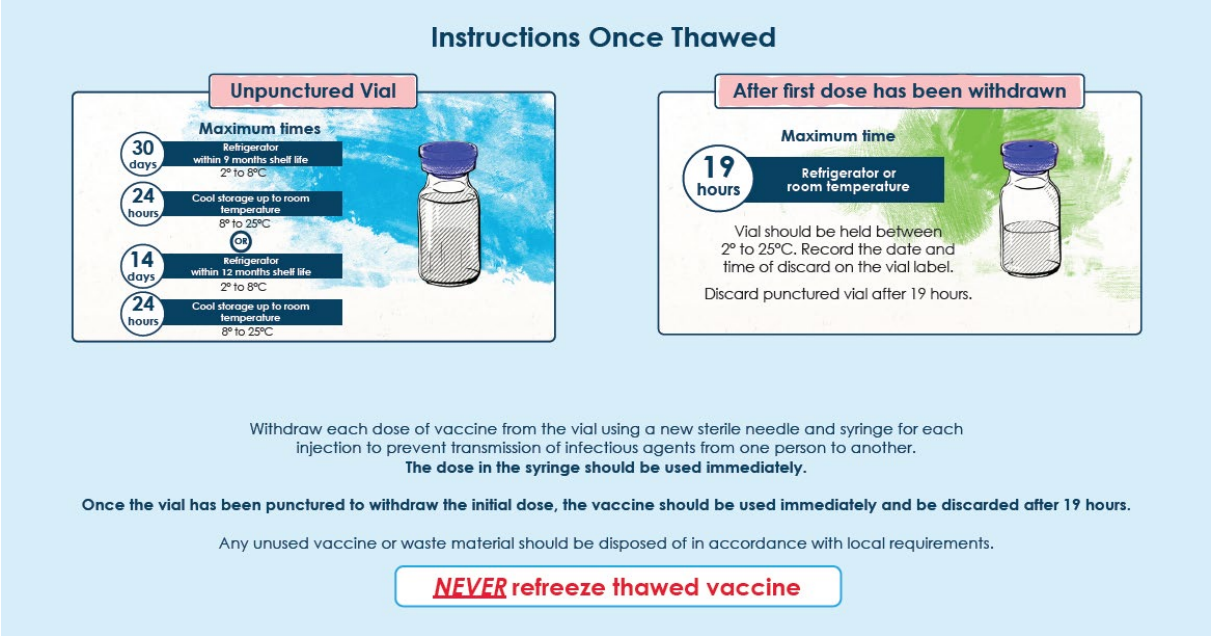
Pierce the stopper preferably at a different site each time. Do not puncture the vial more than 20 times.

An additional overfill is included in each multidose vial to ensure that 5 or 10 doses of 0.5 mL, or 10 or 20 doses of 0.25 mL can be delivered, depending on vial size.

Thaw each multidose vial before use following the instructions below (Table 6).

Table 6. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection (single-dose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 10 vials may be thawed either in the refrigerator or at room temperature (Table 7).

Table 7. Thawing instructions for single-dose vials and carton before use

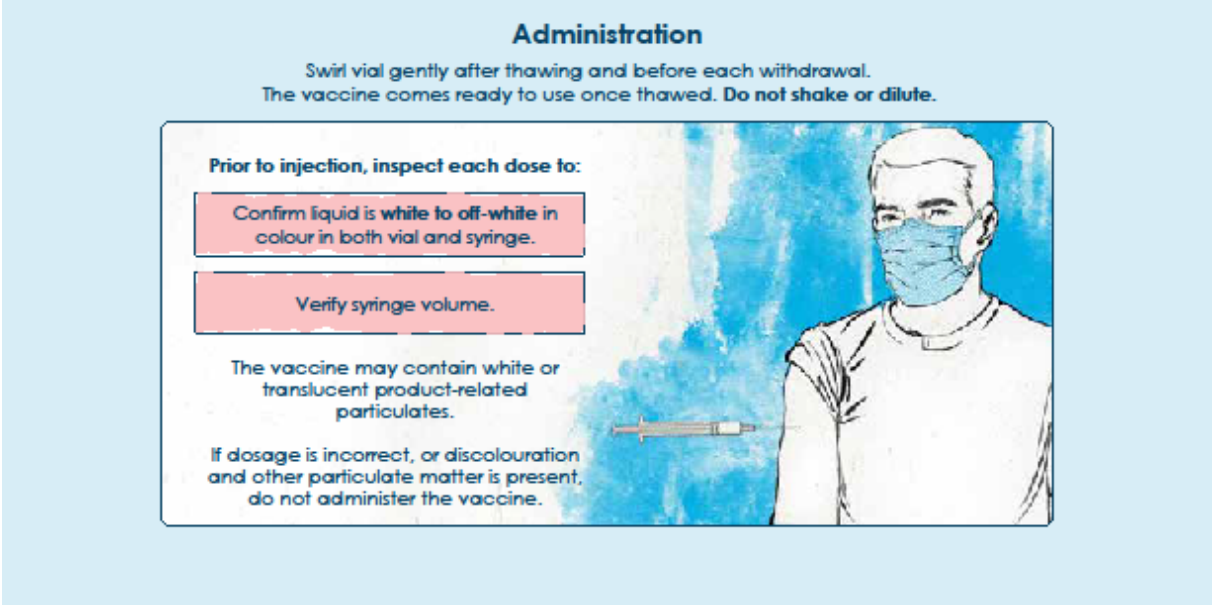
Configuration	Thaw instructions and duration

	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax bivalent Original/Omicron BA.1 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (25 micrograms of elasomeran and 25 micrograms of imelasomeran) mRNA and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 8).

Table 8. Thawing instructions for Spikevax bivalent Original/Omicron BA.1 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a	Thaw duration (minutes)	Thaw temperature (at room	Thaw duration (minutes)

	refrigerator) (°C)		temperature) (°C)	
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax bivalent Original/Omicron BA.1. If the product name is Spikevax 50 micrograms or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the Spikevax bivalent Original/Omicron BA.1 pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax bivalent Original/Omicron BA.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/004
EU/1/20/1507/005
EU/1/20/1507/007
EU/1/20/1507/008

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2021

Date of latest renewal: 03 October 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection
Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection
Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1. Spikevax bivalent Original/Omicron BA.4-5 qualitative and quantitative composition

Strength	**Container**	**Dose(s)**	**Composition per dose**
Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection	Single-dose 0.5 mL vial (blue flip-off cap)	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (original).

Davesomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron BA.4-5). The S-proteins of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 are identical.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection
White to off white dispersion (pH: 7.0 – 8.0).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Spikevax bivalent Original/Omicron BA.4-5 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older (see sections 4.2 and 5.1).

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Table 2. Spikevax bivalent Original/Omicron BA.4-5 posology

Age(s)	**Dose**	**Additional recommendations**
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose (see sections 4.4 and 5.1). If a child has received one prior dose of Spikevax, one dose of Spikevax bivalent Original/Omicron BA.4-5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax bivalent Original/Omicron BA.4-5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	

Age(s)	Dose	Additional recommendations
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 3. Spikevax bivalent Original/Omicron BA.4-5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Paediatric population
The safety and efficacy of Spikevax in children less than 6 months of age have not yet been established (see section 5.1).

Elderly
No dose adjustment is required in elderly individuals ≥65 years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Anaphylaxis has been reported in individuals who have received Spikevax (original). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. Subsequent doses of Spikevax bivalent Original/Omicron BA.4-5 should not be given to those who have experienced anaphylaxis to a prior dose of Spikevax (original).

Myocarditis and pericarditis

There is an increased risk for myocarditis and pericarditis following vaccination with Spikevax.

These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose (see section 4.8).

Available data indicate that most cases recover. Some cases required intensive care support and fatal cases have been observed.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Capillary leak syndrome flare-ups

A few cases of capillary leak syndrome (CLS) flare-ups have been reported in the first days after vaccination with Spikevax (original). Healthcare professionals should be aware of signs and symptoms of CLS to promptly recognise and treat the condition. In individuals with a medical history of CLS, planning of vaccination should be made in collaboration with appropriate medical experts.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical studies.

Limitations of vaccine effectiveness

As with all vaccines, vaccination with Spikevax bivalent Original/Omicron BA.4-5 may not protect all vaccine recipients.

Excipients with known effect

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

Different injectable vaccines should be given at different injection sites.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.4-5 during pregnancy.

However, a large amount of observational data from pregnant women vaccinated with Spikevax (original) during the second and third trimester has not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, Spikevax bivalent Original/ Omicron BA.4-5 can be used during pregnancy.

Breast-feeding

No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.4-5 during breastfeeding.

However, no effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to the vaccine is negligible. Observational data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax bivalent Original/Omicron BA.4-5 can be used during breastfeeding.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

Spikevax bivalent Original/Omicron BA.4-5 has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Adults
The safety of Spikevax (original) was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30 351 participants 18 years of age and older who received at least one dose of Spikevax (original) (n=15 185) or placebo (n=15 166) (NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22 831 (75.2%) of participants were 18 to 64 years of age and 7 520 (24.8%) of participants were 65 years of age and older.

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Adolescents 12 through 17 years of age
Safety data for Spikevax (original) in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study with multiple parts conducted in the United States. The first portion of the study involved 3 726 participants 12 through 17 years of age who received at least one dose of Spikevax (original) (n=2 486) or placebo (n=1 240) (NCT04649151). Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in adolescents 12 to 17 years of age were injection site pain (97%), headache (78%), fatigue (75%), myalgia (54%), chills (49%), axillary swelling/tenderness (35%), arthralgia (35%), nausea/vomiting (29%), injection site swelling (28%), injection site erythema (26%), and fever (14%).

This study transitioned to an open-label Phase 2/3 study in which 1 346 participants 12 years through 17 years of age received a booster dose of Spikevax at least 5 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 years through 11 years of age
Safety data for Spikevax (original) in children were collected in an ongoing Phase 2/3 two-part randomised, observer-blind clinical study conducted in the United States and Canada (NCT04796896). Part 1 is an open-label phase of the study for safety, dose selection, and immunogenicity and included 380 participants 6 years through 11 years of age who received at least 1 dose (0.25 mL) of Spikevax (original). Part 2 is the placebo-controlled phase for safety and included 4 016 participants 6 years through 11 years of age who received at least one dose (0.25 mL) of Spikevax (original) (n=3 012) or placebo (n=1 004). No participants in Part 1 participated in Part 2. Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in participants 6 years through 11 years of age following administration of the primary series (in Part 2) were injection site pain (98.4%), fatigue (73.1%), headache (62.1%), myalgia (35.3%), chills (34.6%), nausea/vomiting (29.3%), axillary swelling/tenderness (27.0%), fever (25.7%), injection site erythema (24.0%), injection site swelling (22.3%), and arthralgia (21.3%).

The study protocol was amended to include an open-label booster dose phase that included 1 294 participants 6 years through 11 years of age who received a booster dose of Spikevax at least 6 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 months through 5 years of age
An ongoing Phase 2/3 randomised, placebo-controlled, observer-blind study to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax was conducted in the United States and Canada. This study involved 10 390 participants 6 months through 11 years of age who received at least one dose of Spikevax (n=7 798) or placebo (n=2 592).

The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months. This paediatric study involved 6 388 participants 6 months through 5 years of age who received at least one dose of Spikevax (n=4 791) or placebo (n=1 597). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

In this clinical study, the adverse reactions in participants 6 months through 23 months of age following administration of the primary series were irritability/crying (81.5%), pain at the injection site (56.2%), sleepiness (51.1%), loss of appetite (45.7%), fever (21.8%), swelling at the injection site (18.4%), erythema at the injection site (17.9%), and axillary swelling/tenderness (12.2%).

The adverse reactions in participants 24 through 36 months of age following administration of the primary series were pain at the injection site (76.8%), irritability/crying (71.0%), sleepiness (49.7%), loss of appetite (42.4%), fever (26.1%), erythema at the injection site (17.9%), swelling at the injection site (15.7%), and axillary swelling/tenderness (11.5%).

The adverse reactions in participants 37 months through 5 years of age following administration of the primary series were pain at the injection site (83.8%), fatigue (61.9%), headache (22.9%), myalgia (22.1%), fever (20.9%), chills (16.8%), nausea/vomiting (15.2%), axillary swelling/tenderness (14.3%), arthralgia (12.8%), erythema at the injection site (9.5%), and swelling at the injection site (8.2%).

Tabulated list of adverse reactions

The safety profile presented below is based on data generated in several placebo-controlled clinical studies:
- 30 351 adults ≥ 18 years of age
- 3 726 adolescents 12 through 17 years of age
- 4 002 children 6 years through 11 years of age
- 6 388 children aged 6 months through 5 years of age

- and post-marketing experience.

Adverse reactions reported are listed according to the following frequency convention:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness (Table 4).

Table 4. Adverse reactions from Spikevax (original) clinical studies and post authorisation experience in children and individuals 6 months of age and older

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Immune system disorders	Not known	Anaphylaxis
		Hypersensitivity
Metabolism and nutrition disorders	Very common	Decreased appetite†
Psychiatric disorders	Very common	Irritability/crying†
Nervous system disorders	Very common	Headache Sleepiness†
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Common	Diarrhoea
	Uncommon	Abdominal pain§
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria¶
	Not known	Erythema multiforme Mechanical urticaria Chronic urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
Reproductive system and breast disorders	Not known	Heavy menstrual bleeding#
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills Pyrexia Injection site swelling Injection site erythema
	Common	Injection site urticaria Injection site rash Delayed injection site reaction♠
	Uncommon	Injection site pruritus
	Rare	Facial swelling♥

MedDRA system organ class	Frequency	Adverse reactions
	Not known	Extensive swelling of vaccinated limb

*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site. Other lymph nodes (e.g., cervical, supraclavicular) were affected in some cases.
† Observed in the paediatric population (6 months to 5 years of age).
‡ Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the Spikevax (original) group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.
§ Abdominal pain was observed in the paediatric population (6 to 11 years of age): 0.2% in the Spikevax (original) group and 0% in the placebo group.
¶ Urticaria has been observed with either acute onset (within a few days after vaccination) or delayed onset (up to approximately two weeks after vaccination).
# Most cases appeared to be non-serious and temporary in nature.
♠ Median time to onset was 9 days after the first injection, and 11 days after the second injection. Median duration was 4 days after the first injection, and 4 days after the second injection.
♥ There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

The reactogenicity and safety profile in 343 subjects receiving Spikevax (original), that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

Adults (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine primary series. In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (0.25 mL, 50 micrograms) was similar to that after the second dose in the primary series.

Spikevax bivalent Original/Omicron BA.1 (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax bivalent Original/Omicron BA.1 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Spikevax bivalent Original/Omicron BA.1 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose. The frequency of adverse reactions after immunisation with Spikevax bivalent Original/Omicron BA.1 was also similar or lower relative to that of a first booster dose of Spikevax (original) (50 micrograms) and relative to the second dose of the Spikevax (original) primary series (100 micrograms). The safety profile of Spikevax bivalent Original/Omicron BA.1 (median follow-up period of 113 days) was similar to the safety profile of Spikevax (original) (median follow-up period of 127 days).

Spikevax bivalent Original/Omicron BA.4-5 (booster dose)
The safety, reactogenicity, and immunogenicity of a bivalent booster dose of Spikevax bivalent Original/Omicron BA.4-5 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received a booster dose of Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms), and 376 participants received a booster dose of Spikevax (original) (50 micrograms).

Spikevax bivalent Original/Omicron BA.4-5 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose.

Spikevax (original) in solid organ transplant recipients

The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose (fourth dose for mRNA vaccines and third dose for non-mRNA vaccines).

Reactogenicity was consistent with the known profile of Spikevax (original). There were no unexpected safety findings.

Description of selected adverse reactions

Myocarditis
The increased risk of myocarditis after vaccination with Spikevax (original) is highest in younger males (see section 4.4).

Two large European pharmacoepidemiological studies have estimated the excess risk in younger males following the second dose of Spikevax (original). One study showed that in a period of 7 days after the second dose, there were about 1.316 (95% CI: 1.299, 1.333) extra cases of myocarditis in 12 to 29 year-old males per 10 000 compared to unexposed persons. In another study, in a period of 28 days after the second dose, there were 1.88 (95% CI: 0.956, 2.804) extra cases of myocarditis in 16 to 24 year-old males per 10 000 compared to unexposed persons.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, COVID-19 vaccines, ATC code: J07BN01

Mechanism of action

Spikevax (elasomeran) and Spikevax bivalent Original/Omicron BA.1 (elasomeran/imelasomeran) both contain mRNA encapsulated in lipid nanoparticles. The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is non-replicating, and is expressed transiently mainly by dendritic cells and subcapsular sinus macrophages. The expressed, membrane-bound spike protein of SARS-CoV-2 is then recognised by immune cells as a foreign antigen. This elicits both T-cell and B-cell responses to generate neutralising antibodies, which may contribute to protection against COVID-19. The nucleoside-modified mRNA in Spikevax bivalent Original/Omicron BA.4-5

(elasomeran/davesomeran) is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

Clinical efficacy

Immunogenicity in participants 18 years of age and older – after Spikevax bivalent Original/Omicron BA.4-5 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.4-5 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received the Spikevax bivalent Original/Omicron BA.4-5 50 microgram booster dose, and 376 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part H evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.4-5 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a first booster dose of Spikevax (original) (50 micrograms). In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part F group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.4-5 group. In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the observed geometric mean titre (GMT) (95% CI) at pre-booster was 87.9 (72.2, 107.1) and increased to 2 324.6 (1 921.2, 2 812.7) 28 days after the Spikevax bivalent Original/Omicron BA.4-5 booster dose. The Day 29 GMR for Spikevax Original/Omicron BA.4-5 50 microgram booster dose versus the Spikevax (original) 50 microgram booster dose was 6.29 (5.27, 7.51), meeting the pre-specified criterion for superiority (lower bound of CI >1).

The estimated neutralising antibody GMTs (95% CI) against Omicron BA.4/BA.5 adjusted for pre-booster titre and age group were 2 747.3 (2 399.2, 3 145.9) and 436.7 (389.1, 490.0) 28 days after Spikevax bivalent Original/Omicron BA.4-5 and Spikevax (original) booster doses, respectively, and the GMR (95% CI) was 6.29 (5.27, 7.51), meeting the pre-specified criterion for non-inferiority (lower bound of CI >0.667).

Immunogenicity in adults – after Spikevax bivalent Original/Omicron BA.1 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.1 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part G evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.1 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a booster dose of Spikevax (original) (50 micrograms) at least 3 months prior to enrolment. In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part G group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.1 group.

In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the original SARS-CoV-2 estimated neutralising antibody geometric mean titre (GMT) and corresponding 95% CI was 6 422.3 (5 990.1, 6 885.7) and 5 286.6 (4 887.1, 5 718.9) 28 days after the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster doses, respectively. These GMTs represent the ratio between response of Spikevax bivalent Original/Omicron BA.1 versus Spikevax (original) against the ancestral SARS-CoV-2 (D614G) strain.

The GMR (97.5% CI) was 1.22 (1.08, 1.37) meeting the pre-specified criterion for non-inferiority (lower bound of 97.5% CI ≥0.67).

The estimated Day 29 neutralising antibody GMTs against Omicron, BA.1 were 2 479.9 (2 264.5, 2 715.8) and 1 421.2 (1 283.0, 1 574.4) in the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster groups, respectively, and the GMR (97.5% CI) was 1.75 (1.49, 2.04), which met the pre-specified superiority criterion (lower bound of CI >1).

Three-month antibody persistence of Spikevax bivalent Original/Omicron BA.1 booster vaccine against COVID-19
Participants in Study P205 Part G were sequentially enrolled to receive 50 micrograms of Spikevax (original) (n = 376) or Spikevax bivalent Original/Omicron BA.1 (n = 437) as second booster doses. In participants with no pre-booster incidence of SARS-CoV-2, Spikevax bivalent Original/Omicron BA.1 elicited Omicron-BA.1-neutralising antibody titres (observed GMT) that were significantly higher (964.4 [834.4, 1 114.7]) than those of Spikevax (original) (624.2 [533.1, 730.9]) and similar between boosters against ancestral SARS-CoV-2 at three months.

Clinical efficacy in adults
The adult study was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or had received immunosuppressants within 6 months, as well as participants who were pregnant, or with a known history of SARS-CoV-2 infection. Participants with stable HIV disease were not excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of Spikevax (original). Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or Spikevax (original).

A total of 30 351 subjects were followed for a median of 92 days (range: 1-122) for the development of COVID-19 disease.

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28 207 subjects who received either Spikevax (original) (n=14 134) or placebo (n=14 073) and had a negative baseline SARS-CoV-2 status. The PPS study population included 47.4% female, 52.6% male, 79.5% White, 9.7% African American, 4.6% Asian, and 6.2% other. 19.7% of participants identified as Hispanic or Latino. The median age of subjects was 53 years (range 18-94). A dosing window of –7 to +14 days for administration of the second dose (scheduled at day 29) was allowed for inclusion in the PPS. 98% of vaccine recipients received the second dose 25 days to 35 days after dose 1 (corresponding to -3 to +7 days around the interval of 28 days).

COVID-19 cases were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT PCR) and by a Clinical Adjudication Committee. Vaccine efficacy overall and by key age groups are presented in Table 5.

Table 5. Vaccine efficacy analysis: confirmed COVID-19[#] regardless of severity starting 14 days after the 2nd dose – PPS

Age group (years)	Spikevax (original)			Placebo			
	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	% Vaccine efficacy (95% CI)*
Overall (≥18)	14 134	11	3.328	14 073	185	56.510	94.1 (89.3, 96.8)**
18 to <65	10 551	7	2.875	10 521	156	64.625	95.6 (90.6, 97.9)
≥65	3 583	4	4.595	3 552	29	33.728	86.4

Age group (years)	Spikevax (original)			Placebo			
	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	% Vaccine efficacy (95% CI)*
							(61.4, 95.2)
≥65 to <75	2 953	4	5.586	2 864	22	31.744	82.4% (48.9, 93.9)
≥75	630	0	0	688	7	41.968	100% (NE, 100)

[#]COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the 2nd dose.
*Vaccine efficacy and 95% confidence interval (CI) from the stratified Cox proportional hazard model
** CI not adjusted for multiplicity. Multiplicity adjusted statistical analyses were carried out in an interim analysis based on less COVID-19 cases, not reported here.

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 of 185 (16%) cases reported in the placebo group. Of the 30 participants with severe disease, 9 were hospitalised, 2 of which were admitted to an intensive care unit. The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO2) criterion for severe disease (≤ 93% on room air).

The vaccine efficacy of Spikevax (original) to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% CI: 88.6, 96.5).

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Immunogenicity in adults – after booster dose (0.25 mL, 50 micrograms)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine as primary series. In an open-label phase, 149 of those participants (Per Protocol Set) received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL, 50 micrograms) was shown to result in a geometric mean fold rise (GMFR) of 12.99 (95% CI: 11.04, 15.29) in neutralising antibodies from pre-booster compared to 28 days after the booster dose. The GMFR in neutralising antibodies was 1.53 (95% CI: 1.32, 1.77) when compared 28 days post dose 2 (primary series) to 28 days after the booster dose.

Immunogenicity of a booster dose following primary vaccination with another authorised COVID-19 vaccine in adults
Safety and immunogenicity of a heterologous booster with Spikevax (original) were studied in an investigator-initiated study with 154 participants. The minimum time interval between primary series using a vector-based or RNA-based COVID-19 vaccine and booster injection with Spikevax (original) was 12 weeks (range: 12 weeks to 20.9 weeks). The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were

assessed on Day 1 prior to administration and at Day 15 and Day 29 after the booster dose. A booster response was demonstrated regardless of primary vaccination.

Only short-term immunogenicity data are available; long-term protection and immunological memory are currently unknown.

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) in the UK
COV-BOOST is a multicentre, randomised Phase 2 investigator-initiated study of third dose booster vaccination against COVID-19 with a subgroup to investigate detailed immunology. Participants were adults aged 30 years or older, in good physical health (mild to moderate well-controlled co-morbidities were permitted), who had received two doses of either Pfizer–BioNTech or Oxford–AstraZeneca (first dose in December 2020, January 2021 or February 2021), and were at least 84 days post second dose by the time of enrolment. Spikevax (original) boosted antibody and neutralising responses and was well tolerated regardless of the prime series. The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 28 after the booster dose.

Pre-boost and post-boost neutralising antibody against the B.1.617.2 (Delta) variant in adults
Results of the pseudovirus neutralisation assay (PsVNA) against the B.1.617.2 (Delta) variant determined pre-booster and on Day 29 post-booster showed that administration of a booster dose of Spikevax (original) (0.25 mL, 50 micrograms) in adults induced a 17-fold rise in neutralising antibodies against the Delta variant compared with pre-booster levels (GMFR = 17.28; 95% CI: 14.38, 20.77; n=295).

Clinical efficacy in adolescents 12 through 17 years of age
The adolescent study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study (NCT04649151) to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in adolescents 12 to 17 years of age. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3 732 participants were randomised 2:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis was performed in 3 181 participants who received 2 doses of either Spikevax (original) (n=2 139) or placebo (n=1 042) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were zero symptomatic COVID-19 cases in the Spikevax (original) group and 4 symptomatic COVID-19 cases in the placebo group.

Immunogenicity in adolescents 12 to 17 years of age – after Spikevax primary vaccination
A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in the per-protocol immunogenicity subsets of adolescents aged 12 through 17 (n=340) in the adolescent study and in participants aged 18 through 25 (n=296) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The geometric mean ratio (GMR) of the neutralising antibody titres in adolescents 12 to 17 years of age compared to the 18- to 25-year-olds was 1.08 (95% CI: 0.94, 1.24). The difference in seroresponse rate was 0.2% (95% CI: -1.8, 2.4). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in adolescents 12 years through 17 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study was to infer efficacy of the booster dose in participants 12 years through 17 years of age by comparing post-booster immune responses (Day 29) to those obtained post-dose 2 of the primary series (Day 57)

in young adults (18 to 25 years of age) in the adult study. Efficacy of the 50 microgram Spikevax booster dose is inferred if post-booster dose immune responses (nAb geometric mean concentration [GMC] and seroresponse rate [SRR]) meet prespecified noninferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy study.

In an open-label phase of this study, participants 12 years through 17 years of age received a single booster dose at least 5 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 257 booster dose participants in this study and a random subset of 295 participants from the young adult study (ages ≥18 to ≤25 years) who previously completed a primary vaccination series of two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

The GMR of the adolescent booster dose Day 29 GMC compared with young adults: Day 57 GMR was 5.1 (95% CI: 4.5, 5.8), meeting the noninferiority criteria (i.e., lower bound of the 95% CI >0.667 (1/1.5); point estimate ≥0.8); the SRR difference was 0.7% (95% CI: -0.8, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

In the 257 participants, pre-booster (booster dose-Day 1) nAb GMC was 400.4 (95% CI: 370.0, 433.4); on BD-Day 29, the GMC was 7 172.0 (95% CI: 6 610.4, 7 781.4). Post-booster booster dose-Day 29 GMC increased approximately 18-fold from pre-booster GMC, demonstrating the potency of the booster dose to adolescents. The SRR was 100 (95% CI: 98.6, 100.0).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of vaccine efficacy from the adult study.

Clinical efficacy in children 6 years through 11 years of age
The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in children aged 6 years through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 4 016 participants were randomised 3:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 10 November 2021 was performed in 3 497 participants who received two doses (0.25 mL at 0 and 1 month) of either Spikevax (original) (n=2 644) or placebo (n=853) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were three COVID-19 cases (0.1%) in the Spikevax (original) group and four COVID-19 cases (0.5%) in the placebo group.

Immunogenicity in children 6 years through 11 years of age
An analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in a subset of children aged 6 years through 11 years (n=319) in the paediatric study and in participants aged 18 through 25 years (n=295) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titres in children 6 years through 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9,

2.1). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in children 6 years through 11 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study is to infer efficacy of the booster dose in participants 6 years through 11 years of age by comparing post-booster dose immune responses (Day 29) to those obtained post dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in that study, where 93% efficacy was demonstrated. Efficacy of the 25 microgram Spikevax booster dose is inferred if post-booster dose immune responses (neutralising antibody [nAb] geometric mean concentration [GMC] and seroresponse rate [SRR]) meet pre-specified non-inferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy trial.

In an open-label phase of this study, participants 6 years through 11 years of age received a single booster dose at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 95 booster dose participants in 6 years through 11 years and a random subset of 295 participants from the young adult study who received two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

In the 95 participants, on booster dose-Day 29, the GMC was 5 847.5 (95% CI: 4 999.6, 6 839.1). The SRR was 100 (95% CI: 95.9, 100.0). Serum nAb levels for children 6 years through 11 years in the per-protocol immunogenicity subset with pre-booster SARS-CoV-2 negative status and the comparison with those from young adults (18 to 25 years of age) were studied. The GMR of booster dose Day 29 GMC compared to young adults Day 57 GMC was 4.2 (95% CI: 3.5, 5.0), meeting the noninferiority criteria (i.e., lower bound of the 95% CI > 0.667); the SRR difference was 0.7% (95% CI: -3.5, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of booster dose vaccine efficacy. The brisk recall response evident within 4 weeks of booster dosing is evidence of the robust priming induced by the Spikevax primary series.

Neutralising antibody against the B.1.617.2 (Delta) variant in children 6 years through 11 years of age
Serum samples of the per-protocol immunogenicity subset (n=134) of the ongoing paediatric study obtained at baseline and on Day 57 were tested in a PsVNA based on the B.1.617.2 (Delta) variant. In children 6 years through 11 years of age, the GMFR from baseline to D57 was 81.77 (95% CI: 70.38, 95.00) for the Delta variant (measured by PsVNA). Furthermore, 99.3% of children met the definition of seroresponse.

Clinical efficacy in children 6 months through 5 years of age
An ongoing Phase 2/3 study was conducted to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax in healthy children 6 months through 11 years of age. The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 21 February 2022 was performed in 5 476 participants 6 months through 5 years of age who received two doses (at 0 and 1 month) of either Spikevax (n=4 105) or placebo (n=1 371) and had a negative baseline SARS-CoV-2 status (referred to as the Per Protocol Set for Efficacy). Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics.

The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 years through 5 years of age and 68 days for participants 6 months through 23 months of age.

Vaccine efficacy in this study was observed during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

Vaccine efficacy (VE) in Part 2 for the Per Protocol Set for Efficacy for COVID-19 cases 14 days or more after dose 2 using the "COVID-19 P301 case definition" (i.e., the definition employed in the pivotal adult efficacy study) was 46.4% (95% CI: 19.8, 63.8) for children 2 years through 5 years of age and 31.5% (95% CI: -27.7, 62.0) for children 6 months through 23 months of age.

Immunogenicity in children 6 months through 5 years of age
For children aged 2 years through 5 years of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 264; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.014 (95% CI: 0.881, 1.167), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The geometric mean fold rise (GMFR) from baseline to Day 57 for these children was 183.3 (95% CI: 164.03, 204.91). The difference in seroresponse rates (SRR) between the children and young adults was -0.4% (95% CI: -2.7%, 1.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the SRR difference > -10%).

For infants and toddlers from 6 months through 23 months of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 230; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.280 (95% CI: 1.115, 1.470), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in SRR rates between the infants/toddlers and young adults was 0.7% (95% CI: -1.0%, 2.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the seroresponse rate difference > -10%).

Accordingly, the prespecified success criteria for the primary immunogenicity objective were met for both age groups, allowing efficacy of 25 micrograms to be inferred in both children 2 years through 5 years and infants and toddlers aged 6 months through 23 months (Tables 6 and 7).

Table 6. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 6 months through 23 months of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		6 months through 23 months n=230	**18 years through 25 years n=291**	**6 months through 23 months/ 18 years through 25 years**	
Assay	**Time point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 780.7 (1 606.4, 1 973.8)	1 390.8 (1 269.1, 1 524.2)	1.3 (1.1, 1.5)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.

[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.

[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.

[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralising antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.

[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 7. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 2 years through 5 years of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		2 years through 5 years n=264	**18 years through 25 years n=291**	**2 years through 5 years/ 18 years through 25 years**	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 410.0 (1 273.8, 1 560.8)	1 390.8 (1 262.5, 1 532.1)	1.0 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

GMC = Geometric mean concentration

n = number of participants with non-missing data at baseline and at Day 57

* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.

[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.

[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.

[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.

[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Available data in children 12 weeks to 6 months of age

The safety and immunogenicity of Spikevax bivalent Original/Omicron BA.1 were evaluated in children 12 weeks to 6 months of age in Study P206. During the dose-finding part of the study, two dose levels (5 mcg and 10 mcg) evaluated as a two-dose regimen were generally well tolerated but did not lead to a substantial immune response.

Immunogenicity in solid organ transplant recipients
The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose.

Immunogenicity in the study was assessed by measurement of neutralising antibodies against pseudovirus expressing the ancestral SARS-CoV-2 (D614G) strain at 1 month after Dose 2, Dose 3, booster dose and up to 12 months from the last dose in Part A, and up to 6 months from booster dose in Part B.

Three doses of Spikevax (original) induced enhanced neutralising antibody titres compared to pre-dose 1 and post-dose 2. A higher proportion of SOT participants who had received three doses achieved seroresponse compared to participants who had received two doses. The neutralising antibody levels observed in SOT liver participants who had received three doses was comparable to the post-dose 2 responses observed in the immunocompetent, baseline SARS-CoV-2-negative adult participants. The neutralising antibody responses continued to be numerically lower post-dose 3 in SOT kidney participants compared to SOT liver participants. The neutralising levels observed one month after Dose 3 persisted through six months with antibody levels maintained at 26-fold higher and seroresponse rate at 67% compared to baseline.

A fourth (booster) dose of Spikevax (original) enhanced neutralising antibody response in SOT participants compared to post-dose 3, regardless of the previous vaccines received [mRNA-1273 (Moderna), BNT162b2 or any mRNA-containing combination]; however, SOT kidney participants had numerically lower neutralising antibody responses compared to SOT liver participants.

Elderly

Spikevax (original) was assessed in individuals 6 months of age and older, including 3 768 subjects 65 years of age and older. The efficacy of Spikevax (original) was consistent between elderly (≥65 years) and younger adult subjects (18-64 years).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with the Spikevax (original) in one or more subsets of the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and reproductive and developmental toxicity.

General toxicity

General toxicity studies were conducted in rats (intramuscularly receiving up to 4 doses exceeding the human dose once every 2 weeks). Transient and reversible injection site oedema and erythema and transient and reversible changes in laboratory tests (including increases in eosinophils, activated partial thromboplastin time, and fibrinogen) were observed. Results suggests the toxicity potential to humans is low.

Genotoxicity/carcinogenicity

In vitro and *in vivo* genotoxicity studies were conducted with the novel lipid component SM-102 of the vaccine. Results suggests the genotoxicity potential to humans is very low. Carcinogenicity studies were not performed.

Reproductive toxicity

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 micrograms) and other ingredients included in a single human dose of Spikevax (original) was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. SARS-CoV-2 antibody responses were present in maternal animals from prior to mating to the end of the study on lactation day 21 as well as in foetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryo foetal or offspring development or postnatal development. No data are available of Spikevax (original) vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate)
Cholesterol
1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
Trometamol
Trometamol hydrochloride
Acetic acid
Sodium acetate trihydrate
Sucrose
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened multidose vial (Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, the unopened vaccine vial may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. Within this period, up to 12 hours may be used for transportation at 2°C to 8°C (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened vaccine vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the unopened vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

The unopened vaccine may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Punctured multidose vials (Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection)

Chemical and physical in-use stability has been demonstrated for 19 hours at 2°C to 25ºC after initial puncture (within the allowed use period of 30 days or 14 days, respectively, at 2°C to 8ºC and including 24 hours at 8°C to 25ºC). From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

Unopened single-dose vial (Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, single-dose vials may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. Within this period, single-dose vials may be transported up to 12 hours at 2°C to 8°C (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened single-dose vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the single-dose vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

Single-dose vials may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, pre-filled syringes may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened pre-filled syringes when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the pre-filled syringe will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

Once thawed, the vaccine should not be refrozen.

Pre-filled syringes may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

6.4 Special precautions for storage

Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials)

Store in a freezer at -50ºC to -15ºC.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.
For storage conditions of the multidose vial after first opening, see section 6.3.

Transportation of thawed multidose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 12 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection) (single-dose vials)

Store in a freezer at -50ºC to -15ºC.
Keep the single-dose vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of single-dose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed single-dose vials in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, single-dose vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Store in a freezer at -50ºC to -15ºC.
Keep the pre-filled syringe in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use.

6.5 Nature and contents of container

Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials)

2.5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection (single-dose vials)

0.5 mL dispersion in a (type 1 glass or type 1 equivalent glass) single-dose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size: 10 single-dose vials. Each vial contains 0.5 mL.

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

0.5 mL dispersion in a pre-filled syringe (cyclic olefin polymer) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack size: 10 pre-filled syringes. Each pre-filled syringe contains 0.5 mL.

6.6 Special precautions for disposal and other handling

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.

Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.4-5. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL or Spikevax bivalent Original/Omicron BA.1, please make reference to the Summary of Product Characteristics for that formulation.

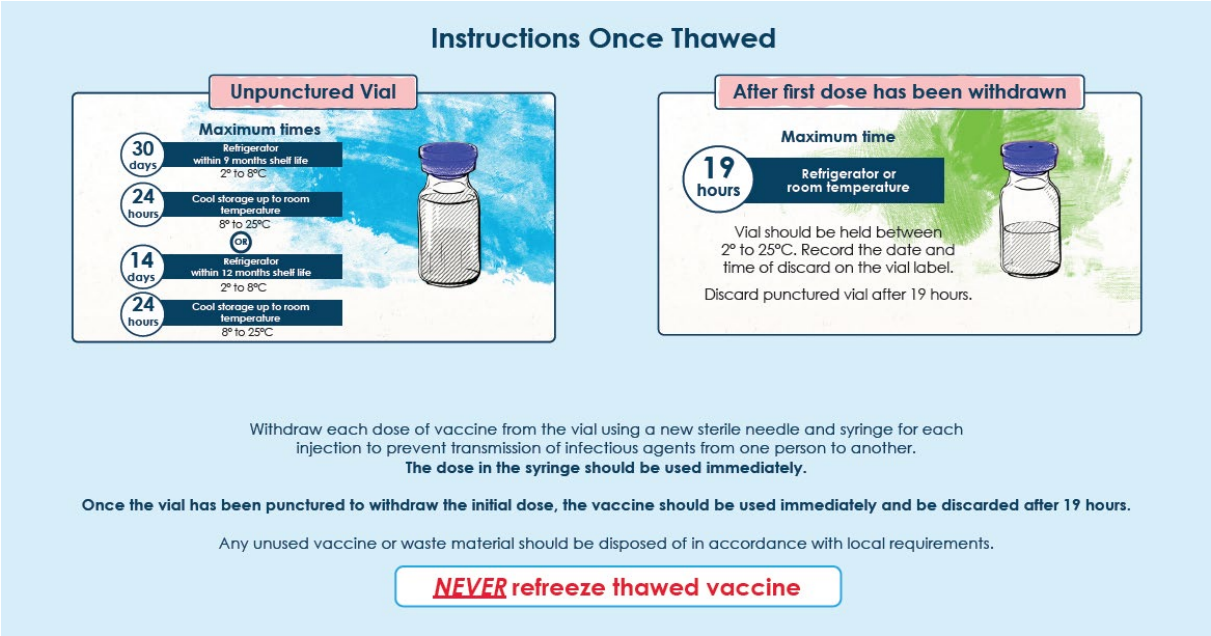
Pierce the stopper preferably at a different site each time.

An additional overfill is included in each multidose vial to ensure that 5 doses of 0.5 mL or a maximum of 10 doses of 0.25 mL can be delivered, depending on the individual's age.

Thaw each multidose vial before use following the instructions below (Table 8).

Table 8. Thawing instructions for multidose vials before use

Configuration	**Thaw instructions and duration**			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection (single-dose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.4-5. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 10 vials may be thawed either in the refrigerator or at room temperature (Table 9).

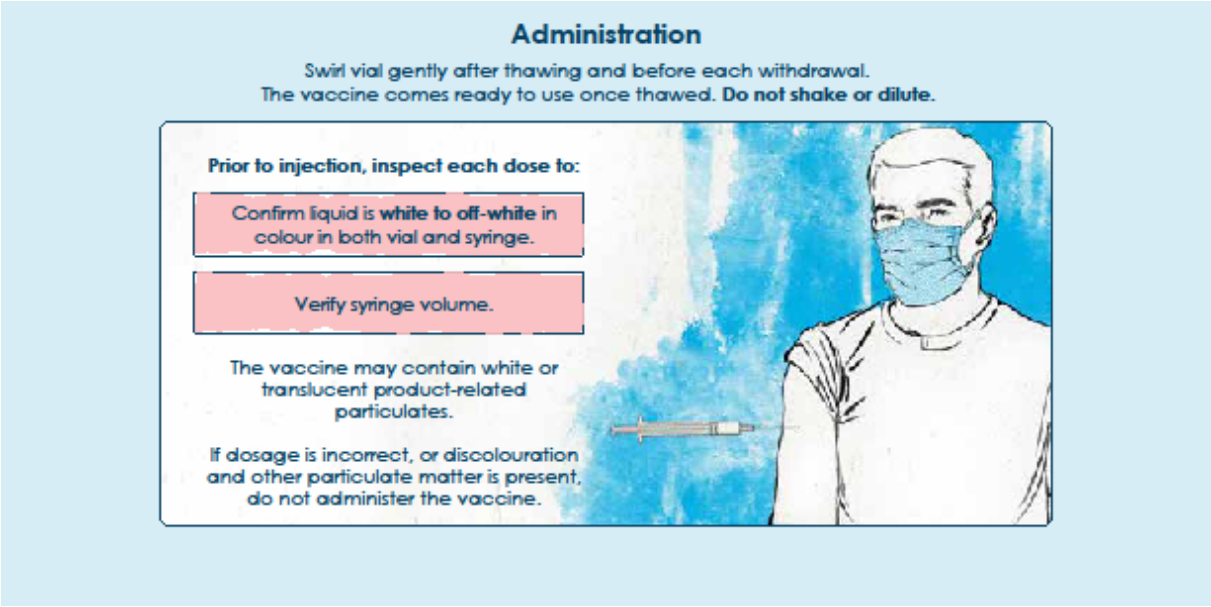
Table 9. Thawing instructions for single-dose vials and carton before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax bivalent Original/Omicron BA.4-5 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (25 micrograms of elasomeran and 25 micrograms of davesomeran) mRNA and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 10).

Table 10. Thawing instructions for Spikevax bivalent Original/Omicron BA.4-5 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax bivalent Original/Omicron BA.4-5. If the product name is Spikevax 50 micrograms or Spikevax bivalent Original/Omicron BA.1, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the Spikevax bivalent Original/Omicron BA.4-5 pre-filled syringes

- Do not shake.

- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax bivalent Original/Omicron BA.4-5 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/006
EU/1/20/1507/009
EU/1/20/1507/010

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2021
Date of latest renewal: 03 October 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection
Spikevax XBB.1.5 50 micrograms dispersion for injection
Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe
Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1. Spikevax XBB.1.5 qualitative and quantitative composition

Strength	Container	Dose(s)	Composition per dose
Spikevax XBB.1.5 0.1 mg/mL dispersion for injection	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax XBB.1.5 50 micrograms dispersion for injection	Single-dose 0.5 mL vial (blue flip-off cap)	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.25 mL For single-use only.	One dose (0.25 mL) contains 25 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

Andusomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron XBB.1.5).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection
White to off white dispersion (pH: 7.0 – 8.0).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Spikevax XBB.1.5 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older (see sections 4.2 and 5.1).

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Table 2. Spikevax XBB.1.5 posology

Age(s)	**Dose**	**Additional recommendations**
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose (see sections 4.4 and 5.1). If a child has received one prior dose of any Spikevax vaccine, one dose of Spikevax XBB.1.5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax XBB.1.5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after

Age(s)	Dose	Additional recommendations
		the most recent dose of a COVID-19 vaccine.

* Do not use the 0.5 mL single-dose vial or 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 3. Spikevax XBB.1.5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the 0.5 mL single-dose vial or 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Paediatric population
The safety and efficacy of Spikevax in children less than 6 months of age have not yet been established (see section 5.1).

Elderly
No dose adjustment is required in elderly individuals ≥65 years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Anaphylaxis has been reported in individuals who have received Spikevax (original). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. Subsequent doses of Spikevax XBB.1.5 should not be given to those who have experienced anaphylaxis to a prior dose of Spikevax (original).

Myocarditis and pericarditis

There is an increased risk for myocarditis and pericarditis following vaccination with Spikevax.

These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose (see section 4.8).

Available data indicate that most cases recover. Some cases required intensive care support and fatal cases have been observed.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Capillary leak syndrome flare-ups

A few cases of capillary leak syndrome (CLS) flare-ups have been reported in the first days after vaccination with Spikevax (original). Healthcare professionals should be aware of signs and symptoms of CLS to promptly recognise and treat the condition. In individuals with a medical history of CLS, planning of vaccination should be made in collaboration with appropriate medical experts.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical studies.

Limitations of vaccine effectiveness

As with all vaccines, vaccination with Spikevax XBB.1.5 may not protect all vaccine recipients.

Excipients with known effect

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

Different injectable vaccines should be given at different injection sites.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data are available yet regarding the use of andusomeran during pregnancy.

However, a large amount of observational data from pregnant women vaccinated with Spikevax (original) during the second and third trimester has not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, andusomeran can be used during pregnancy.

Breast-feeding

No data are available yet regarding the use of andusomeran during breastfeeding.

However, no effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to the vaccine is negligible. Observational data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Andusomeran can be used during breastfeeding.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

Andusomeran has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Adults
The safety of Spikevax (original) was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30 351 participants 18 years of age and older who received at least one dose of Spikevax (original) (n=15 185) or placebo (n=15 166) (NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22 831 (75.2%) of participants were 18 to 64 years of age and 7 520 (24.8%) of participants were 65 years of age and older.

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Adolescents 12 through 17 years of age
Safety data for Spikevax (original) in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study with multiple parts conducted in the United States. The first portion of the study involved 3 726 participants 12 through 17 years of age who received at least one dose of Spikevax (original) (n=2 486) or placebo (n=1 240) (NCT04649151). Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in adolescents 12 to 17 years of age were injection site pain (97%), headache (78%), fatigue (75%), myalgia (54%), chills (49%), axillary swelling/tenderness (35%), arthralgia (35%), nausea/vomiting (29%), injection site swelling (28%), injection site erythema (26%), and fever (14%).

This study transitioned to an open-label Phase 2/3 study in which 1 346 participants 12 years through 17 years of age received a booster dose of Spikevax at least 5 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 years through 11 years of age
Safety data for Spikevax (original) in children were collected in an ongoing Phase 2/3 two-part randomised, observer-blind clinical study conducted in the United States and Canada (NCT04796896). Part 1 is an open-label phase of the study for safety, dose selection, and immunogenicity and included 380 participants 6 years through 11 years of age who received at least 1 dose (0.25 mL) of Spikevax (original). Part 2 is the placebo-controlled phase for safety and included 4 016 participants 6 years through 11 years of age who received at least one dose (0.25 mL) of Spikevax (original) (n=3 012) or placebo (n=1 004). No participants in Part 1 participated in Part 2. Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in participants 6 years through 11 years of age following administration of the primary series (in Part 2) were injection site pain (98.4%), fatigue (73.1%), headache (62.1%), myalgia (35.3%), chills (34.6%), nausea/vomiting (29.3%), axillary swelling/tenderness (27.0%), fever (25.7%), injection site erythema (24.0%), injection site swelling (22.3%), and arthralgia (21.3%).

The study protocol was amended to include an open-label booster dose phase that included 1 294 participants 6 years through 11 years of age who received a booster dose of Spikevax at least 6 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 months through 5 years of age
An ongoing Phase 2/3 randomised, placebo-controlled, observer-blind study to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax was conducted in the United States and Canada. This study involved 10 390 participants 6 months through 11 years of age who received at least one dose of Spikevax (n=7 798) or placebo (n=2 592).

The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months. This paediatric study involved 6 388 participants 6 months through 5 years of age who received at least one dose of Spikevax (n=4 791) or placebo (n=1 597). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

In this clinical study, the adverse reactions in participants 6 months through 23 months of age following administration of the primary series were irritability/crying (81.5%), pain at the injection site (56.2%), sleepiness (51.1%), loss of appetite (45.7%), fever (21.8%), swelling at the injection site (18.4%), erythema at the injection site (17.9%), and axillary swelling/tenderness (12.2%).

The adverse reactions in participants 24 through 36 months of age following administration of the primary series were pain at the injection site (76.8%), irritability/crying (71.0%), sleepiness (49.7%), loss of appetite (42.4%), fever (26.1%), erythema at the injection site (17.9%), swelling at the injection site (15.7%), and axillary swelling/tenderness (11.5%).

The adverse reactions in participants 37 months through 5 years of age following administration of the primary series were pain at the injection site (83.8%), fatigue (61.9%), headache (22.9%), myalgia (22.1%), fever (20.9%), chills (16.8%), nausea/vomiting (15.2%), axillary swelling/tenderness (14.3%), arthralgia (12.8%), erythema at the injection site (9.5%), and swelling at the injection site (8.2%).

Tabulated list of adverse reactions

The safety profile presented below is based on data generated in several placebo-controlled clinical studies:
- 30 351 adults ≥ 18 years of age
- 3 726 adolescents 12 through 17 years of age
- 4 002 children 6 years through 11 years of age
- 6 388 children aged 6 months through 5 years of age
- and post-marketing experience.

Adverse reactions reported are listed according to the following frequency convention:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness (Table 4).

Table 4. Adverse reactions from Spikevax (original) clinical studies and post authorisation experience in children and individuals 6 months of age and older

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Immune system disorders	Not known	Anaphylaxis
		Hypersensitivity
Metabolism and nutrition disorders	Very common	Decreased appetite†
Psychiatric disorders	Very common	Irritability/crying†
Nervous system disorders	Very common	Headache Sleepiness†
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Common	Diarrhoea
	Uncommon	Abdominal pain§
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria¶
	Not known	Erythema multiforme Mechanical urticaria Chronic urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
Reproductive system and breast disorders	Not known	Heavy menstrual bleeding#
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills Pyrexia Injection site swelling Injection site erythema
	Common	Injection site urticaria Injection site rash Delayed injection site reaction♠
	Uncommon	Injection site pruritus
	Rare	Facial swelling♥
	Not known	Extensive swelling of vaccinated limb

*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site. Other lymph nodes (e.g., cervical, supraclavicular) were affected in some cases.

† Observed in the paediatric population (6 months to 5 years of age).

‡ Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the Spikevax (original) group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.

§ Abdominal pain was observed in the paediatric population (6 to 11 years of age): 0.2% in the Spikevax (original) group and 0% in the placebo group.

¶ Urticaria has been observed with either acute onset (within a few days after vaccination) or delayed onset (up to approximately two weeks after vaccination).

Most cases appeared to be non-serious and temporary in nature.

♠ Median time to onset was 9 days after the first injection, and 11 days after the second injection. Median duration was 4 days after the first injection, and 4 days after the second injection.

♥ There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

The reactogenicity and safety profile in 343 subjects receiving Spikevax (original), that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

Adults (booster dose)

The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine primary series. In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (0.25 mL, 50 micrograms) was similar to that after the second dose in the primary series.

Spikevax bivalent Original/Omicron BA.1 (booster dose)

The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax bivalent Original/Omicron BA.1 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Spikevax bivalent Original/Omicron BA.1 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose. The frequency of adverse reactions after immunisation with Spikevax bivalent Original/Omicron BA.1 was also similar or lower relative to that of a first booster dose of Spikevax (original) (50 micrograms) and relative to the second dose of the Spikevax (original) primary series (100 micrograms). The safety profile of Spikevax bivalent Original/Omicron BA.1 (median follow-up period of 113 days) was similar to the safety profile of Spikevax (original) (median follow-up period of 127 days).

Spikevax bivalent Original/Omicron BA.4-5 (booster dose)

The safety, reactogenicity, and immunogenicity of a bivalent booster dose of Spikevax bivalent Original/Omicron BA.4-5 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received a booster dose of Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms), and 376 participants received a booster dose of Spikevax (original) (50 micrograms).

Spikevax bivalent Original/Omicron BA.4-5 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose.

Spikevax XBB.1.5 (booster dose)

The safety, reactogenicity and immunogenicity of a booster dose of Spikevax XBB.1.5 are evaluated in an ongoing Phase 2/3 open-label study in adults (mRNA-1273-P205, Part J). In this study, 50 participants received a booster dose of Spikevax XBB.1.5 (50 micrograms) and 51 participants received a booster dose of an investigational bivalent Omicron XBB.1.5/BA.4-5 vaccine (50 micrograms).

The reactogenicity profile of Spikevax XBB.1.5 was similar to that of Spikevax (original) and Spikevax bivalent Original/Omicron BA.4-5. The median follow-up time for both vaccine groups in this interim analysis was 20 days (range of 20 to 22 days with data cut-off date of 16 May 2023).

Spikevax (original) in solid organ transplant recipients

The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose (fourth dose for mRNA vaccines and third dose for non-mRNA vaccines).

Reactogenicity was consistent with the known profile of Spikevax (original). There were no unexpected safety findings.

Description of selected adverse reactions

Myocarditis
The increased risk of myocarditis after vaccination with Spikevax (original) is highest in younger males (see section 4.4).

Two large European pharmacoepidemiological studies have estimated the excess risk in younger males following the second dose of Spikevax (original). One study showed that in a period of 7 days after the second dose, there were about 1.316 (95% CI: 1.299, 1.333) extra cases of myocarditis in 12 to 29 year-old males per 10 000 compared to unexposed persons. In another study, in a period of 28 days after the second dose, there were 1.88 (95% CI: 0.956, 2.804) extra cases of myocarditis in 16 to 24 year-old males per 10 000 compared to unexposed persons.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, COVID-19 vaccines, ATC code: J07BN01

Mechanism of action

Elasomeran and elasomeran/imelasomeran both contain mRNA encapsulated in lipid nanoparticles. The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is non-replicating, and is expressed transiently mainly by dendritic cells and subcapsular sinus macrophages. The expressed, membrane-bound spike protein of SARS-CoV-2 is then recognised by immune cells as a foreign antigen. This elicits both T-cell and B-cell responses to generate neutralising antibodies, which may contribute to protection against COVID-19. The nucleoside-modified mRNA in elasomeran/davesomeran and in andusomeran is formulated in lipid particles, which enable delivery of

the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

Clinical efficacy

Immunogenicity in adults – after Spikevax XBB.1.5 dose (0.5 mL, 50 micrograms) versus an investigational bivalent XBB.1.5/BA.4-5 dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity and immunogenicity of Spikevax XBB.1.5 50 micrograms and of a bivalent vaccine that contains equal mRNA amounts of Omicron XBB.1.5 and Omicron BA.4-5 spike proteins (25 micrograms XBB.1.5 / 25 micrograms BA.4-5) are evaluated in a Phase 2/3 open-label study in adults. In this study, 50 participants received Spikevax XBB.1.5 and 51 participants received the investigational bivalent XBB.1.5/BA.4-5 (mRNA-1273- P205, Part J). The two groups were randomised 1:1.

The vaccines were administered as a fifth dose to adults who previously received a two-dose primary series of any mRNA COVID-19 vaccine, a booster dose of any mRNA COVID-19 vaccine, and a booster dose of any mRNA bivalent Original/Omicron BA.4-5 vaccine.

Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 elicited potent neutralising responses at Day 15 against XBB.1.5, XBB.1.16, BA.4-5, BQ.1.1 and D614G. In the per-protocol immunogenicity set that includes all participants, with and without prior SARS-CoV-2 infection (N=49 and N=50 for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 groups, respectively), the Day 15 GMFR (95% CI) for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 was 16.7 (12.8, 21.7) and 11.6 (8.7, 15.4), respectively, against XBB.1.5 and 6.3 (4.8, 8.2) and 5.3 (3.9, 7.1) against BA.4-5.

For variants not contained in the vaccines, the Day 15 GMFR (95% CI) for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 was 11.4 (8.5, 15.4) and 9.3 (7.0, 12.3) against XBB.1.16; 5.8 (4.7, 7.3) and 6.1 (4.6, 7.9) against BQ.1.1 and 2.8 (2.2, 3.5) and 2.3 (1.9, 2.8) against D614G.

Immunogenicity in participants 18 years of age and older – after Spikevax bivalent Original/Omicron BA.4-5 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.4-5 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received the Spikevax bivalent Original/Omicron BA.4-5 50 microgram booster dose, and 376 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part H evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.4-5 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a first booster dose of Spikevax (original) (50 micrograms). In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part F group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.4-5 group. In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the observed geometric mean titre (GMT) (95% CI) at pre-booster was 87.9 (72.2, 107.1) and increased to 2 324.6 (1 921.2, 2 812.7) 28 days after the Spikevax bivalent Original/Omicron BA.4-5 booster dose. The Day 29 GMR for Spikevax Original/Omicron BA.4-5 50 microgram booster dose versus the Spikevax (original) 50 microgram booster dose was 6.29 (5.27, 7.51), meeting the pre-specified criterion for superiority (lower bound of CI >1).

The estimated neutralising antibody GMTs (95% CI) against Omicron BA.4/BA.5 adjusted for pre-booster titre and age group were 2 747.3 (2 399.2, 3 145.9) and 436.7 (389.1, 490.0) 28 days after Spikevax bivalent Original/Omicron BA.4-5 and Spikevax (original) booster doses, respectively, and the GMR (95% CI) was 6.29 (5.27, 7.51), meeting the pre-specified criterion for non-inferiority (lower bound of CI >0.667).

Immunogenicity in adults – after Spikevax bivalent Original/Omicron BA.1 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.1 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part G evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.1 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a booster dose of Spikevax (original) (50 micrograms) at least 3 months prior to enrolment. In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part G group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.1 group.

In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the original SARS-CoV-2 estimated neutralising antibody geometric mean titre (GMT) and corresponding 95% CI was 6 422.3 (5 990.1, 6 885.7) and 5 286.6 (4 887.1, 5 718.9) 28 days after the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster doses, respectively. These GMTs represent the ratio between response of Spikevax bivalent Original/Omicron BA.1 versus Spikevax (original) against the ancestral SARS-CoV-2 (D614G) strain. The GMR (97.5% CI) was 1.22 (1.08, 1.37) meeting the pre-specified criterion for non-inferiority (lower bound of 97.5% CI ≥0.67).

The estimated Day 29 neutralising antibody GMTs against Omicron, BA.1 were 2 479.9 (2 264.5, 2 715.8) and 1 421.2 (1 283.0, 1 574.4) in the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster groups, respectively, and the GMR (97.5% CI) was 1.75 (1.49, 2.04), which met the pre-specified superiority criterion (lower bound of CI >1).

Three-month antibody persistence of Spikevax bivalent Original/Omicron BA.1 booster vaccine against COVID-19
Participants in Study P205 Part G were sequentially enrolled to receive 50 micrograms of Spikevax (original) (n = 376) or Spikevax bivalent Original/Omicron BA.1 (n = 437) as second booster doses. In participants with no pre-booster incidence of SARS-CoV-2, Spikevax bivalent Original/Omicron BA.1 elicited Omicron-BA.1-neutralising antibody titres (observed GMT) that were significantly higher (964.4 [834.4, 1 114.7]) than those of Spikevax (original) (624.2 [533.1, 730.9]) and similar between boosters against ancestral SARS-CoV-2 at three months.

Clinical efficacy in adults
The adult study was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or had received immunosuppressants within 6 months, as well as participants who were pregnant, or with a known history of SARS-CoV-2 infection. Participants with stable HIV disease were not excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of Spikevax (original). Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or Spikevax (original).

A total of 30 351 subjects were followed for a median of 92 days (range: 1-122) for the development of COVID-19 disease.

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28 207 subjects who received either Spikevax (original) (n=14 134) or placebo (n=14 073) and had a negative baseline SARS-CoV-2 status. The PPS study population included 47.4% female, 52.6% male, 79.5% White, 9.7% African American, 4.6% Asian, and 6.2% other. 19.7% of participants identified

as Hispanic or Latino. The median age of subjects was 53 years (range 18-94). A dosing window of –7 to +14 days for administration of the second dose (scheduled at day 29) was allowed for inclusion in the PPS. 98% of vaccine recipients received the second dose 25 days to 35 days after dose 1 (corresponding to -3 to +7 days around the interval of 28 days).

COVID-19 cases were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT PCR) and by a Clinical Adjudication Committee. Vaccine efficacy overall and by key age groups are presented in Table 5.

Table 5. Vaccine efficacy analysis: confirmed COVID-19[#] regardless of severity starting 14 days after the 2nd dose – PPS

Age group (years)	Spikevax (original)			Placebo			
	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	% Vaccine efficacy (95% CI)*
Overall (≥18)	14 134	11	3.328	14 073	185	56.510	94.1 (89.3, 96.8)**
18 to <65	10 551	7	2.875	10 521	156	64.625	95.6 (90.6, 97.9)
≥65	3 583	4	4.595	3 552	29	33.728	86.4 (61.4, 95.2)
≥65 to <75	2 953	4	5.586	2 864	22	31.744	82.4% (48.9, 93.9)
≥75	630	0	0	688	7	41.968	100% (NE, 100)

[#]COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the 2nd dose.
*Vaccine efficacy and 95% confidence interval (CI) from the stratified Cox proportional hazard model
** CI not adjusted for multiplicity. Multiplicity adjusted statistical analyses were carried out in an interim analysis based on less COVID-19 cases, not reported here.

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 of 185 (16%) cases reported in the placebo group. Of the 30 participants with severe disease, 9 were hospitalised, 2 of which were admitted to an intensive care unit. The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO2) criterion for severe disease (≤ 93% on room air).

The vaccine efficacy of Spikevax (original) to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% CI: 88.6, 96.5).

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Immunogenicity in adults – after booster dose (0.25 mL, 50 micrograms)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine as primary series. In an open-label phase, 149 of those participants (Per Protocol Set) received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL, 50 micrograms) was shown to result in a geometric mean fold rise (GMFR) of 12.99 (95% CI: 11.04, 15.29) in neutralising antibodies from pre-booster compared to

28 days after the booster dose. The GMFR in neutralising antibodies was 1.53 (95% CI: 1.32, 1.77) when compared 28 days post dose 2 (primary series) to 28 days after the booster dose.

Immunogenicity of a booster dose following primary vaccination with another authorised COVID-19 vaccine in adults
Safety and immunogenicity of a heterologous booster with Spikevax (original) were studied in an investigator-initiated study with 154 participants. The minimum time interval between primary series using a vector-based or RNA-based COVID-19 vaccine and booster injection with Spikevax (original) was 12 weeks (range: 12 weeks to 20.9 weeks). The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 1 prior to administration and at Day 15 and Day 29 after the booster dose. A booster response was demonstrated regardless of primary vaccination.

Only short-term immunogenicity data are available; long-term protection and immunological memory are currently unknown.

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) in the UK
COV-BOOST is a multicentre, randomised Phase 2 investigator-initiated study of third dose booster vaccination against COVID-19 with a subgroup to investigate detailed immunology. Participants were adults aged 30 years or older, in good physical health (mild to moderate well-controlled co-morbidities were permitted), who had received two doses of either Pfizer–BioNTech or Oxford–AstraZeneca (first dose in December 2020, January 2021 or February 2021), and were at least 84 days post second dose by the time of enrolment. Spikevax (original) boosted antibody and neutralising responses and was well tolerated regardless of the prime series. The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 28 after the booster dose.

Clinical efficacy in adolescents 12 through 17 years of age
The adolescent study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study (NCT04649151) to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in adolescents 12 to 17 years of age. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3 732 participants were randomised 2:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis was performed in 3 181 participants who received 2 doses of either Spikevax (original) (n=2 139) or placebo (n=1 042) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were zero symptomatic COVID-19 cases in the Spikevax (original) group and 4 symptomatic COVID-19 cases in the placebo group.

Immunogenicity in adolescents 12 to 17 years of age – after Spikevax primary vaccination
A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in the per-protocol immunogenicity subsets of adolescents aged 12 through 17 (n=340) in the adolescent study and in participants aged 18 through 25 (n=296) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The geometric mean ratio (GMR) of the neutralising antibody titres in adolescents 12 to 17 years of age compared to the 18- to 25-year-olds was 1.08 (95% CI: 0.94, 1.24). The difference in seroresponse rate was 0.2% (95% CI: -1.8, 2.4). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in adolescents 12 years through 17 years of age – after Spikevax (original) booster dose

The primary immunogenicity objective of the booster phase of this study was to infer efficacy of the booster dose in participants 12 years through 17 years of age by comparing post-booster immune responses (Day 29) to those obtained post-dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in the adult study. Efficacy of the 50 microgram Spikevax booster dose is inferred if post-booster dose immune responses (nAb geometric mean concentration [GMC] and seroresponse rate [SRR]) meet prespecified noninferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy study.

In an open-label phase of this study, participants 12 years through 17 years of age received a single booster dose at least 5 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 257 booster dose participants in this study and a random subset of 295 participants from the young adult study (ages ≥18 to ≤25 years) who previously completed a primary vaccination series of two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

The GMR of the adolescent booster dose Day 29 GMC compared with young adults: Day 57 GMR was 5.1 (95% CI: 4.5, 5.8), meeting the noninferiority criteria (i.e., lower bound of the 95% CI >0.667 (1/1.5); point estimate ≥0.8); the SRR difference was 0.7% (95% CI: -0.8, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

In the 257 participants, pre-booster (booster dose-Day 1) nAb GMC was 400.4 (95% CI: 370.0, 433.4); on BD-Day 29, the GMC was 7 172.0 (95% CI: 6 610.4, 7 781.4). Post-booster booster dose-Day 29 GMC increased approximately 18-fold from pre-booster GMC, demonstrating the potency of the booster dose to adolescents. The SRR was 100 (95% CI: 98.6, 100.0).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of vaccine efficacy from the adult study.

Clinical efficacy in children 6 years through 11 years of age
The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in children aged 6 years through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 4 016 participants were randomised 3:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 10 November 2021 was performed in 3 497 participants who received two doses (0.25 mL at 0 and 1 month) of either Spikevax (original) (n=2 644) or placebo (n=853) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were three COVID-19 cases (0.1%) in the Spikevax (original) group and four COVID-19 cases (0.5%) in the placebo group.

Immunogenicity in children 6 years through 11 years of age
An analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in a subset of children aged 6 years through 11 years (n=319) in the paediatric study and in participants aged 18 through 25 years (n=295) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titres in children 6 years through 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9,

2.1). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in children 6 years through 11 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study is to infer efficacy of the booster dose in participants 6 years through 11 years of age by comparing post-booster dose immune responses (Day 29) to those obtained post dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in that study, where 93% efficacy was demonstrated. Efficacy of the 25 microgram Spikevax booster dose is inferred if post-booster dose immune responses (neutralising antibody [nAb] geometric mean concentration [GMC] and seroresponse rate [SRR]) meet pre-specified non-inferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy trial.

In an open-label phase of this study, participants 6 years through 11 years of age received a single booster dose at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 95 booster dose participants in 6 years through 11 years and a random subset of 295 participants from the young adult study who received two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

In the 95 participants, on booster dose-Day 29, the GMC was 5 847.5 (95% CI: 4 999.6, 6 839.1). The SRR was 100 (95% CI: 95.9, 100.0). Serum nAb levels for children 6 years through 11 years in the per-protocol immunogenicity subset with pre-booster SARS-CoV-2 negative status and the comparison with those from young adults (18 to 25 years of age) were studied. The GMR of booster dose Day 29 GMC compared to young adults Day 57 GMC was 4.2 (95% CI: 3.5, 5.0), meeting the noninferiority criteria (i.e., lower bound of the 95% CI > 0.667); the SRR difference was 0.7% (95% CI: -3.5, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of booster dose vaccine efficacy. The brisk recall response evident within 4 weeks of booster dosing is evidence of the robust priming induced by the Spikevax primary series.

Clinical efficacy in children 6 months through 5 years of age
An ongoing Phase 2/3 study was conducted to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax in healthy children 6 months through 11 years of age. The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 21 February 2022 was performed in 5 476 participants 6 months through 5 years of age who received two doses (at 0 and 1 month) of either Spikevax (n=4 105) or placebo (n=1 371) and had a negative baseline SARS-CoV-2 status (referred to as the Per Protocol Set for Efficacy). Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics.

The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 years through 5 years of age and 68 days for participants 6 months through 23 months of age.

Vaccine efficacy in this study was observed during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

Vaccine efficacy (VE) in Part 2 for the Per Protocol Set for Efficacy for COVID-19 cases 14 days or more after dose 2 using the “COVID-19 P301 case definition” (i.e., the definition employed in the

pivotal adult efficacy study) was 46.4% (95% CI: 19.8, 63.8) for children 2 years through 5 years of age and 31.5% (95% CI: -27.7, 62.0) for children 6 months through 23 months of age.

Immunogenicity in children 6 months through 5 years of age
For children aged 2 years through 5 years of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 264; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.014 (95% CI: 0.881, 1.167), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The geometric mean fold rise (GMFR) from baseline to Day 57 for these children was 183.3 (95% CI: 164.03, 204.91). The difference in seroresponse rates (SRR) between the children and young adults was -0.4% (95% CI: -2.7%, 1.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the SRR difference > -10%).

For infants and toddlers from 6 months through 23 months of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 230; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.280 (95% CI: 1.115, 1.470), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in SRR rates between the infants/toddlers and young adults was 0.7% (95% CI: -1.0%, 2.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the seroresponse rate difference > -10%).

Accordingly, the prespecified success criteria for the primary immunogenicity objective were met for both age groups, allowing efficacy of 25 micrograms to be inferred in both children 2 years through 5 years and infants and toddlers aged 6 months through 23 months (Tables 6 and 7).

Table 6. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 6 months through 23 months of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		6 months through 23 months n=230	**18 years through 25 years n=291**	**6 months through 23 months/ 18 years through 25 years**	
Assay	**Time point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 780.7 (1 606.4, 1 973.8)	1 390.8 (1 269.1, 1 524.2)	1.3 (1.1, 1.5)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.

[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralising antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 7. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 2 years through 5 years of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		2 years through 5 years n=264	**18 years through 25 years n=291**	**2 years through 5 years/ 18 years through 25 years**	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 410.0 (1 273.8, 1 560.8)	1 390.8 (1 262.5, 1 532.1)	1.0 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Available data in children 12 weeks to 6 months of age
The safety and immunogenicity of Spikevax bivalent Original/Omicron BA.1 were evaluated in children 12 weeks to 6 months of age in Study P206. During the dose-finding part of the study, two dose levels (5 mcg and 10 mcg) evaluated as a two-dose regimen were generally well tolerated but did not lead to a substantial immune response.

Immunogenicity in solid organ transplant recipients

The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose.

Immunogenicity in the study was assessed by measurement of neutralising antibodies against pseudovirus expressing the ancestral SARS-CoV-2 (D614G) strain at 1 month after Dose 2, Dose 3, booster dose and up to 12 months from the last dose in Part A, and up to 6 months from booster dose in Part B.

Three doses of Spikevax (original) induced enhanced neutralising antibody titres compared to pre-dose 1 and post-dose 2. A higher proportion of SOT participants who had received three doses achieved seroresponse compared to participants who had received two doses. The neutralising antibody levels observed in SOT liver participants who had received three doses was comparable to the post-dose 2 responses observed in the immunocompetent, baseline SARS-CoV-2-negative adult participants. The neutralising antibody responses continued to be numerically lower post-dose 3 in SOT kidney participants compared to SOT liver participants. The neutralising levels observed one month after Dose 3 persisted through six months with antibody levels maintained at 26-fold higher and seroresponse rate at 67% compared to baseline.

A fourth (booster) dose of Spikevax (original) enhanced neutralising antibody response in SOT participants compared to post-dose 3, regardless of the previous vaccines received [mRNA-1273 (Moderna), BNT162b2 or any mRNA-containing combination]; however, SOT kidney participants had numerically lower neutralising antibody responses compared to SOT liver participants.

Elderly

Spikevax (original) was assessed in individuals 6 months of age and older, including 3 768 subjects 65 years of age and older. The efficacy of Spikevax (original) was consistent between elderly (≥65 years) and younger adult subjects (18-64 years).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Spikevax (original) in one or more subsets of the paediatric population in the prevention of COVID-19 (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and reproductive and developmental toxicity.

General toxicity

General toxicity studies were conducted in rats (intramuscularly receiving up to 4 doses exceeding the human dose once every 2 weeks). Transient and reversible injection site oedema and erythema and transient and reversible changes in laboratory tests (including increases in eosinophils, activated

partial thromboplastin time, and fibrinogen) were observed. Results suggests the toxicity potential to humans is low.

Genotoxicity/carcinogenicity

In vitro and *in vivo* genotoxicity studies were conducted with the novel lipid component SM-102 of the vaccine. Results suggests the genotoxicity potential to humans is very low. Carcinogenicity studies were not performed.

Reproductive toxicity

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 micrograms) and other ingredients included in a single human dose of Spikevax (original) was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. SARS-CoV-2 antibody responses were present in maternal animals from prior to mating to the end of the study on lactation day 21 as well as in foetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryo foetal or offspring development or postnatal development. No data are available of Spikevax (original) vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate)
Cholesterol
1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
Trometamol
Trometamol hydrochloride
Acetic acid
Sodium acetate trihydrate
Sucrose
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened multidose vial (Spikevax XBB.1.5 0.1 mg/mL dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, the unopened vaccine vial may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days.

Chemical and physical stability has also been demonstrated for unopened vaccine vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the unopened vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on

the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C (see section 6.4).

Once thawed, the vaccine should not be refrozen.

The unopened vaccine may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Punctured multidose vials (Spikevax XBB.1.5 0.1 mg/mL dispersion for injection)

Chemical and physical in-use stability has been demonstrated for 19 hours at 2°C to 25ºC after initial puncture (within the allowed use period of 30 days or 14 days, respectively, at 2°C to 8ºC and including 24 hours at 8°C to 25ºC). From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

Unopened single-dose vial (Spikevax XBB.1.5 50 micrograms dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, single-dose vials may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days.

Chemical and physical stability has also been demonstrated for unopened single-dose vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the single-dose vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, single-dose vials may be transported up to 36 hours at 2°C to 8°C (see section 6.4).

Once thawed, the vaccine should not be refrozen.

Single-dose vials may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe and Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, pre-filled syringes may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened pre-filled syringes when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the pre-filled syringe will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Pre-filled syringe transport duration is limited by the shipper qualification duration.

Once thawed, the vaccine should not be refrozen.

Pre-filled syringes may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

6.4 Special precautions for storage

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection (multidose vials)

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.
For storage conditions of the multidose vial after first opening, see section 6.3.

Transportation of thawed multidose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 36 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax XBB.1.5 50 micrograms dispersion for injection (single-dose vials)

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the single-dose vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of single-dose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed single-dose vials in liquid state for up to 36 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, single-dose vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe and Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use. Pre-filled syringe transport duration is limited by the shipper qualification duration.

6.5 Nature and contents of container

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection (multidose vials)

2.5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax XBB.1.5 50 micrograms dispersion for injection (single-dose vials)

0.5 mL dispersion in a (type 1 glass or type 1 equivalent glass) single-dose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack sizes:
1 single-dose vial
10 single-dose vials
Each vial contains 0.5 mL.

Not all pack sizes may be marketed.

Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe and Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe

0.25 mL or 0.5 mL dispersion in a pre-filled syringe (cyclic olefin copolymer) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in a paper inner tray within a carton or in 1 clear blister containing 1 pre-filled syringe or 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack sizes:
1 pre-filled syringe
10 pre-filled syringes
Each pre-filled syringe contains 0.25 mL or 0.5 mL, depending on labelled syringe volume.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection (multidose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax XBB.1.5. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL, Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

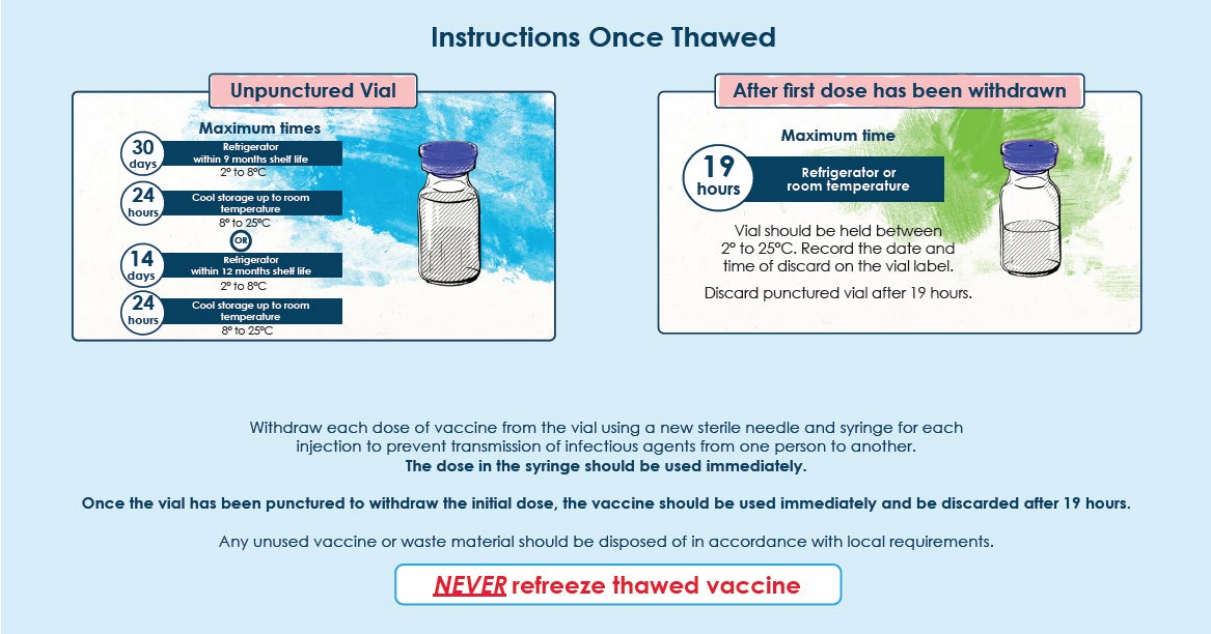
Pierce the stopper preferably at a different site each time.

An additional overfill is included in each multidose vial to ensure that 5 doses of 0.5 mL or a maximum of 10 doses of 0.25 mL can be delivered, depending on the individual's age.

Thaw each multidose vial before use following the instructions below (Table 8).

Table 8. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax XBB.1.5 50 micrograms dispersion for injection (single-dose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax XBB.1.5. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 1 or 10 vials may be thawed either in the refrigerator or at room temperature (Table 9).

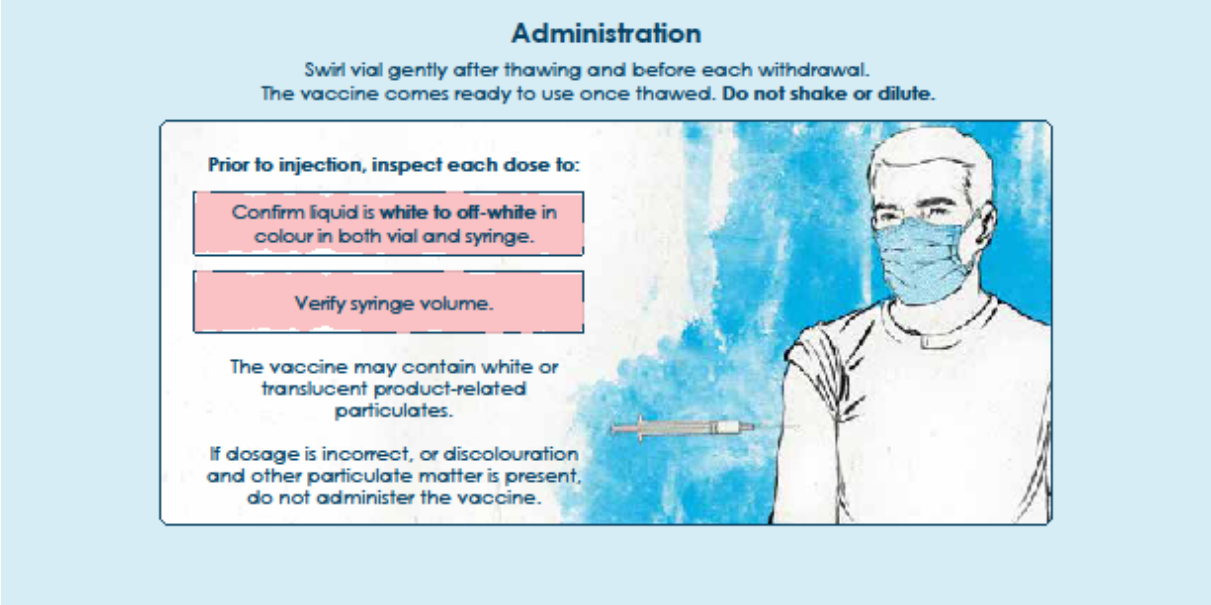
Table 9. Thawing instructions for single-dose vials and carton before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe and Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.25 mL or 0.5 mL can be administered from each pre-filled syringe, depending on labelled syringe volume. Do not use the 0.5 mL pre-filled syringe to administer a 0.25 mL dose.

Spikevax XBB.1.5 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.25 mL (25 micrograms of andusomeran) or 0.5 mL (50 micrograms of andusomeran) mRNA and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 1 or 2 pre-filled syringes, depending on pack size) or in the carton itself, either in the refrigerator or at room temperature (Table 10).

Table 10. Thawing instructions for Spikevax XBB.1.5 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax XBB.1.5. If the product name is Spikevax 50 micrograms, Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the Spikevax XBB.1.5 pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax XBB.1.5 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/011
EU/1/20/1507/012

EU/1/20/1507/013
EU/1/20/1507/014
EU/1/20/1507/015
EU/1/20/1507/016
EU/1/20/1507/017
EU/1/20/1507/018
EU/1/20/1507/027
EU/1/20/1507/028
EU/1/20/1507/029
EU/1/20/1507/030

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2021
Date of latest renewal: 03 October 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Spikevax JN.1 0.1 mg/mL dispersion for injection
Spikevax JN.1 50 micrograms dispersion for injection
Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1. Spikevax JN.1 qualitative and quantitative composition

Strength	Container	Dose(s)	Composition per dose
Spikevax JN.1 0.1 mg/mL dispersion for injection	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 JN.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of SARS-CoV-2 JN.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax JN.1 50 micrograms dispersion for injection	Single-dose 0.5 mL vial (blue flip-off cap)	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 JN.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 JN.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

SARS-CoV-2 JN.1 mRNA is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (JN.1).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection
White to off white dispersion (pH: 7.0 – 8.0).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Spikevax JN.1 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older (see sections 4.2 and 5.1).

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Table 2. Spikevax JN.1 posology

Age(s)	**Dose**	**Additional recommendations**
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose (see sections 4.4 and 5.1). If a child has received one prior dose of any Spikevax vaccine, one dose of Spikevax JN.1 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax JN.1 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 3. Spikevax JN.1 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Paediatric population
The safety and efficacy of Spikevax in children less than 6 months of age have not yet been established (see section 5.1).

Elderly
No dose adjustment is required in elderly individuals ≥65 years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Anaphylaxis has been reported in individuals who have received Spikevax (original). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. Subsequent doses of Spikevax JN.1 should not be given to those who have experienced anaphylaxis to a prior dose of any Spikevax vaccine.

Myocarditis and pericarditis

There is an increased risk for myocarditis and pericarditis following vaccination with Spikevax.

These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose (see section 4.8).

Available data indicate that most cases recover. Some cases required intensive care support and fatal cases have been observed.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Capillary leak syndrome flare-ups

A few cases of capillary leak syndrome (CLS) flare-ups have been reported in the first days after vaccination with Spikevax (original). Healthcare professionals should be aware of signs and symptoms of CLS to promptly recognise and treat the condition. In individuals with a medical history of CLS, planning of vaccination should be made in collaboration with appropriate medical experts.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical studies.

Limitations of vaccine effectiveness

As with all vaccines, vaccination with Spikevax JN.1 may not protect all vaccine recipients.

Excipients with known effect

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

Different injectable vaccines should be given at different injection sites.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data are available yet regarding the use of SARS-CoV-2 JN.1 mRNA during pregnancy.

However, a large amount of observational data from pregnant women vaccinated with Spikevax (original) during the second and third trimester has not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, SARS-CoV-2 JN.1 mRNA can be used during pregnancy.

Breast-feeding

No data are available yet regarding the use of SARS-CoV-2 JN.1 mRNA during breastfeeding.

However, no effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to the vaccine is negligible. Observational data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. SARS-CoV-2 JN.1 mRNA can be used during breastfeeding.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

SARS-CoV-2 JN.1 mRNA has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Adults
The safety of Spikevax (original) was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30 351 participants 18 years of age and older who received at least one dose of Spikevax (original) (n=15 185) or placebo (n=15 166) (NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22 831 (75.2%) of participants were 18 to 64 years of age and 7 520 (24.8%) of participants were 65 years of age and older.

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Adolescents 12 through 17 years of age
Safety data for Spikevax (original) in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study with multiple parts conducted in the United States. The first portion of the study involved 3 726 participants 12 through 17 years of age who received at least one dose of Spikevax (original) (n=2 486) or placebo (n=1 240) (NCT04649151). Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in adolescents 12 to 17 years of age were injection site pain (97%), headache (78%), fatigue (75%), myalgia (54%), chills (49%), axillary swelling/tenderness (35%), arthralgia (35%), nausea/vomiting (29%), injection site swelling (28%), injection site erythema (26%), and fever (14%).

This study transitioned to an open-label Phase 2/3 study in which 1 346 participants 12 years through 17 years of age received a booster dose of Spikevax at least 5 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 years through 11 years of age
Safety data for Spikevax (original) in children were collected in an ongoing Phase 2/3 two-part randomised, observer-blind clinical study conducted in the United States and Canada (NCT04796896). Part 1 is an open-label phase of the study for safety, dose selection, and immunogenicity and included 380 participants 6 years through 11 years of age who received at least 1 dose (0.25 mL) of Spikevax (original). Part 2 is the placebo-controlled phase for safety and included 4 016 participants 6 years through 11 years of age who received at least one dose (0.25 mL) of Spikevax (original) (n=3 012) or placebo (n=1 004). No participants in Part 1 participated in Part 2. Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in participants 6 years through 11 years of age following administration of the primary series (in Part 2) were injection site pain (98.4%), fatigue (73.1%), headache (62.1%), myalgia (35.3%), chills (34.6%), nausea/vomiting (29.3%), axillary swelling/tenderness (27.0%), fever (25.7%), injection site erythema (24.0%), injection site swelling (22.3%), and arthralgia (21.3%).

The study protocol was amended to include an open-label booster dose phase that included 1 294 participants 6 years through 11 years of age who received a booster dose of Spikevax at least 6 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 months through 5 years of age
An ongoing Phase 2/3 randomised, placebo-controlled, observer-blind study to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax was conducted in the United States and Canada. This study involved 10 390 participants 6 months through 11 years of age who received at least one dose of Spikevax (n=7 798) or placebo (n=2 592).

The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months. This paediatric study involved 6 388 participants 6 months through 5 years of age who received at least one dose of Spikevax (n=4 791) or placebo (n=1 597). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

In this clinical study, the adverse reactions in participants 6 months through 23 months of age following administration of the primary series were irritability/crying (81.5%), pain at the injection site (56.2%), sleepiness (51.1%), loss of appetite (45.7%), fever (21.8%), swelling at the injection site (18.4%), erythema at the injection site (17.9%), and axillary swelling/tenderness (12.2%).

The adverse reactions in participants 24 through 36 months of age following administration of the primary series were pain at the injection site (76.8%), irritability/crying (71.0%), sleepiness (49.7%), loss of appetite (42.4%), fever (26.1%), erythema at the injection site (17.9%), swelling at the injection site (15.7%), and axillary swelling/tenderness (11.5%).

The adverse reactions in participants 37 months through 5 years of age following administration of the primary series were pain at the injection site (83.8%), fatigue (61.9%), headache (22.9%), myalgia (22.1%), fever (20.9%), chills (16.8%), nausea/vomiting (15.2%), axillary swelling/tenderness (14.3%), arthralgia (12.8%), erythema at the injection site (9.5%), and swelling at the injection site (8.2%).

Tabulated list of adverse reactions

The safety profile presented below is based on data generated in several placebo-controlled clinical studies:

- 30 351 adults ≥ 18 years of age
- 3 726 adolescents 12 through 17 years of age
- 4 002 children 6 years through 11 years of age
- 6 388 children aged 6 months through 5 years of age
- and post-marketing experience.

Adverse reactions reported are listed according to the following frequency convention:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness (Table 4).

Table 4. Adverse reactions from Spikevax (original) clinical studies and post authorisation experience in children and individuals 6 months of age and older

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Immune system disorders	Not known	Anaphylaxis
		Hypersensitivity
Metabolism and nutrition disorders	Very common	Decreased appetite†
Psychiatric disorders	Very common	Irritability/crying†
Nervous system disorders	Very common	Headache Sleepiness†
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Common	Diarrhoea
	Uncommon	Abdominal pain§
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria¶
	Not known	Erythema multiforme Mechanical urticaria Chronic urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
Reproductive system and breast disorders	Not known	Heavy menstrual bleeding#
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills Pyrexia Injection site swelling Injection site erythema
	Common	Injection site urticaria Injection site rash Delayed injection site reaction♠
	Uncommon	Injection site pruritus
	Rare	Facial swelling♥
	Not known	Extensive swelling of vaccinated limb

*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site. Other lymph nodes (e.g., cervical, supraclavicular) were affected in some cases.

† Observed in the paediatric population (6 months to 5 years of age).

‡ Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the Spikevax (original) group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.

§ Abdominal pain was observed in the paediatric population (6 to 11 years of age): 0.2% in the Spikevax (original) group and 0% in the placebo group.

¶ Urticaria has been observed with either acute onset (within a few days after vaccination) or delayed onset (up to approximately two weeks after vaccination).

Most cases appeared to be non-serious and temporary in nature.

♠ Median time to onset was 9 days after the first injection, and 11 days after the second injection. Median duration was 4 days after the first injection, and 4 days after the second injection.

♥ There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

The reactogenicity and safety profile in 343 subjects receiving Spikevax (original), that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

Adults (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine primary series. In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (0.25 mL, 50 micrograms) was similar to that after the second dose in the primary series.

Spikevax bivalent Original/Omicron BA.1 (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax bivalent Original/Omicron BA.1 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Spikevax bivalent Original/Omicron BA.1 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose. The frequency of adverse reactions after immunisation with Spikevax bivalent Original/Omicron BA.1 was also similar or lower relative to that of a first booster dose of Spikevax (original) (50 micrograms) and relative to the second dose of the Spikevax (original) primary series (100 micrograms). The safety profile of Spikevax bivalent Original/Omicron BA.1 (median follow-up period of 113 days) was similar to the safety profile of Spikevax (original) (median follow-up period of 127 days).

Spikevax bivalent Original/Omicron BA.4-5 (booster dose)
The safety, reactogenicity, and immunogenicity of a bivalent booster dose of Spikevax bivalent Original/Omicron BA.4-5 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received a booster dose of Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms), and 376 participants received a booster dose of Spikevax (original) (50 micrograms).

Spikevax bivalent Original/Omicron BA.4-5 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose.

Spikevax XBB.1.5 (booster dose)
The safety, reactogenicity and immunogenicity of a booster dose of Spikevax XBB.1.5 are evaluated in an ongoing Phase 2/3 open-label study in adults (mRNA-1273-P205, Part J). In this study, 50 participants received a booster dose of Spikevax XBB.1.5 (50 micrograms) and 51 participants received a booster dose of an investigational bivalent Omicron XBB.1.5/BA.4-5 vaccine (50 micrograms).

The reactogenicity profile of Spikevax XBB.1.5 was similar to that of Spikevax (original) and Spikevax bivalent Original/Omicron BA.4-5. The median follow-up time for both vaccine groups in this interim analysis was 20 days (range of 20 to 22 days with data cut-off date of 16 May 2023).

Spikevax (original) in solid organ transplant recipients
The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose (fourth dose for mRNA vaccines and third dose for non-mRNA vaccines).

Reactogenicity was consistent with the known profile of Spikevax (original). There were no unexpected safety findings.

Description of selected adverse reactions

Myocarditis
The increased risk of myocarditis after vaccination with Spikevax (original) is highest in younger males (see section 4.4).

Two large European pharmacoepidemiological studies have estimated the excess risk in younger males following the second dose of Spikevax (original). One study showed that in a period of 7 days after the second dose, there were about 1.316 (95% CI: 1.299, 1.333) extra cases of myocarditis in 12 to 29 year-old males per 10 000 compared to unexposed persons. In another study, in a period of 28 days after the second dose, there were 1.88 (95% CI: 0.956, 2.804) extra cases of myocarditis in 16 to 24 year-old males per 10 000 compared to unexposed persons.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, COVID-19 vaccines, ATC code: J07BN01

Mechanism of action

Elasomeran and elasomeran/imelasomeran both contain mRNA encapsulated in lipid nanoparticles. The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is non-replicating, and is expressed transiently mainly by dendritic cells and subcapsular sinus macrophages. The expressed, membrane-bound spike protein of SARS-CoV-2 is then recognised by immune cells as a foreign antigen. This elicits both T-cell and B-cell responses to generate neutralising antibodies, which may contribute to protection against COVID-19. The nucleoside-modified mRNA in elasomeran/davesomeran, andusomeran and SARS-CoV-2 JN.1 mRNA is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

Clinical efficacy

Immunogenicity in adults – after Spikevax XBB.1.5 dose (0.5 mL, 50 micrograms) versus an investigational bivalent XBB.1.5/BA.4-5 dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity and immunogenicity of Spikevax XBB.1.5 50 micrograms and of a bivalent vaccine that contains equal mRNA amounts of Omicron XBB.1.5 and Omicron BA.4-5 spike proteins (25 micrograms XBB.1.5 / 25 micrograms BA.4-5) are evaluated in a Phase 2/3 open-label study in adults. In this study, 50 participants received Spikevax XBB.1.5 and 51 participants received the investigational bivalent XBB.1.5/BA.4-5 (mRNA-1273- P205, Part J). The two groups were randomised 1:1.

The vaccines were administered as a fifth dose to adults who previously received a two-dose primary series of any mRNA COVID-19 vaccine, a booster dose of any mRNA COVID-19 vaccine, and a booster dose of any mRNA bivalent Original/Omicron BA.4-5 vaccine.

Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 elicited potent neutralising responses at Day 15 against XBB.1.5, XBB.1.16, BA.4-5, BQ.1.1 and D614G. In the per-protocol immunogenicity set that includes all participants, with and without prior SARS-CoV-2 infection (N=49 and N=50 for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 groups, respectively), the Day 15 GMFR (95% CI) for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 was 16.7 (12.8, 21.7) and 11.6 (8.7, 15.4), respectively, against XBB.1.5 and 6.3 (4.8, 8.2) and 5.3 (3.9, 7.1) against BA.4-5.

For variants not contained in the vaccines, the Day 15 GMFR (95% CI) for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 was 11.4 (8.5, 15.4) and 9.3 (7.0, 12.3) against XBB.1.16; 5.8 (4.7, 7.3) and 6.1 (4.6, 7.9) against BQ.1.1 and 2.8 (2.2, 3.5) and 2.3 (1.9, 2.8) against D614G.

Immunogenicity in participants 18 years of age and older – after Spikevax bivalent Original/Omicron BA.4-5 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.4-5 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received the Spikevax bivalent Original/Omicron BA.4-5 50 microgram booster dose, and 376 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part H evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.4-5 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a first booster dose of Spikevax (original) (50 micrograms). In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part F group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.4-5 group. In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the observed geometric mean titre (GMT) (95% CI) at pre-booster was 87.9 (72.2, 107.1) and increased to 2 324.6 (1 921.2, 2 812.7) 28 days after the Spikevax bivalent Original/Omicron BA.4-5 booster dose. The Day 29 GMR for Spikevax Original/Omicron BA.4-5 50 microgram booster dose versus the Spikevax (original) 50 microgram booster dose was 6.29 (5.27, 7.51), meeting the pre-specified criterion for superiority (lower bound of CI >1).

The estimated neutralising antibody GMTs (95% CI) against Omicron BA.4/BA.5 adjusted for pre-booster titre and age group were 2 747.3 (2 399.2, 3 145.9) and 436.7 (389.1, 490.0) 28 days after Spikevax bivalent Original/Omicron BA.4-5 and Spikevax (original) booster doses, respectively, and the GMR (95% CI) was 6.29 (5.27, 7.51), meeting the pre-specified criterion for non-inferiority (lower bound of CI >0.667).

Immunogenicity in adults – after Spikevax bivalent Original/Omicron BA.1 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.1 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age

and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part G evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.1 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a booster dose of Spikevax (original) (50 micrograms) at least 3 months prior to enrolment. In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part G group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.1 group.

In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the original SARS-CoV-2 estimated neutralising antibody geometric mean titre (GMT) and corresponding 95% CI was 6 422.3 (5 990.1, 6 885.7) and 5 286.6 (4 887.1, 5 718.9) 28 days after the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster doses, respectively. These GMTs represent the ratio between response of Spikevax bivalent Original/Omicron BA.1 versus Spikevax (original) against the ancestral SARS-CoV-2 (D614G) strain. The GMR (97.5% CI) was 1.22 (1.08, 1.37) meeting the pre-specified criterion for non-inferiority (lower bound of 97.5% CI ≥0.67).

The estimated Day 29 neutralising antibody GMTs against Omicron, BA.1 were 2 479.9 (2 264.5, 2 715.8) and 1 421.2 (1 283.0, 1 574.4) in the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster groups, respectively, and the GMR (97.5% CI) was 1.75 (1.49, 2.04), which met the pre-specified superiority criterion (lower bound of CI >1).

Three-month antibody persistence of Spikevax bivalent Original/Omicron BA.1 booster vaccine against COVID-19
Participants in Study P205 Part G were sequentially enrolled to receive 50 micrograms of Spikevax (original) (n = 376) or Spikevax bivalent Original/Omicron BA.1 (n = 437) as second booster doses. In participants with no pre-booster incidence of SARS-CoV-2, Spikevax bivalent Original/Omicron BA.1 elicited Omicron-BA.1-neutralising antibody titres (observed GMT) that were significantly higher (964.4 [834.4, 1 114.7]) than those of Spikevax (original) (624.2 [533.1, 730.9]) and similar between boosters against ancestral SARS-CoV-2 at three months.

Clinical efficacy in adults
The adult study was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or had received immunosuppressants within 6 months, as well as participants who were pregnant, or with a known history of SARS-CoV-2 infection. Participants with stable HIV disease were not excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of Spikevax (original). Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or Spikevax (original).

A total of 30 351 subjects were followed for a median of 92 days (range: 1-122) for the development of COVID-19 disease.

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28 207 subjects who received either Spikevax (original) (n=14 134) or placebo (n=14 073) and had a negative baseline SARS-CoV-2 status. The PPS study population included 47.4% female, 52.6% male, 79.5% White, 9.7% African American, 4.6% Asian, and 6.2% other. 19.7% of participants identified as Hispanic or Latino. The median age of subjects was 53 years (range 18-94). A dosing window of –7 to +14 days for administration of the second dose (scheduled at day 29) was allowed for inclusion in the PPS. 98% of vaccine recipients received the second dose 25 days to 35 days after dose 1 (corresponding to -3 to +7 days around the interval of 28 days).

COVID-19 cases were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT PCR) and by a Clinical Adjudication Committee. Vaccine efficacy overall and by key age groups are presented in Table 5.

Table 5. Vaccine efficacy analysis: confirmed COVID-19[#] regardless of severity starting 14 days after the 2nd dose – PPS

Age group (years)	Spikevax (original)			Placebo			
	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	% Vaccine efficacy (95% CI)*
Overall (≥18)	14 134	11	3.328	14 073	185	56.510	94.1 (89.3, 96.8)**
18 to <65	10 551	7	2.875	10 521	156	64.625	95.6 (90.6, 97.9)
≥65	3 583	4	4.595	3 552	29	33.728	86.4 (61.4, 95.2)
≥65 to <75	2 953	4	5.586	2 864	22	31.744	82.4% (48.9, 93.9)
≥75	630	0	0	688	7	41.968	100% (NE, 100)

[#]COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the 2nd dose.
*Vaccine efficacy and 95% confidence interval (CI) from the stratified Cox proportional hazard model
** CI not adjusted for multiplicity. Multiplicity adjusted statistical analyses were carried out in an interim analysis based on less COVID-19 cases, not reported here.

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 of 185 (16%) cases reported in the placebo group. Of the 30 participants with severe disease, 9 were hospitalised, 2 of which were admitted to an intensive care unit. The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO2) criterion for severe disease (≤ 93% on room air).

The vaccine efficacy of Spikevax (original) to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% CI: 88.6, 96.5).

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Immunogenicity in adults – after booster dose (0.25 mL, 50 micrograms)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine as primary series. In an open-label phase, 149 of those participants (Per Protocol Set) received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL, 50 micrograms) was shown to result in a geometric mean fold rise (GMFR) of 12.99 (95% CI: 11.04, 15.29) in neutralising antibodies from pre-booster compared to

28 days after the booster dose. The GMFR in neutralising antibodies was 1.53 (95% CI: 1.32, 1.77) when compared 28 days post dose 2 (primary series) to 28 days after the booster dose.

Immunogenicity of a booster dose following primary vaccination with another authorised COVID-19 vaccine in adults
Safety and immunogenicity of a heterologous booster with Spikevax (original) were studied in an investigator-initiated study with 154 participants. The minimum time interval between primary series using a vector-based or RNA-based COVID-19 vaccine and booster injection with Spikevax (original) was 12 weeks (range: 12 weeks to 20.9 weeks). The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 1 prior to administration and at Day 15 and Day 29 after the booster dose. A booster response was demonstrated regardless of primary vaccination.

Only short-term immunogenicity data are available; long-term protection and immunological memory are currently unknown.

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) in the UK
COV-BOOST is a multicentre, randomised Phase 2 investigator-initiated study of third dose booster vaccination against COVID-19 with a subgroup to investigate detailed immunology. Participants were adults aged 30 years or older, in good physical health (mild to moderate well-controlled co-morbidities were permitted), who had received two doses of either Pfizer–BioNTech or Oxford–AstraZeneca (first dose in December 2020, January 2021 or February 2021), and were at least 84 days post second dose by the time of enrolment. Spikevax (original) boosted antibody and neutralising responses and was well tolerated regardless of the prime series. The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 28 after the booster dose.

Clinical efficacy in adolescents 12 through 17 years of age
The adolescent study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study (NCT04649151) to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in adolescents 12 to 17 years of age. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3 732 participants were randomised 2:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis was performed in 3 181 participants who received 2 doses of either Spikevax (original) (n=2 139) or placebo (n=1 042) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were zero symptomatic COVID-19 cases in the Spikevax (original) group and 4 symptomatic COVID-19 cases in the placebo group.

Immunogenicity in adolescents 12 to 17 years of age – after Spikevax primary vaccination
A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in the per-protocol immunogenicity subsets of adolescents aged 12 through 17 (n=340) in the adolescent study and in participants aged 18 through 25 (n=296) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The geometric mean ratio (GMR) of the neutralising antibody titres in adolescents 12 to 17 years of age compared to the 18- to 25-year-olds was 1.08 (95% CI: 0.94, 1.24). The difference in seroresponse rate was 0.2% (95% CI: -1.8, 2.4). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in adolescents 12 years through 17 years of age – after Spikevax (original) booster dose

The primary immunogenicity objective of the booster phase of this study was to infer efficacy of the booster dose in participants 12 years through 17 years of age by comparing post-booster immune responses (Day 29) to those obtained post-dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in the adult study. Efficacy of the 50 microgram Spikevax booster dose is inferred if post-booster dose immune responses (nAb geometric mean concentration [GMC] and seroresponse rate [SRR]) meet prespecified noninferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy study.

In an open-label phase of this study, participants 12 years through 17 years of age received a single booster dose at least 5 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 257 booster dose participants in this study and a random subset of 295 participants from the young adult study (ages ≥18 to ≤25 years) who previously completed a primary vaccination series of two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

The GMR of the adolescent booster dose Day 29 GMC compared with young adults: Day 57 GMR was 5.1 (95% CI: 4.5, 5.8), meeting the noninferiority criteria (i.e., lower bound of the 95% CI >0.667 (1/1.5); point estimate ≥0.8); the SRR difference was 0.7% (95% CI: -0.8, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

In the 257 participants, pre-booster (booster dose-Day 1) nAb GMC was 400.4 (95% CI: 370.0, 433.4); on BD-Day 29, the GMC was 7 172.0 (95% CI: 6 610.4, 7 781.4). Post-booster booster dose-Day 29 GMC increased approximately 18-fold from pre-booster GMC, demonstrating the potency of the booster dose to adolescents. The SRR was 100 (95% CI: 98.6, 100.0).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of vaccine efficacy from the adult study.

Clinical efficacy in children 6 years through 11 years of age
The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in children aged 6 years through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 4 016 participants were randomised 3:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 10 November 2021 was performed in 3 497 participants who received two doses (0.25 mL at 0 and 1 month) of either Spikevax (original) (n=2 644) or placebo (n=853) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were three COVID-19 cases (0.1%) in the Spikevax (original) group and four COVID-19 cases (0.5%) in the placebo group.

Immunogenicity in children 6 years through 11 years of age
An analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in a subset of children aged 6 years through 11 years (n=319) in the paediatric study and in participants aged 18 through 25 years (n=295) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titres in children 6 years through 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9,

2.1). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in children 6 years through 11 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study is to infer efficacy of the booster dose in participants 6 years through 11 years of age by comparing post-booster dose immune responses (Day 29) to those obtained post dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in that study, where 93% efficacy was demonstrated. Efficacy of the 25 microgram Spikevax booster dose is inferred if post-booster dose immune responses (neutralising antibody [nAb] geometric mean concentration [GMC] and seroresponse rate [SRR]) meet pre-specified non-inferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy trial.

In an open-label phase of this study, participants 6 years through 11 years of age received a single booster dose at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 95 booster dose participants in 6 years through 11 years and a random subset of 295 participants from the young adult study who received two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

In the 95 participants, on booster dose-Day 29, the GMC was 5 847.5 (95% CI: 4 999.6, 6 839.1). The SRR was 100 (95% CI: 95.9, 100.0). Serum nAb levels for children 6 years through 11 years in the per-protocol immunogenicity subset with pre-booster SARS-CoV-2 negative status and the comparison with those from young adults (18 to 25 years of age) were studied. The GMR of booster dose Day 29 GMC compared to young adults Day 57 GMC was 4.2 (95% CI: 3.5, 5.0), meeting the noninferiority criteria (i.e., lower bound of the 95% CI > 0.667); the SRR difference was 0.7% (95% CI: -3.5, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of booster dose vaccine efficacy. The brisk recall response evident within 4 weeks of booster dosing is evidence of the robust priming induced by the Spikevax primary series.

Clinical efficacy in children 6 months through 5 years of age
An ongoing Phase 2/3 study was conducted to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax in healthy children 6 months through 11 years of age. The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 21 February 2022 was performed in 5 476 participants 6 months through 5 years of age who received two doses (at 0 and 1 month) of either Spikevax (n=4 105) or placebo (n=1 371) and had a negative baseline SARS-CoV-2 status (referred to as the Per Protocol Set for Efficacy). Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics.

The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 years through 5 years of age and 68 days for participants 6 months through 23 months of age.

Vaccine efficacy in this study was observed during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

Vaccine efficacy (VE) in Part 2 for the Per Protocol Set for Efficacy for COVID-19 cases 14 days or more after dose 2 using the “COVID-19 P301 case definition” (i.e., the definition employed in the

pivotal adult efficacy study) was 46.4% (95% CI: 19.8, 63.8) for children 2 years through 5 years of age and 31.5% (95% CI: -27.7, 62.0) for children 6 months through 23 months of age.

Immunogenicity in children 6 months through 5 years of age
For children aged 2 years through 5 years of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 264; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.014 (95% CI: 0.881, 1.167), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The geometric mean fold rise (GMFR) from baseline to Day 57 for these children was 183.3 (95% CI: 164.03, 204.91). The difference in seroresponse rates (SRR) between the children and young adults was -0.4% (95% CI: -2.7%, 1.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the SRR difference > -10%).

For infants and toddlers from 6 months through 23 months of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 230; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.280 (95% CI: 1.115, 1.470), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in SRR rates between the infants/toddlers and young adults was 0.7% (95% CI: -1.0%, 2.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the seroresponse rate difference > -10%).

Accordingly, the prespecified success criteria for the primary immunogenicity objective were met for both age groups, allowing efficacy of 25 micrograms to be inferred in both children 2 years through 5 years and infants and toddlers aged 6 months through 23 months (Tables 6 and 7).

Table 6. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 6 months through 23 months of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		6 months through 23 months n=230	**18 years through 25 years n=291**	**6 months through 23 months/ 18 years through 25 years**	
Assay	**Time point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 780.7 (1 606.4, 1 973.8)	1 390.8 (1 269.1, 1 524.2)	1.3 (1.1, 1.5)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.

[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralising antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 7. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 2 years through 5 years of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		2 years through 5 years n=264	**18 years through 25 years n=291**	**2 years through 5 years/ 18 years through 25 years**	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 410.0 (1 273.8, 1 560.8)	1 390.8 (1 262.5, 1 532.1)	1.0 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Available data in children 12 weeks to 6 months of age
The safety and immunogenicity of Spikevax bivalent Original/Omicron BA.1 were evaluated in children 12 weeks to 6 months of age in Study P206. During the dose-finding part of the study, two dose levels (5 mcg and 10 mcg) evaluated as a two-dose regimen were generally well tolerated but did not lead to a substantial immune response.

Immunogenicity in solid organ transplant recipients

The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose.

Immunogenicity in the study was assessed by measurement of neutralising antibodies against pseudovirus expressing the ancestral SARS-CoV-2 (D614G) strain at 1 month after Dose 2, Dose 3, booster dose and up to 12 months from the last dose in Part A, and up to 6 months from booster dose in Part B.

Three doses of Spikevax (original) induced enhanced neutralising antibody titres compared to pre-dose 1 and post-dose 2. A higher proportion of SOT participants who had received three doses achieved seroresponse compared to participants who had received two doses. The neutralising antibody levels observed in SOT liver participants who had received three doses was comparable to the post-dose 2 responses observed in the immunocompetent, baseline SARS-CoV-2-negative adult participants. The neutralising antibody responses continued to be numerically lower post-dose 3 in SOT kidney participants compared to SOT liver participants. The neutralising levels observed one month after Dose 3 persisted through six months with antibody levels maintained at 26-fold higher and seroresponse rate at 67% compared to baseline.

A fourth (booster) dose of Spikevax (original) enhanced neutralising antibody response in SOT participants compared to post-dose 3, regardless of the previous vaccines received [mRNA-1273 (Moderna), BNT162b2 or any mRNA-containing combination]; however, SOT kidney participants had numerically lower neutralising antibody responses compared to SOT liver participants.

Elderly

Spikevax (original) was assessed in individuals 6 months of age and older, including 3 768 subjects 65 years of age and older. The efficacy of Spikevax (original) was consistent between elderly (≥65 years) and younger adult subjects (18-64 years).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Spikevax (original) in one or more subsets of the paediatric population in the prevention of COVID-19 (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and reproductive and developmental toxicity.

General toxicity

General toxicity studies were conducted in rats (intramuscularly receiving up to 4 doses exceeding the human dose once every 2 weeks). Transient and reversible injection site oedema and erythema and transient and reversible changes in laboratory tests (including increases in eosinophils, activated

partial thromboplastin time, and fibrinogen) were observed. Results suggests the toxicity potential to humans is low.

Genotoxicity/carcinogenicity

In vitro and *in vivo* genotoxicity studies were conducted with the novel lipid component SM-102 of the vaccine. Results suggests the genotoxicity potential to humans is very low. Carcinogenicity studies were not performed.

Reproductive toxicity

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 micrograms) and other ingredients included in a single human dose of Spikevax (original) was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. SARS-CoV-2 antibody responses were present in maternal animals from prior to mating to the end of the study on lactation day 21 as well as in foetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryo foetal or offspring development or postnatal development. No data are available of Spikevax (original) vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate)
Cholesterol
1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
Trometamol
Trometamol hydrochloride
Acetic acid
Sodium acetate trihydrate
Sucrose
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened multidose vial (Spikevax JN.1 0.1 mg/mL dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, the unopened vaccine vial may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days.

Chemical and physical stability has also been demonstrated for unopened vaccine vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the unopened vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on

the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C (see section 6.4).

Once thawed, the vaccine should not be refrozen.

The unopened vaccine may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Punctured multidose vials (Spikevax JN.1 0.1 mg/mL dispersion for injection)

Chemical and physical in-use stability has been demonstrated for 19 hours at 2°C to 25ºC after initial puncture (within the allowed use period of 30 days or 14 days, respectively, at 2°C to 8ºC and including 24 hours at 8°C to 25ºC). From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

Unopened single-dose vial (Spikevax JN.1 50 micrograms dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, single-dose vials may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days.

Chemical and physical stability has also been demonstrated for unopened single-dose vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the single-dose vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, single-dose vials may be transported up to 36 hours at 2°C to 8°C (see section 6.4).

Once thawed, the vaccine should not be refrozen.

Single-dose vials may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, pre-filled syringes may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened pre-filled syringes when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the pre-filled syringe will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Pre-filled syringe transport duration is limited by the shipper qualification duration.

Once thawed, the vaccine should not be refrozen.

Pre-filled syringes may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

6.4 Special precautions for storage

Spikevax JN.1 0.1 mg/mL dispersion for injection (multidose vials)

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.
For storage conditions of the multidose vial after first opening, see section 6.3.

Transportation of thawed multidose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 36 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax JN.1 50 micrograms dispersion for injection (single-dose vials)

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the single-dose vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of single-dose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed single-dose vials in liquid state for up to 36 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, single-dose vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use. Pre-filled syringe transport duration is limited by the shipper qualification duration.

6.5 Nature and contents of container

Spikevax JN.1 0.1 mg/mL dispersion for injection (multidose vials)

2.5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax JN.1 50 micrograms dispersion for injection (single-dose vials)

0.5 mL dispersion in a (type 1 glass or type 1 equivalent glass) single-dose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack sizes:
1 single-dose vial
10 single-dose vials
Each vial contains 0.5 mL.

Not all pack sizes may be marketed.

Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe

0.5 mL dispersion in a pre-filled syringe (cyclic olefin copolymer) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in a paper inner tray within a carton or in 1 clear blister containing 1 pre-filled syringe or 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack sizes:
1 pre-filled syringe
10 pre-filled syringes
Each pre-filled syringe contains 0.5 mL.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.

Spikevax JN.1 0.1 mg/mL dispersion for injection (multidose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax JN.1. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 or Spikevax XBB.1.5, please make reference to the Summary of Product Characteristics for that formulation.

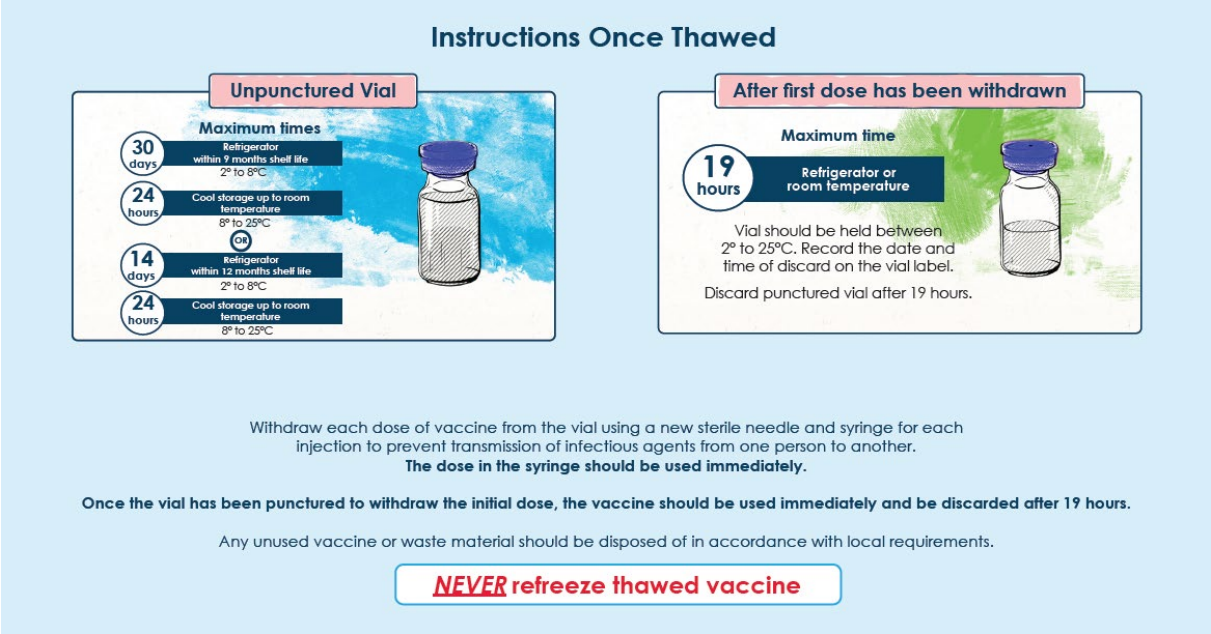
Pierce the stopper preferably at a different site each time.

An additional overfill is included in each multidose vial to ensure that 5 doses of 0.5 mL or a maximum of 10 doses of 0.25 mL can be delivered, depending on the individual's age.

Thaw each multidose vial before use following the instructions below (Table 8).

Table 8. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax JN.1 50 micrograms dispersion for injection (single-dose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax JN.1. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 or Spikevax XBB.1.5, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 1 or 10 vials may be thawed either in the refrigerator or at room temperature (Table 9).

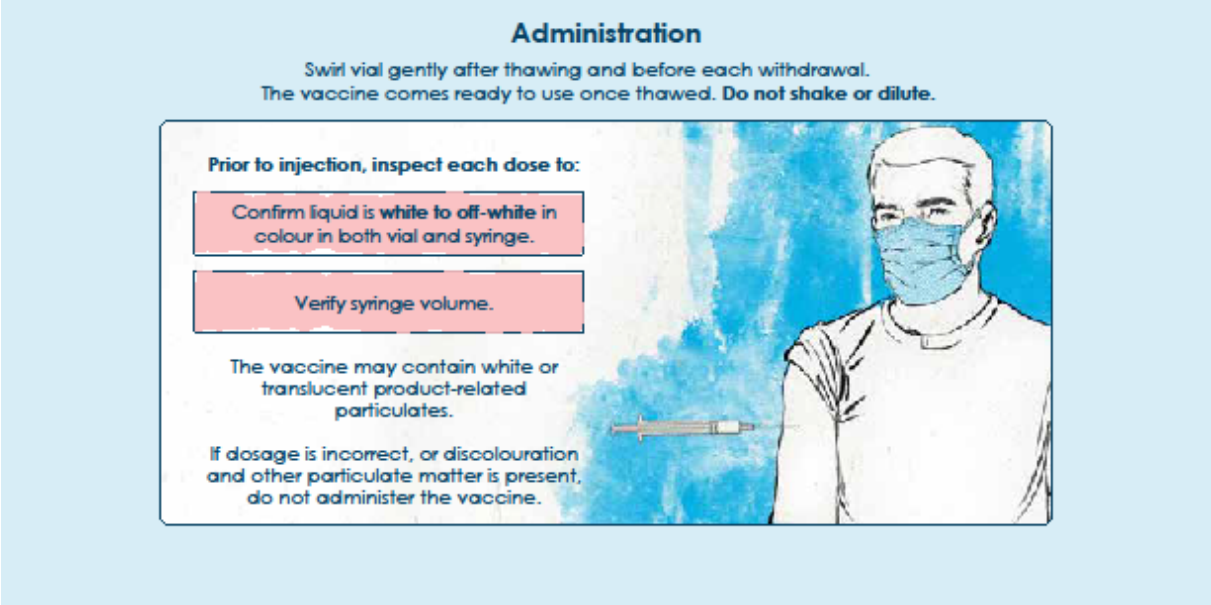
Table 9. Thawing instructions for single-dose vials and carton before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax JN.1 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (50 micrograms of SARS-CoV-2 JN.1 mRNA) and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 1 or 2 pre-filled syringes, depending on pack size) or in the carton itself, either in the refrigerator or at room temperature (Table 10).

Table 10. Thawing instructions for Spikevax JN.1 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a	Thaw duration (minutes)	Thaw temperature (at room	Thaw duration (minutes)

	refrigerator) (°C)		temperature) (°C)	
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax JN.1. If the product name is Spikevax 50 micrograms, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 or Spikevax XBB.1.5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the Spikevax JN.1 pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax JN.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/019
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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2021
Date of latest renewal: 03 October 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Spikevax LP.8.1 0.1 mg/mL dispersion for injection
Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe
Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1. Spikevax LP.8.1 qualitative and quantitative composition

Strength	**Container**	**Dose(s)**	**Composition per dose**
Spikevax LP.8.1 0.1 mg/mL dispersion for injection	Multidose 2.5 mL vial (blue flip-off cap)	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).
Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.25 mL For single-use only.	One dose (0.25 mL) contains 25 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in lipid nanoparticles).

SARS-CoV-2 LP.8.1 mRNA is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (LP.8.1).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection
White to off white dispersion (pH: 7.0 – 8.0).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Spikevax LP.8.1 is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older (see sections 4.2 and 5.1).

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Table 2. Spikevax LP.8.1 posology

Age(s)	**Dose**	**Additional recommendations**
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose (see sections 4.4 and 5.1). If a child has received one prior dose of any Spikevax vaccine, one dose of Spikevax LP.8.1 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax LP.8.1 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 3. Spikevax LP.8.1 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Paediatric population
The safety and efficacy of Spikevax in children less than 6 months of age have not yet been established (see section 5.1).

Elderly
No dose adjustment is required in elderly individuals ≥65 years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Anaphylaxis has been reported in individuals who have received Spikevax (original). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. Subsequent doses of Spikevax LP.8.1 should not be given to those who have experienced anaphylaxis to a prior dose of any Spikevax vaccine.

Myocarditis and pericarditis

There is an increased risk for myocarditis and pericarditis following vaccination with Spikevax.

These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose (see section 4.8).

Available data indicate that most cases recover. Some cases required intensive care support and fatal cases have been observed.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Capillary leak syndrome flare-ups

A few cases of capillary leak syndrome (CLS) flare-ups have been reported in the first days after vaccination with Spikevax (original). Healthcare professionals should be aware of signs and symptoms of CLS to promptly recognise and treat the condition. In individuals with a medical history of CLS, planning of vaccination should be made in collaboration with appropriate medical experts.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical studies.

Limitations of vaccine effectiveness

As with all vaccines, vaccination with Spikevax LP.8.1 may not protect all vaccine recipients.

Excipients with known effect

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

Different injectable vaccines should be given at different injection sites.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data are available yet regarding the use of SARS-CoV-2 LP.8.1 mRNA during pregnancy.

However, a large amount of observational data from pregnant women vaccinated with Spikevax (original) during the second and third trimester has not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, SARS-CoV-2 LP.8.1 mRNA can be used during pregnancy.

Breast-feeding

No data are available yet regarding the use of SARS-CoV-2 LP.8.1 mRNA during breastfeeding.

However, no effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to the vaccine is negligible. Observational data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. SARS-CoV-2 LP.8.1 mRNA can be used during breastfeeding.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

SARS-CoV-2 LP.8.1 mRNA has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Adults
The safety of Spikevax (original) was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30 351 participants 18 years of age and older who received at least one dose of Spikevax (original) (n=15 185) or placebo (n=15 166) (NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22 831 (75.2%) of participants were 18 to 64 years of age and 7 520 (24.8%) of participants were 65 years of age and older.

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Adolescents 12 through 17 years of age
Safety data for Spikevax (original) in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study with multiple parts conducted in the United States. The first portion of the study involved 3 726 participants 12 through 17 years of age who received at least one dose of Spikevax (original) (n=2 486) or placebo (n=1 240) (NCT04649151). Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in adolescents 12 to 17 years of age were injection site pain (97%), headache (78%), fatigue (75%), myalgia (54%), chills (49%), axillary swelling/tenderness (35%), arthralgia (35%), nausea/vomiting (29%), injection site swelling (28%), injection site erythema (26%), and fever (14%).

This study transitioned to an open-label Phase 2/3 study in which 1 346 participants 12 years through 17 years of age received a booster dose of Spikevax at least 5 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 years through 11 years of age
Safety data for Spikevax (original) in children were collected in an ongoing Phase 2/3 two-part randomised, observer-blind clinical study conducted in the United States and Canada (NCT04796896). Part 1 is an open-label phase of the study for safety, dose selection, and immunogenicity and included 380 participants 6 years through 11 years of age who received at least 1 dose (0.25 mL) of Spikevax (original). Part 2 is the placebo-controlled phase for safety and included 4 016 participants 6 years through 11 years of age who received at least one dose (0.25 mL) of Spikevax (original) (n=3 012) or placebo (n=1 004). No participants in Part 1 participated in Part 2. Demographic characteristics were similar among participants who received Spikevax (original) and those who received placebo.

The most frequent adverse reactions in participants 6 years through 11 years of age following administration of the primary series (in Part 2) were injection site pain (98.4%), fatigue (73.1%), headache (62.1%), myalgia (35.3%), chills (34.6%), nausea/vomiting (29.3%), axillary swelling/tenderness (27.0%), fever (25.7%), injection site erythema (24.0%), injection site swelling (22.3%), and arthralgia (21.3%).

The study protocol was amended to include an open-label booster dose phase that included 1 294 participants 6 years through 11 years of age who received a booster dose of Spikevax at least 6 months after the second dose of the primary series. No additional adverse reactions were identified in the open-label portion of the study.

Children 6 months through 5 years of age
An ongoing Phase 2/3 randomised, placebo-controlled, observer-blind study to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax was conducted in the United States and Canada. This study involved 10 390 participants 6 months through 11 years of age who received at least one dose of Spikevax (n=7 798) or placebo (n=2 592).

The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months. This paediatric study involved 6 388 participants 6 months through 5 years of age who received at least one dose of Spikevax (n=4 791) or placebo (n=1 597). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

In this clinical study, the adverse reactions in participants 6 months through 23 months of age following administration of the primary series were irritability/crying (81.5%), pain at the injection site (56.2%), sleepiness (51.1%), loss of appetite (45.7%), fever (21.8%), swelling at the injection site (18.4%), erythema at the injection site (17.9%), and axillary swelling/tenderness (12.2%).

The adverse reactions in participants 24 through 36 months of age following administration of the primary series were pain at the injection site (76.8%), irritability/crying (71.0%), sleepiness (49.7%), loss of appetite (42.4%), fever (26.1%), erythema at the injection site (17.9%), swelling at the injection site (15.7%), and axillary swelling/tenderness (11.5%).

The adverse reactions in participants 37 months through 5 years of age following administration of the primary series were pain at the injection site (83.8%), fatigue (61.9%), headache (22.9%), myalgia (22.1%), fever (20.9%), chills (16.8%), nausea/vomiting (15.2%), axillary swelling/tenderness (14.3%), arthralgia (12.8%), erythema at the injection site (9.5%), and swelling at the injection site (8.2%).

Tabulated list of adverse reactions

The safety profile presented below is based on data generated in several placebo-controlled clinical studies:

- 30 351 adults ≥ 18 years of age
- 3 726 adolescents 12 through 17 years of age
- 4 002 children 6 years through 11 years of age
- 6 388 children aged 6 months through 5 years of age
- and post-marketing experience.

Adverse reactions reported are listed according to the following frequency convention:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥1/10 000 to <1/1 000)
Very rare (<1/10 000)
Not known (cannot be estimated from the available data)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness (Table 4).

Table 4. Adverse reactions from Spikevax (original) clinical studies and post authorisation experience in children and individuals 6 months of age and older

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Immune system disorders	Not known	Anaphylaxis
		Hypersensitivity
Metabolism and nutrition disorders	Very common	Decreased appetite†
Psychiatric disorders	Very common	Irritability/crying†
Nervous system disorders	Very common	Headache Sleepiness†
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Common	Diarrhoea
	Uncommon	Abdominal pain§
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria¶
	Not known	Erythema multiforme Mechanical urticaria Chronic urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
Reproductive system and breast disorders	Not known	Heavy menstrual bleeding#
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills Pyrexia Injection site swelling Injection site erythema
	Common	Injection site urticaria Injection site rash Delayed injection site reaction♠
	Uncommon	Injection site pruritus
	Rare	Facial swelling♥
	Not known	Extensive swelling of vaccinated limb

*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site. Other lymph nodes (e.g., cervical, supraclavicular) were affected in some cases.

† Observed in the paediatric population (6 months to 5 years of age).

‡ Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the Spikevax (original) group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.

§ Abdominal pain was observed in the paediatric population (6 to 11 years of age): 0.2% in the Spikevax (original) group and 0% in the placebo group.

¶ Urticaria has been observed with either acute onset (within a few days after vaccination) or delayed onset (up to approximately two weeks after vaccination).

Most cases appeared to be non-serious and temporary in nature.

♠ Median time to onset was 9 days after the first injection, and 11 days after the second injection. Median duration was 4 days after the first injection, and 4 days after the second injection.

♥ There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

The reactogenicity and safety profile in 343 subjects receiving Spikevax (original), that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

Adults (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine primary series. In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (0.25 mL, 50 micrograms) was similar to that after the second dose in the primary series.

Spikevax bivalent Original/Omicron BA.1 (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax bivalent Original/Omicron BA.1 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Spikevax bivalent Original/Omicron BA.1 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose. The frequency of adverse reactions after immunisation with Spikevax bivalent Original/Omicron BA.1 was also similar or lower relative to that of a first booster dose of Spikevax (original) (50 micrograms) and relative to the second dose of the Spikevax (original) primary series (100 micrograms). The safety profile of Spikevax bivalent Original/Omicron BA.1 (median follow-up period of 113 days) was similar to the safety profile of Spikevax (original) (median follow-up period of 127 days).

Spikevax bivalent Original/Omicron BA.4-5 (booster dose)
The safety, reactogenicity, and immunogenicity of a bivalent booster dose of Spikevax bivalent Original/Omicron BA.4-5 are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received a booster dose of Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms), and 376 participants received a booster dose of Spikevax (original) (50 micrograms).

Spikevax bivalent Original/Omicron BA.4-5 had a reactogenicity profile similar to that of the Spikevax (original) booster given as a second booster dose.

Spikevax XBB.1.5 (booster dose)
The safety, reactogenicity and immunogenicity of a booster dose of Spikevax XBB.1.5 are evaluated in an ongoing Phase 2/3 open-label study in adults (mRNA-1273-P205, Part J). In this study, 50 participants received a booster dose of Spikevax XBB.1.5 (50 micrograms) and 51 participants received a booster dose of an investigational bivalent Omicron XBB.1.5/BA.4-5 vaccine (50 micrograms).

The reactogenicity profile of Spikevax XBB.1.5 was similar to that of Spikevax (original) and Spikevax bivalent Original/Omicron BA.4-5. The median follow-up time for both vaccine groups in this interim analysis was 20 days (range of 20 to 22 days with data cut-off date of 16 May 2023).

Spikevax (original) in solid organ transplant recipients
The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose (fourth dose for mRNA vaccines and third dose for non-mRNA vaccines).

Reactogenicity was consistent with the known profile of Spikevax (original). There were no unexpected safety findings.

Description of selected adverse reactions

Myocarditis
The increased risk of myocarditis after vaccination with Spikevax (original) is highest in younger males (see section 4.4).

Two large European pharmacoepidemiological studies have estimated the excess risk in younger males following the second dose of Spikevax (original). One study showed that in a period of 7 days after the second dose, there were about 1.316 (95% CI: 1.299, 1.333) extra cases of myocarditis in 12 to 29 year-old males per 10 000 compared to unexposed persons. In another study, in a period of 28 days after the second dose, there were 1.88 (95% CI: 0.956, 2.804) extra cases of myocarditis in 16 to 24 year-old males per 10 000 compared to unexposed persons.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, COVID-19 vaccines, ATC code: J07BN01

Mechanism of action

Elasomeran and elasomeran/imelasomeran both contain mRNA encapsulated in lipid nanoparticles. The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is non-replicating, and is expressed transiently mainly by dendritic cells and subcapsular sinus macrophages. The expressed, membrane-bound spike protein of SARS-CoV-2 is then recognised by immune cells as a foreign antigen. This elicits both T-cell and B-cell responses to generate neutralising antibodies, which may contribute to protection against COVID-19. The nucleoside-modified mRNA in elasomeran/davesomeran, andusomeran, SARS-CoV-2 JN.1 mRNA and SARS-CoV-2 LP.8.1 mRNA is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

Clinical efficacy

Immunogenicity in adults – after Spikevax XBB.1.5 dose (0.5 mL, 50 micrograms) versus an investigational bivalent XBB.1.5/BA.4-5 dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity and immunogenicity of Spikevax XBB.1.5 50 micrograms and of a bivalent vaccine that contains equal mRNA amounts of Omicron XBB.1.5 and Omicron BA.4-5 spike proteins (25 micrograms XBB.1.5 / 25 micrograms BA.4-5) are evaluated in a Phase 2/3 open-label study in adults. In this study, 50 participants received Spikevax XBB.1.5 and 51 participants received the investigational bivalent XBB.1.5/BA.4-5 (mRNA-1273- P205, Part J). The two groups were randomised 1:1.

The vaccines were administered as a fifth dose to adults who previously received a two-dose primary series of any mRNA COVID-19 vaccine, a booster dose of any mRNA COVID-19 vaccine, and a booster dose of any mRNA bivalent Original/Omicron BA.4-5 vaccine.

Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 elicited potent neutralising responses at Day 15 against XBB.1.5, XBB.1.16, BA.4-5, BQ.1.1 and D614G. In the per-protocol immunogenicity set that includes all participants, with and without prior SARS-CoV-2 infection (N=49 and N=50 for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 groups, respectively), the Day 15 GMFR (95% CI) for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 was 16.7 (12.8, 21.7) and 11.6 (8.7, 15.4), respectively, against XBB.1.5 and 6.3 (4.8, 8.2) and 5.3 (3.9, 7.1) against BA.4-5.

For variants not contained in the vaccines, the Day 15 GMFR (95% CI) for Spikevax XBB.1.5 and bivalent XBB.1.5/BA.4-5 was 11.4 (8.5, 15.4) and 9.3 (7.0, 12.3) against XBB.1.16; 5.8 (4.7, 7.3) and 6.1 (4.6, 7.9) against BQ.1.1 and 2.8 (2.2, 3.5) and 2.3 (1.9, 2.8) against D614G.

Immunogenicity in participants 18 years of age and older – after Spikevax bivalent Original/Omicron BA.4-5 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.4-5 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age and older (mRNA-1273-P205). In this study, 511 participants received the Spikevax bivalent Original/Omicron BA.4-5 50 microgram booster dose, and 376 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part H evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.4-5 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a first booster dose of Spikevax (original) (50 micrograms). In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part F group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.4-5 group. In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the observed geometric mean titre (GMT) (95% CI) at pre-booster was 87.9 (72.2, 107.1) and increased to 2 324.6 (1 921.2, 2 812.7) 28 days after the Spikevax bivalent Original/Omicron BA.4-5 booster dose. The Day 29 GMR for Spikevax Original/Omicron BA.4-5 50 microgram booster dose versus the Spikevax (original) 50 microgram booster dose was 6.29 (5.27, 7.51), meeting the pre-specified criterion for superiority (lower bound of CI >1).

The estimated neutralising antibody GMTs (95% CI) against Omicron BA.4/BA.5 adjusted for pre-booster titre and age group were 2 747.3 (2 399.2, 3 145.9) and 436.7 (389.1, 490.0) 28 days after Spikevax bivalent Original/Omicron BA.4-5 and Spikevax (original) booster doses, respectively, and the GMR (95% CI) was 6.29 (5.27, 7.51), meeting the pre-specified criterion for non-inferiority (lower bound of CI >0.667).

Immunogenicity in adults – after Spikevax bivalent Original/Omicron BA.1 booster dose (0.5 mL, 25 micrograms/25 micrograms)
The safety, reactogenicity, and immunogenicity of a Spikevax bivalent Original/Omicron BA.1 booster dose are evaluated in an ongoing Phase 2/3 open-label study in participants 18 years of age

and older (mRNA-1273-P205). In this study, 437 participants received the Spikevax bivalent Original/Omicron BA.1 50 microgram booster dose, and 377 participants received the Spikevax (original) 50 microgram booster dose.

Study P205 Part G evaluated the safety, reactogenicity and immunogenicity of Spikevax bivalent Original/Omicron BA.1 when administered as a second booster dose to adults who previously received 2 doses of Spikevax (original) (100 microgram) as a primary series and a booster dose of Spikevax (original) (50 micrograms) at least 3 months prior to enrolment. In P205 Part F, study participants received Spikevax (original) (50 micrograms) as a second booster dose and the Part G group serves as a within-study, non-contemporaneous comparator group to the Spikevax bivalent Original/Omicron BA.1 group.

In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster). In the primary analysis, the original SARS-CoV-2 estimated neutralising antibody geometric mean titre (GMT) and corresponding 95% CI was 6 422.3 (5 990.1, 6 885.7) and 5 286.6 (4 887.1, 5 718.9) 28 days after the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster doses, respectively. These GMTs represent the ratio between response of Spikevax bivalent Original/Omicron BA.1 versus Spikevax (original) against the ancestral SARS-CoV-2 (D614G) strain. The GMR (97.5% CI) was 1.22 (1.08, 1.37) meeting the pre-specified criterion for non-inferiority (lower bound of 97.5% CI ≥0.67).

The estimated Day 29 neutralising antibody GMTs against Omicron, BA.1 were 2 479.9 (2 264.5, 2 715.8) and 1 421.2 (1 283.0, 1 574.4) in the Spikevax bivalent Original/Omicron BA.1 and Spikevax (original) booster groups, respectively, and the GMR (97.5% CI) was 1.75 (1.49, 2.04), which met the pre-specified superiority criterion (lower bound of CI >1).

Three-month antibody persistence of Spikevax bivalent Original/Omicron BA.1 booster vaccine against COVID-19
Participants in Study P205 Part G were sequentially enrolled to receive 50 micrograms of Spikevax (original) (n = 376) or Spikevax bivalent Original/Omicron BA.1 (n = 437) as second booster doses. In participants with no pre-booster incidence of SARS-CoV-2, Spikevax bivalent Original/Omicron BA.1 elicited Omicron-BA.1-neutralising antibody titres (observed GMT) that were significantly higher (964.4 [834.4, 1 114.7]) than those of Spikevax (original) (624.2 [533.1, 730.9]) and similar between boosters against ancestral SARS-CoV-2 at three months.

Clinical efficacy in adults
The adult study was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or had received immunosuppressants within 6 months, as well as participants who were pregnant, or with a known history of SARS-CoV-2 infection. Participants with stable HIV disease were not excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of Spikevax (original). Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or Spikevax (original).

A total of 30 351 subjects were followed for a median of 92 days (range: 1-122) for the development of COVID-19 disease.

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28 207 subjects who received either Spikevax (original) (n=14 134) or placebo (n=14 073) and had a negative baseline SARS-CoV-2 status. The PPS study population included 47.4% female, 52.6% male, 79.5% White, 9.7% African American, 4.6% Asian, and 6.2% other. 19.7% of participants identified as Hispanic or Latino. The median age of subjects was 53 years (range 18-94). A dosing window of –7 to +14 days for administration of the second dose (scheduled at day 29) was allowed for inclusion in the PPS. 98% of vaccine recipients received the second dose 25 days to 35 days after dose 1 (corresponding to -3 to +7 days around the interval of 28 days).

COVID-19 cases were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT PCR) and by a Clinical Adjudication Committee. Vaccine efficacy overall and by key age groups are presented in Table 5.

Table 5. Vaccine efficacy analysis: confirmed COVID-19[#] regardless of severity starting 14 days after the 2nd dose – PPS

Age group (years)	Spikevax (original)			Placebo			
	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	Subjects N	COVID-19 cases n	Incidence rate of COVID-19 per 1 000 person-years	% Vaccine efficacy (95% CI)*
Overall (≥18)	14 134	11	3.328	14 073	185	56.510	94.1 (89.3, 96.8)**
18 to <65	10 551	7	2.875	10 521	156	64.625	95.6 (90.6, 97.9)
≥65	3 583	4	4.595	3 552	29	33.728	86.4 (61.4, 95.2)
≥65 to <75	2 953	4	5.586	2 864	22	31.744	82.4% (48.9, 93.9)
≥75	630	0	0	688	7	41.968	100% (NE, 100)

[#]COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the 2nd dose.
*Vaccine efficacy and 95% confidence interval (CI) from the stratified Cox proportional hazard model
** CI not adjusted for multiplicity. Multiplicity adjusted statistical analyses were carried out in an interim analysis based on less COVID-19 cases, not reported here.

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 of 185 (16%) cases reported in the placebo group. Of the 30 participants with severe disease, 9 were hospitalised, 2 of which were admitted to an intensive care unit. The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO2) criterion for severe disease (≤ 93% on room air).

The vaccine efficacy of Spikevax (original) to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% CI: 88.6, 96.5).

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Immunogenicity in adults – after booster dose (0.25 mL, 50 micrograms)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax (original) are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax (original) vaccine as primary series. In an open-label phase, 149 of those participants (Per Protocol Set) received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL, 50 micrograms) was shown to result in a geometric mean fold rise (GMFR) of 12.99 (95% CI: 11.04, 15.29) in neutralising antibodies from pre-booster compared to

28 days after the booster dose. The GMFR in neutralising antibodies was 1.53 (95% CI: 1.32, 1.77) when compared 28 days post dose 2 (primary series) to 28 days after the booster dose.

Immunogenicity of a booster dose following primary vaccination with another authorised COVID-19 vaccine in adults
Safety and immunogenicity of a heterologous booster with Spikevax (original) were studied in an investigator-initiated study with 154 participants. The minimum time interval between primary series using a vector-based or RNA-based COVID-19 vaccine and booster injection with Spikevax (original) was 12 weeks (range: 12 weeks to 20.9 weeks). The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 1 prior to administration and at Day 15 and Day 29 after the booster dose. A booster response was demonstrated regardless of primary vaccination.

Only short-term immunogenicity data are available; long-term protection and immunological memory are currently unknown.

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) in the UK
COV-BOOST is a multicentre, randomised Phase 2 investigator-initiated study of third dose booster vaccination against COVID-19 with a subgroup to investigate detailed immunology. Participants were adults aged 30 years or older, in good physical health (mild to moderate well-controlled co-morbidities were permitted), who had received two doses of either Pfizer–BioNTech or Oxford–AstraZeneca (first dose in December 2020, January 2021 or February 2021), and were at least 84 days post second dose by the time of enrolment. Spikevax (original) boosted antibody and neutralising responses and was well tolerated regardless of the prime series. The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 28 after the booster dose.

Clinical efficacy in adolescents 12 through 17 years of age
The adolescent study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study (NCT04649151) to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in adolescents 12 to 17 years of age. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3 732 participants were randomised 2:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis was performed in 3 181 participants who received 2 doses of either Spikevax (original) (n=2 139) or placebo (n=1 042) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were zero symptomatic COVID-19 cases in the Spikevax (original) group and 4 symptomatic COVID-19 cases in the placebo group.

Immunogenicity in adolescents 12 to 17 years of age – after Spikevax primary vaccination
A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in the per-protocol immunogenicity subsets of adolescents aged 12 through 17 (n=340) in the adolescent study and in participants aged 18 through 25 (n=296) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The geometric mean ratio (GMR) of the neutralising antibody titres in adolescents 12 to 17 years of age compared to the 18- to 25-year-olds was 1.08 (95% CI: 0.94, 1.24). The difference in seroresponse rate was 0.2% (95% CI: -1.8, 2.4). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in adolescents 12 years through 17 years of age – after Spikevax (original) booster dose

The primary immunogenicity objective of the booster phase of this study was to infer efficacy of the booster dose in participants 12 years through 17 years of age by comparing post-booster immune responses (Day 29) to those obtained post-dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in the adult study. Efficacy of the 50 microgram Spikevax booster dose is inferred if post-booster dose immune responses (nAb geometric mean concentration [GMC] and seroresponse rate [SRR]) meet prespecified noninferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy study.

In an open-label phase of this study, participants 12 years through 17 years of age received a single booster dose at least 5 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 257 booster dose participants in this study and a random subset of 295 participants from the young adult study (ages ≥18 to ≤25 years) who previously completed a primary vaccination series of two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

The GMR of the adolescent booster dose Day 29 GMC compared with young adults: Day 57 GMR was 5.1 (95% CI: 4.5, 5.8), meeting the noninferiority criteria (i.e., lower bound of the 95% CI >0.667 (1/1.5); point estimate ≥0.8); the SRR difference was 0.7% (95% CI: -0.8, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

In the 257 participants, pre-booster (booster dose-Day 1) nAb GMC was 400.4 (95% CI: 370.0, 433.4); on BD-Day 29, the GMC was 7 172.0 (95% CI: 6 610.4, 7 781.4). Post-booster booster dose-Day 29 GMC increased approximately 18-fold from pre-booster GMC, demonstrating the potency of the booster dose to adolescents. The SRR was 100 (95% CI: 98.6, 100.0).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of vaccine efficacy from the adult study.

Clinical efficacy in children 6 years through 11 years of age
The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study to evaluate the safety, reactogenicity, and efficacy of Spikevax (original) in children aged 6 years through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 4 016 participants were randomised 3:1 to receive 2 doses of Spikevax (original) or saline placebo 1 month apart.

A secondary efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 10 November 2021 was performed in 3 497 participants who received two doses (0.25 mL at 0 and 1 month) of either Spikevax (original) (n=2 644) or placebo (n=853) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax (original) and those who received placebo, there were no notable differences in demographics.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose.

There were three COVID-19 cases (0.1%) in the Spikevax (original) group and four COVID-19 cases (0.5%) in the placebo group.

Immunogenicity in children 6 years through 11 years of age
An analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in a subset of children aged 6 years through 11 years (n=319) in the paediatric study and in participants aged 18 through 25 years (n=295) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titres in children 6 years through 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9,

2.1). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

Immunogenicity in children 6 years through 11 years of age – after Spikevax (original) booster dose
The primary immunogenicity objective of the booster phase of this study is to infer efficacy of the booster dose in participants 6 years through 11 years of age by comparing post-booster dose immune responses (Day 29) to those obtained post dose 2 of the primary series (Day 57) in young adults (18 to 25 years of age) in that study, where 93% efficacy was demonstrated. Efficacy of the 25 microgram Spikevax booster dose is inferred if post-booster dose immune responses (neutralising antibody [nAb] geometric mean concentration [GMC] and seroresponse rate [SRR]) meet pre-specified non-inferiority criteria (for both GMC and SRR) compared to those measured following completion of the 100 microgram Spikevax primary series among a subset of young adults (18 to 25 years) in the pivotal adult efficacy trial.

In an open-label phase of this study, participants 6 years through 11 years of age received a single booster dose at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 95 booster dose participants in 6 years through 11 years and a random subset of 295 participants from the young adult study who received two doses 1 month apart of Spikevax. Both groups of participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively.

In the 95 participants, on booster dose-Day 29, the GMC was 5 847.5 (95% CI: 4 999.6, 6 839.1). The SRR was 100 (95% CI: 95.9, 100.0). Serum nAb levels for children 6 years through 11 years in the per-protocol immunogenicity subset with pre-booster SARS-CoV-2 negative status and the comparison with those from young adults (18 to 25 years of age) were studied. The GMR of booster dose Day 29 GMC compared to young adults Day 57 GMC was 4.2 (95% CI: 3.5, 5.0), meeting the noninferiority criteria (i.e., lower bound of the 95% CI > 0.667); the SRR difference was 0.7% (95% CI: -3.5, 2.4), meeting the noninferiority criteria (lower bound of the 95% of the SRR difference >-10%).

The prespecified success criteria for the primary immunogenicity objective were met, thus enabling the inference of booster dose vaccine efficacy. The brisk recall response evident within 4 weeks of booster dosing is evidence of the robust priming induced by the Spikevax primary series.

Clinical efficacy in children 6 months through 5 years of age
An ongoing Phase 2/3 study was conducted to evaluate the safety, tolerability, reactogenicity, and efficacy of Spikevax in healthy children 6 months through 11 years of age. The study enrolled children in 3 age groups: 6 years through 11 years; 2 years through 5 years; and 6 months through 23 months.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 21 February 2022 was performed in 5 476 participants 6 months through 5 years of age who received two doses (at 0 and 1 month) of either Spikevax (n=4 105) or placebo (n=1 371) and had a negative baseline SARS-CoV-2 status (referred to as the Per Protocol Set for Efficacy). Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics.

The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 years through 5 years of age and 68 days for participants 6 months through 23 months of age.

Vaccine efficacy in this study was observed during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

Vaccine efficacy (VE) in Part 2 for the Per Protocol Set for Efficacy for COVID-19 cases 14 days or more after dose 2 using the “COVID-19 P301 case definition” (i.e., the definition employed in the

pivotal adult efficacy study) was 46.4% (95% CI: 19.8, 63.8) for children 2 years through 5 years of age and 31.5% (95% CI: -27.7, 62.0) for children 6 months through 23 months of age.

Immunogenicity in children 6 months through 5 years of age
For children aged 2 years through 5 years of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 264; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.014 (95% CI: 0.881, 1.167), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The geometric mean fold rise (GMFR) from baseline to Day 57 for these children was 183.3 (95% CI: 164.03, 204.91). The difference in seroresponse rates (SRR) between the children and young adults was -0.4% (95% CI: -2.7%, 1.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the SRR difference > -10%).

For infants and toddlers from 6 months through 23 months of age, comparison of Day 57 nAb responses in this Part 2 per-protocol immunogenicity subset (n = 230; 25 micrograms) to those of young adults (n = 295; 100 micrograms) demonstrated a GMR of 1.280 (95% CI: 1.115, 1.470), meeting the noninferiority success criteria (i.e., lower bound of the 95% CI for GMR ≥ 0.67; point estimate ≥ 0.8). The difference in SRR rates between the infants/toddlers and young adults was 0.7% (95% CI: -1.0%, 2.5%), also meeting the noninferiority success criteria (lower bound of the 95% CI of the seroresponse rate difference > -10%).

Accordingly, the prespecified success criteria for the primary immunogenicity objective were met for both age groups, allowing efficacy of 25 micrograms to be inferred in both children 2 years through 5 years and infants and toddlers aged 6 months through 23 months (Tables 6 and 7).

Table 6. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 6 months through 23 months of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		6 months through 23 months n=230	**18 years through 25 years n=291**	**6 months through 23 months/ 18 years through 25 years**	
Assay	**Time point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 780.7 (1 606.4, 1 973.8)	1 390.8 (1 269.1, 1 524.2)	1.3 (1.1, 1.5)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.

[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralising antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 7. Summary of geometric mean concentration ratio and seroresponse rate – comparison of individuals 2 years through 5 years of age to participants 18 years through 25 years of age – per-protocol immunogenicity set

		2 years through 5 years n=264	**18 years through 25 years n=291**	**2 years through 5 years/ 18 years through 25 years**	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met noninferiority objective (Y/N)[b]**
SARS-CoV-2 neutralisation assay[c]	28 days after Dose 2	1 410.0 (1 273.8, 1 560.8)	1 390.8 (1 262.5, 1 532.1)	1.0 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in seroresponse rate % (95% CI)[e]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (participants 6 months through 5 years of age and young adults) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[c] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralisation assay.
[d] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Available data in children 12 weeks to 6 months of age
The safety and immunogenicity of Spikevax bivalent Original/Omicron BA.1 were evaluated in children 12 weeks to 6 months of age in Study P206. During the dose-finding part of the study, two dose levels (5 mcg and 10 mcg) evaluated as a two-dose regimen were generally well tolerated but did not lead to a substantial immune response.

Immunogenicity in solid organ transplant recipients

The safety, reactogenicity, and immunogenicity of Spikevax (original) were evaluated in a two-part Phase 3b open-label study in adult solid organ transplant (SOT) recipients, including kidney and liver transplants (mRNA-1273-P304). A 100 microgram (0.5 mL) dose was administered, which was the dose authorised at the time of study conduct.

In Part A, 128 SOT recipients received a third dose of Spikevax (original). In Part B, 159 SOT recipients received a booster dose at least 4 months after the last dose.

Immunogenicity in the study was assessed by measurement of neutralising antibodies against pseudovirus expressing the ancestral SARS-CoV-2 (D614G) strain at 1 month after Dose 2, Dose 3, booster dose and up to 12 months from the last dose in Part A, and up to 6 months from booster dose in Part B.

Three doses of Spikevax (original) induced enhanced neutralising antibody titres compared to pre-dose 1 and post-dose 2. A higher proportion of SOT participants who had received three doses achieved seroresponse compared to participants who had received two doses. The neutralising antibody levels observed in SOT liver participants who had received three doses was comparable to the post-dose 2 responses observed in the immunocompetent, baseline SARS-CoV-2-negative adult participants. The neutralising antibody responses continued to be numerically lower post-dose 3 in SOT kidney participants compared to SOT liver participants. The neutralising levels observed one month after Dose 3 persisted through six months with antibody levels maintained at 26-fold higher and seroresponse rate at 67% compared to baseline.

A fourth (booster) dose of Spikevax (original) enhanced neutralising antibody response in SOT participants compared to post-dose 3, regardless of the previous vaccines received [mRNA-1273 (Moderna), BNT162b2 or any mRNA-containing combination]; however, SOT kidney participants had numerically lower neutralising antibody responses compared to SOT liver participants.

Elderly

Spikevax (original) was assessed in individuals 6 months of age and older, including 3 768 subjects 65 years of age and older. The efficacy of Spikevax (original) was consistent between elderly (≥65 years) and younger adult subjects (18-64 years).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Spikevax (original) in one or more subsets of the paediatric population in the prevention of COVID-19 (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and reproductive and developmental toxicity.

General toxicity

General toxicity studies were conducted in rats (intramuscularly receiving up to 4 doses exceeding the human dose once every 2 weeks). Transient and reversible injection site oedema and erythema and transient and reversible changes in laboratory tests (including increases in eosinophils, activated

partial thromboplastin time, and fibrinogen) were observed. Results suggests the toxicity potential to humans is low.

Genotoxicity/carcinogenicity

In vitro and *in vivo* genotoxicity studies were conducted with the novel lipid component SM-102 of the vaccine. Results suggests the genotoxicity potential to humans is very low. Carcinogenicity studies were not performed.

Reproductive toxicity

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 micrograms) and other ingredients included in a single human dose of Spikevax (original) was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. SARS-CoV-2 antibody responses were present in maternal animals from prior to mating to the end of the study on lactation day 21 as well as in foetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryo foetal or offspring development or postnatal development. No data are available of Spikevax (original) vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate)
Cholesterol
1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
Trometamol
Trometamol hydrochloride
Acetic acid
Sodium acetate trihydrate
Sucrose
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened multidose vial (Spikevax LP.8.1 0.1 mg/mL dispersion for injection)

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, the unopened vaccine vial may be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days.

Chemical and physical stability has also been demonstrated for unopened vaccine vials when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the unopened vial will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on

the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C (see section 6.4).

Once thawed, the vaccine should not be refrozen.

The unopened vaccine may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

Punctured multidose vials (Spikevax LP.8.1 0.1 mg/mL dispersion for injection)

Chemical and physical in-use stability has been demonstrated for 19 hours at 2°C to 25ºC after initial puncture (within the allowed use period of 30 days or 14 days, respectively, at 2°C to 8ºC and including 24 hours at 8°C to 25ºC). From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe and Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe

9 months at -50ºC to -15ºC.

Within the period of 9 months, after removal from the freezer, pre-filled syringes may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened pre-filled syringes when stored for 12 months at -50°C to -15°C **provided that once thawed and stored at 2°C to 8°C,** protected from light, **the pre-filled syringe will be used up within a maximum of 14 days** (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months.

- Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C.
- If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Pre-filled syringe transport duration is limited by the shipper qualification duration.

Once thawed, the vaccine should not be refrozen.

Pre-filled syringes may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

6.4 Special precautions for storage

Spikevax LP.8.1 0.1 mg/mL dispersion for injection (multidose vials)

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.
For storage conditions of the multidose vial after first opening, see section 6.3.

Transportation of thawed multidose vials in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 36 hours at 2°C to 8°C (within the 30 days or 14 days shelf life,

respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use.

Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe and Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe

Store in a freezer at -50ºC to -15ºC.
Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
For storage conditions after thawing, see section 6.3.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C
If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use. Pre-filled syringe transport duration is limited by the shipper qualification duration.

6.5 Nature and contents of container

Spikevax LP.8.1 0.1 mg/mL dispersion for injection (multidose vials)

2.5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe and Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe

0.25 mL or 0.5 mL dispersion in a pre-filled syringe (cyclic olefin copolymer) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in a paper inner tray within a carton or in 1 clear blister containing 1 pre-filled syringe or 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack sizes:
1 pre-filled syringe
10 pre-filled syringes
Each pre-filled syringe contains 0.25 mL or 0.5 mL, depending on labelled syringe volume.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.

Spikevax LP.8.1 0.1 mg/mL dispersion for injection (multidose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax LP.8.1. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL, Spikevax bivalent Original/Omicron

BA.1, Spikevax bivalent Original/Omicron BA.4-5, Spikevax XBB.1.5 or Spikevax JN.1, please make reference to the Summary of Product Characteristics for that formulation.

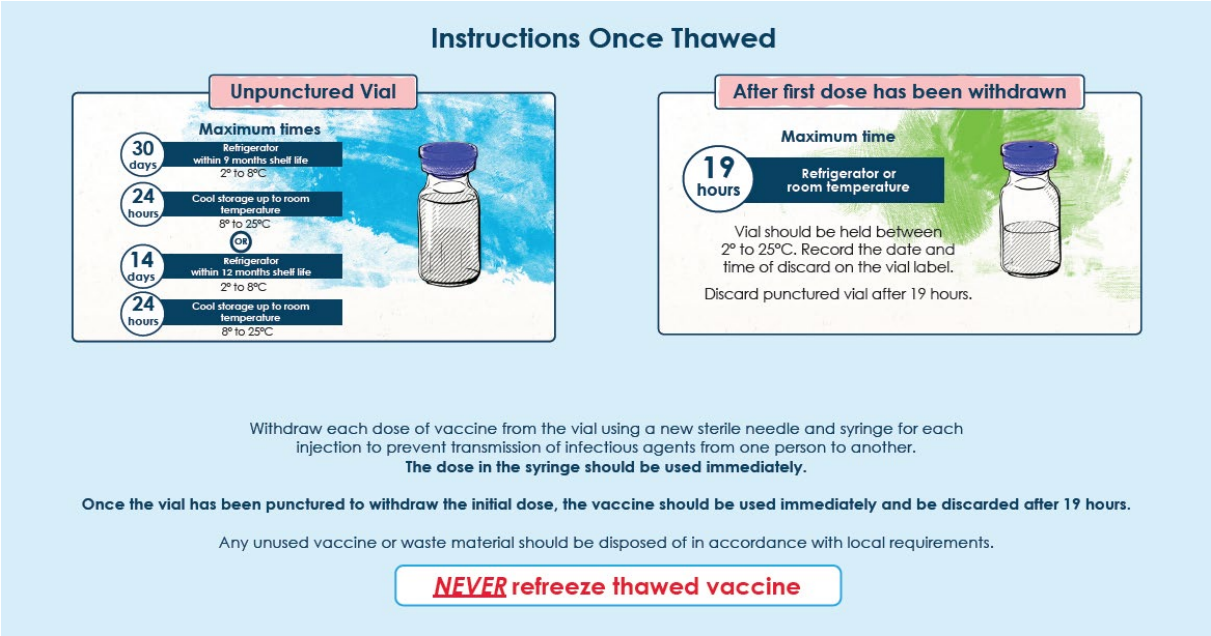
Pierce the stopper preferably at a different site each time.

An additional overfill is included in each multidose vial to ensure that 5 doses of 0.5 mL or a maximum of 10 doses of 0.25 mL can be delivered, depending on the individual's age.

Thaw each multidose vial before use following the instructions below (Table 8).

Table 8. Thawing instructions for multidose vials before use

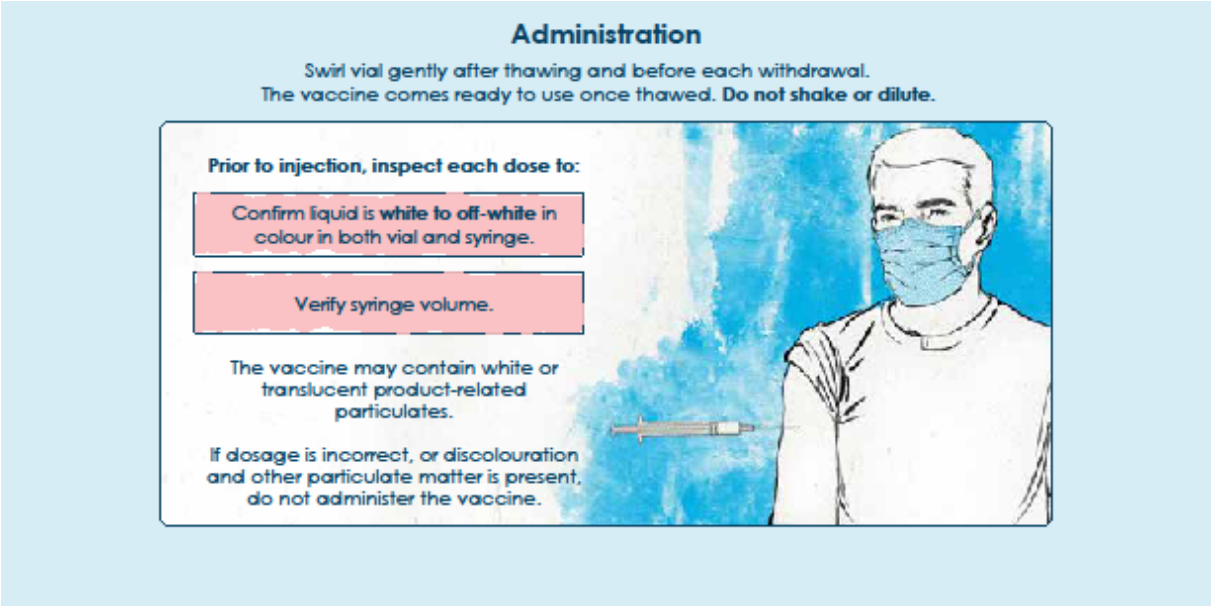
Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe and Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.25 mL or 0.5 mL can be administered from each pre-filled syringe, depending on labelled syringe volume. Do not use the 0.5 mL pre-filled syringe to administer a 0.25 mL dose.

Spikevax LP.8.1 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.25 mL (25 micrograms of SARS-CoV-2 LP.8.1 mRNA) or 0.5 mL (50 micrograms of SARS-CoV-2 LP.8.1 mRNA) and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 1 or 2 pre-filled syringes, depending on pack size) or in the carton itself, either in the refrigerator or at room temperature (Table 9).

Table 9. Thawing instructions for Spikevax LP.8.1 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax LP.8.1. If the product name is Spikevax 50 micrograms, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, Spikevax XBB.1.5 or Spikevax JN.1, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the Spikevax LP.8.1 pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax LP.8.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/031
EU/1/20/1507/032
EU/1/20/1507/033
EU/1/20/1507/034
EU/1/20/1507/035
EU/1/20/1507/036
EU/1/20/1507/037
EU/1/20/1507/038
EU/1/20/1507/039
EU/1/20/1507/040

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2021
Date of latest renewal: 03 October 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substances

ModernaTX, Inc.
One Moderna Way
Norwood, MA 02062
USA

Name and address of the manufacturers responsible for batch release

Rovi Pharma Industrial Services, S.A.
Paseo de Europa, 50
28703. San Sebastián de los Reyes
Madrid
Spain

Recipharm Monts
18 Rue de Montbazon
Monts, France 37260

Moderna Biotech Spain S.L.
C/ Julián Camarillo n° 31
28037 Madrid
Spain

Rovi Pharma Industrial Services, S.A.
Calle Julián Camarillo n°35
28037 Madrid
Spain

Patheon Italia S.p.a.
Viale G.B. Stucchi
110
20900 Monza
Italy

Patheon Italia S.p.A.
2 Trav. SX Via Morolense 5
03013 Ferentino (FR)
Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Periodic safety update reports (PSURs)

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax 0.2 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 5 mL.
One dose (0.5 mL) contains 100 micrograms of elasomeran.
One dose (0.25 mL) contains 50 micrograms of elasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax 0.2 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 2.5 mL. One dose (0.5 mL) contains 50 micrograms of elasomeran. One dose (0.25 mL) contains 25 micrograms of elasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
2.5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
elasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.5 mL. One dose (0.5 mL) contains 50 micrograms of elasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC

SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax 50 micrograms dispersion for injection
elasomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/imelasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 2.5 mL. One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran. One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of imelasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax bivalent Original/Omicron BA.1 (50 mcg/50 mcg)/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/imelasomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
2.5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/imelasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 5 mL. One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran. One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of imelasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax bivalent Original/Omicron BA.1 (50 mcg/50 mcg)/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/imelasomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (SINGLE-DOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/imelasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each single-dose vial contains 0.5 mL. One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 single-dose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/008

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SINGLE-DOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax bivalent Original/Omicron BA.1 25 mcg/25 mcg dispersion for injection
elasomeran/imelasomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Single-dose vial
0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
elasomeran/imelasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.5 mL. One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax bivalent Original/Omicron BA.1 25 mcg/25 mcg dispersion for injection
elasomeran/imelasomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/davesomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 2.5 mL. One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran. One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of davesomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax bivalent Original/Omicron BA.4-5 (50 mcg/50 mcg)/mL dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/davesomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
2.5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (SINGLE-DOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection
COVID-19 mRNA Vaccine
elasomeran/davesomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each single-dose vial contains 0.5 mL. One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 single-dose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/009

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SINGLE-DOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax bivalent Original/Omicron BA.4-5 25 mcg/25 mcg dispersion for injection
elasomeran/davesomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Single-dose vial
0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
elasomeran/davesomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.5 mL. One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/010

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax bivalent Original/Omicron BA.4-5 25 mcg/25 mcg dispersion for injection
elasomeran/davesomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
andusomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 2.5 mL. One dose (0.5 mL) contains 50 micrograms of andusomeran.
One dose (0.25 mL) contains 25 micrograms of andusomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/011 (glass)
EU/1/20/1507/012 (cyclic olefin polymer)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
andusomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
2.5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (SINGLE-DOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax XBB.1.5 50 micrograms dispersion for injection
COVID-19 mRNA Vaccine
andusomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each single-dose vial contains 0.5 mL. One dose (0.5 mL) contains 50 micrograms of andusomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 single-dose vial
10 single-dose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/013
EU/1/20/1507/014

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SINGLE-DOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax XBB.1.5 50 mcg dispersion for injection
andusomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Single-dose vial
0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
andusomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.5 mL. One dose (0.5 mL) contains 50 micrograms of andusomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 pre-filled syringe
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/015 (blister pack of 1)
EU/1/20/1507/016 (blister pack of 10)
EU/1/20/1507/017 (paper inner tray of 1)
EU/1/20/1507/018 (paper inner tray of 10)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax XBB.1.5 50 mcg dispersion for injection
andusomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
andusomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.25 mL. One dose (0.25 mL) contains 25 micrograms of andusomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 pre-filled syringe
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/027 (blister pack of 1)
EU/1/20/1507/028 (blister pack of 10)
EU/1/20/1507/029 (paper inner tray of 1)
EU/1/20/1507/030 (paper inner tray of 10)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax XBB.1.5 25 mcg dispersion for injection
andusomeran
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.25 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax JN.1 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 2.5 mL. One dose (0.5 mL) contains 50 micrograms of **SARS-CoV-2 JN.1 mRNA**. One dose (0.25 mL) contains 25 micrograms of **SARS-CoV-2 JN.1 mRNA**.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/019 (glass)
EU/1/20/1507/020 (cyclic olefin polymer)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax JN.1 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
2.5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (SINGLE-DOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax JN.1 50 micrograms dispersion for injection
COVID-19 mRNA Vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One single-dose vial contains 0.5 mL. One dose (0.5 mL) contains 50 micrograms of **SARS-CoV-2 JN.1 mRNA**.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 single-dose vial
10 single-dose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/021
EU/1/20/1507/022

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SINGLE-DOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax JN.1 50 mcg dispersion for injection
COVID-19 mRNA Vaccine
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Single-dose vial
0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.5 mL. One dose (0.5 mL) contains 50 micrograms of **SARS-CoV-2 JN.1 mRNA**.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 pre-filled syringe
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/023(blister pack of 1)
EU/1/20/1507/024 (blister pack of 10)
EU/1/20/1507/025 (paper inner tray of 1)
EU/1/20/1507/026 (paper inner tray of 10)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax JN.1 50 mcg dispersion for injection
COVID-19 mRNA Vaccine
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax LP.8.1 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 2.5 mL. One dose (0.5 mL) contains 50 micrograms of **SARS-CoV-2 LP.8.1 mRNA**. One dose (0.25 mL) contains 25 micrograms of **SARS-CoV-2 LP.8.1 mRNA**.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/031 (glass)
EU/1/20/1507/032 (cyclic olefin polymer)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax LP.8.1 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial
2.5 mL

6. OTHER

Scan here for package leaflet or visit www.modernacovid19global.com.
Discard date/time:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.5 mL. One dose (0.5 mL) contains 50 micrograms of **SARS-CoV-2 LP.8.1 mRNA**.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 pre-filled syringe
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/033 (blister pack of 1)
EU/1/20/1507/034 (blister pack of 10)
EU/1/20/1507/035 (paper inner tray of 1)
EU/1/20/1507/036 (paper inner tray of 10)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax LP.8.1 50 mcg dispersion for injection
COVID-19 mRNA Vaccine
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.25 mL. One dose (0.25 mL) contains 25 micrograms of **SARS-CoV-2 LP.8.1 mRNA**.

3. LIST OF EXCIPIENTS

Excipients: SM-102, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 pre-filled syringe
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (-50°C - ≤ -15°C)
EXP (2-8°C)

9. SPECIAL STORAGE CONDITIONS

Store in a freezer at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/037 (blister pack of 1)
EU/1/20/1507/038 (blister pack of 10)
EU/1/20/1507/039 (paper inner tray of 1)
EU/1/20/1507/040 (paper inner tray of 10)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Spikevax LP.8.1 25 mcg dispersion for injection
COVID-19 mRNA Vaccine
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.25 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Spikevax 0.2 mg/mL dispersion for injection
Spikevax 0.1 mg/mL dispersion for injection
Spikevax 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
elasomeran

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Spikevax is and what it is used for

Spikevax is a vaccine used to prevent COVID-19 caused by SARS-CoV-2. It is given to adults and children aged 6 months and older. The active substance in Spikevax is mRNA encoding the SARS-CoV-2 spike protein. The mRNA is embedded in SM-102 lipid nanoparticles.

As Spikevax does not contain the virus, it cannot give you COVID-19.

How the vaccine works
Spikevax stimulates the body's natural defences (immune system). The vaccine works by causing the body to produce protection (antibodies) against the virus that causes COVID-19. Spikevax uses a substance called messenger ribonucleic acid (mRNA) to carry instructions that cells in the body can use to make the spike protein that is also on the virus. The cells then make antibodies against the spike protein to help fight off the virus. This will help to protect you against COVID-19.

2. What you need to know before you are given Spikevax

The vaccine must not be given if you are **allergic** to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Spikevax if:

- you have previously had a severe, life-threatening **allergic** reaction after any other vaccine injection or after you were given Spikevax in the past.

- you have a very weak or compromised immune system
- you have ever fainted following any needle injection.
- you have a bleeding disorder
- you have a high fever or severe infection; however, you can have your vaccination if you have a mild fever or upper airway infection like a cold
- you have any serious illness
- if you have anxiety related to injections

There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) after vaccination with Spikevax (see section 4).

These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose.

Most cases of myocarditis and pericarditis recover. Some cases required intensive care support and fatal cases have been seen.

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Spikevax.

Capillary leak syndrome (CLS) flare-ups
A few cases of capillary leak syndrome flare-ups (causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint, low blood pressure) have been reported following vaccination with Spikevax. If you have previously had episodes of CLS, talk to a doctor before you are given Spikevax.

Duration of protection
As with any vaccine, the primary 2-dose vaccination course of Spikevax may not fully protect all those who receive it and it is not known how long you will be protected.

Children
Spikevax is not recommended for children aged under 6 months.

Other medicines and Spikevax
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Spikevax may affect the way other medicines work, and other medicines may affect how Spikevax works.

Immunocompromised individuals
If you are immunocompromised, you may receive a third dose of Spikevax. The efficacy of Spikevax even after a third dose may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Pregnancy and breast-feeding
If you are pregnant or think you may be pregnant, tell your doctor, nurse or pharmacist before you receive this vaccine. Spikevax can be used during pregnancy. A large amount of information from pregnant women vaccinated with Spikevax during the second and third trimester have not shown negative effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no change to the risk for miscarriage has been seen.

Spikevax can be given during breastfeeding.

Driving and using machines
Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Spikevax contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How you will be given Spikevax

Table 1. Spikevax dosing for primary series, a third dose in severely immunocompromised and booster doses

Strength	Vaccination type	Age(s)	Dose	Recommendations
Spikevax 0.2 mg/mL dispersion for injection	Primary series	Individuals 12 years of age and older	2 (two) doses (0.5 mL each, containing 100 micrograms mRNA)	It is recommended to administer the second dose 28 days after the first dose.
		Children 6 years through 11 years of age	2 (two) doses (0.25 mL each, containing 50 micrograms mRNA, which is half of the primary dose for individuals 12 years and older)	
	Third dose in severely immuno-compromised	Individuals 12 years of age and older	1 (one) dose of 0.5 mL, containing 100 micrograms mRNA	A third dose may be given at least 28 days after the second dose.
		Children 6 years through 11 years of age	1 (one) dose of 0.25 mL, containing 50 micrograms mRNA	
	Booster dose	Individuals 12 years of age and older	1 (one) dose of 0.25 mL, containing 50 micrograms mRNA	Spikevax may be used to boost individuals 12 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector

Strength	Vaccination type	Age(s)	Dose	Recommendations
				vaccine at least 3 months after completion of the primary series.
Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe*	Primary series†	Children 6 years through 11 years of age	2 (two) doses (0.5 mL each, containing 50 micrograms mRNA each)	It is recommended to administer the second dose 28 days after the first dose.
		Children 6 months through 5 years of age	2 (two) doses (0.25 mL each, containing 25 micrograms mRNA each, which is half of the primary dose for children 6 years through 11 years of age)*	
	Third dose in severely immuno-compromised‡	Children 6 years through 11 years of age	1 (one) dose of 0.5 mL, containing 50 micrograms mRNA	A third dose may be given at least 28 days after the second dose.
		Children 6 months through 5 years of age	1 (one) dose of 0.25 mL, containing 25 micrograms mRNA*	
	Booster dose	Individuals 12 years of age and older	1 (one) dose of 0.5 mL, containing 50 micrograms mRNA	Spikevax may be used to boost individuals 6 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector vaccine at least 3 months after completion of the primary series.
		Children 6 years through 11 years of age	1 (one) dose of 0.25 mL, containing 25 micrograms mRNA*	

*Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.
†For primary series for individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.
‡For the third dose in severely immunocompromised individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.

If you miss an appointment for your primary 2nd dose of Spikevax
- If you miss an appointment, arrange another visit as soon as possible with your doctor, pharmacist or nurse.
- If you miss a scheduled injection, you may not be fully protected against COVID-19.

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.

After each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least **15 minutes** to monitor for signs of an allergic reaction.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:
- feeling faint or light-headed;
- changes in your heartbeat;
- shortness of breath;
- wheezing;
- swelling of your lips, face, or throat;
- hives or rash;
- nausea or vomiting;
- stomach pain.

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common (may affect more than 1 in 10 people):
- swelling/tenderness in the underarm
- decreased appetite (observed in 6 month to 5 year olds)
- irritability/crying (observed in 6 month to 5 year olds)
- headache
- sleepiness (observed in 6 month to 5 year olds)
- nausea
- vomiting
- muscle ache, joint aches, and stiffness
- pain or swelling at the injection site
- redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)
- feeling very tired
- chills
- fever

Common (may affect up to 1 in 10 people):
- diarrhoea
- rash
- rash or hives at the injection site (some of which may occur approximately 9 to 11 days after the injection)

Uncommon (may affect up to 1 in 100 people):
- itchiness at the injection site
- dizziness

- stomach pain
- raised, itchy rash (urticaria) (which may occur from the time of injection and up to approximately two weeks after the injection)

Rare (may affect up to 1 in 1 000 people)
- temporary one-sided facial drooping (Bell's palsy)
- swelling of the face (swelling of the face may occur in individuals who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

Very rare (may affect up to 1 in 10 000 people)
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain

Frequency not known
- severe allergic reactions with breathing difficulties (anaphylaxis)
- reaction of increased sensitivity or intolerance by the immune system (hypersensitivity)
- a skin reaction that causes red spots or patches on the skin that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme)
- extensive swelling of the vaccinated limb
- heavy menstrual bleeding (most cases appeared to be non-serious and temporary in nature)
- rash elicited by external stimulus such as firm stroking, scratching, or pressure to the skin (mechanical urticaria)
- raised, itchy rash with a duration of more than six weeks (chronic urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this vaccine.

5. How to store Spikevax

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Information about storage, expiry, and use and handling are described in the section intended for healthcare professionals at the end of the package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Spikevax contains

Table 2. Composition by container type

Strength	Container	Dose(s)	Composition
Spikevax 0.2 mg/mL dispersion for injection	Multidose vial	Maximum 10 doses of 0.5 mL each	One dose (0.5 mL) contains 100 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
		Maximum 20 doses of 0.25 mL each	One dose (0.25 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax 0.1 mg/mL dispersion for injection	Multidose vial	5 doses of 0.5 mL each Maximum 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax 50 micrograms dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only. Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.	One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).

Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (original).

The other ingredients are SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate), cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

What Spikevax looks like and contents of the pack

Spikevax 0.2 mg/mL dispersion for injection

Spikevax is a white to off white dispersion supplied in a 5 mL glass vial with a rubber stopper and red flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials

Spikevax 0.1 mg/mL dispersion for injection

Spikevax is a white to off white dispersion supplied in a 2.5 mL glass vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials

Spikevax 50 micrograms dispersion for injection in pre-filled syringe

Spikevax is a white to off white dispersion supplied in a pre-filled syringe (cyclic olefin polymer) with plunger stopper and a tip cap (without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack size: 10 pre-filled syringes

Marketing Authorisation Holder
MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

Manufacturers

For multidose vials

Rovi Pharma Industrial Services, S.A.
Paseo de Europa, 50
28703. San Sebastián de los Reyes
Madrid
Spain

Recipharm Monts
18 Rue de Montbazon
Monts, France 37260

Moderna Biotech Spain S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

For pre-filled syringe

Rovi Pharma Industrial Services, S.A.
Calle Julián Camarillo n°35
28037 Madrid
Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien **Lietuva**

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Sími: 800 4382

Italia
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Κύπρος
Τηλ: 80091080

Latvija
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Tel: 88 003 1114

Luxembourg/Luxemburg
Tél/Tel: 800 85 499

Magyarország
Tel: 06 809 87488

Malta
Tel: 8006 5066

Nederland
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Norge
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Österreich
Tel: 0800 909636

Polska
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Portugal
Tel: 800 210 256

România
Tel: 0800 400 625

Slovenija
Tel: 080 083082

Slovenská republika
Tel: 0800 191 647

Suomi/Finland
Puh/Tel: 0800 774198

Sverige
Tel: 020 10 92 13

This leaflet was last revised in

Scan the code with a mobile device to get the package leaflet in different languages.

Or visit the URL https://www.ModernaCovid19Global.com

Detailed information on this vaccine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Storage and preparation for administration

Spikevax should be administered by a trained healthcare professional.

The vaccine comes ready to use once thawed.

Do not shake or dilute.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration.

Spikevax is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.

Store vials and pre-filled syringes in a freezer at -50ºC to -15ºC.

Keep the vial and pre-filled syringe in the outer carton in order to protect from light.

Spikevax 0.2 mg/mL dispersion for injection (multidose vials with a red flip-off cap)

Ten (10) doses (of 0.5 mL each) or a maximum of twenty (20) doses (of 0.25 mL each) can be withdrawn from each multidose vial.

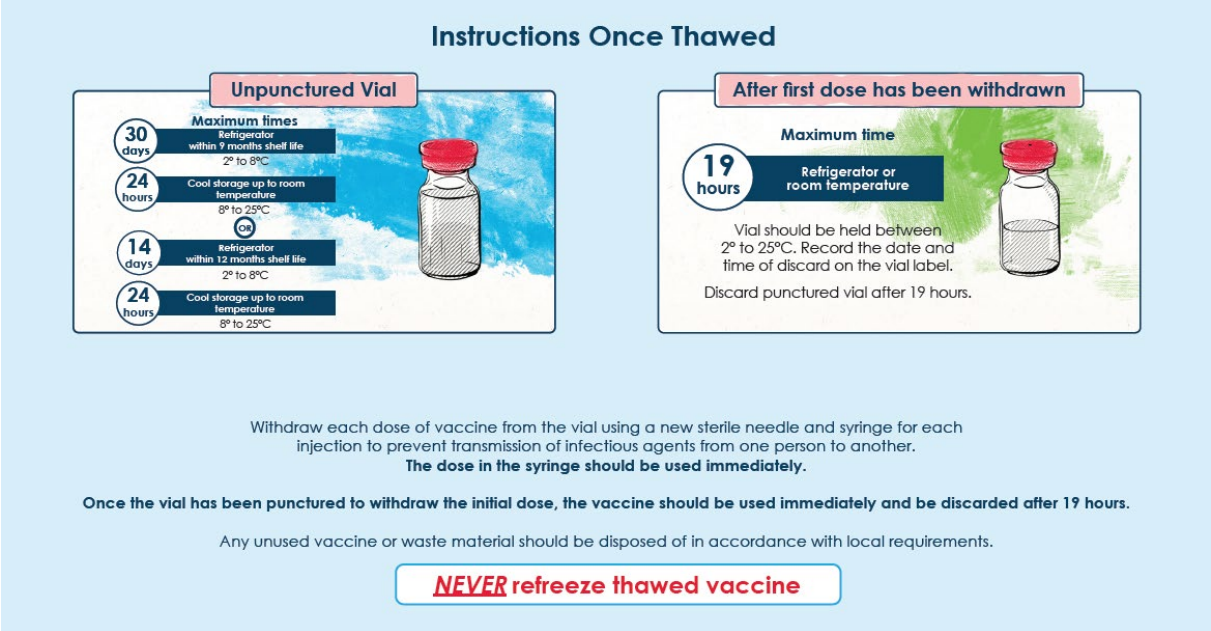
Pierce the stopper preferably at a different site each time. Do not puncture the red-cap vial more than 20 times.

Verify that the vial has a red flip-off cap and the product name is Spikevax 0.2 mg/mL. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each multidose vial before use following the instructions below (Table 3).

Table 3. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax 0.1 mg/mL dispersion for injection (multidose vials with a blue flip-off cap)

Five (5) doses (of 0.5 mL each) or a maximum of ten (10) doses (of 0.25 mL each) can be withdrawn from each multidose vial.

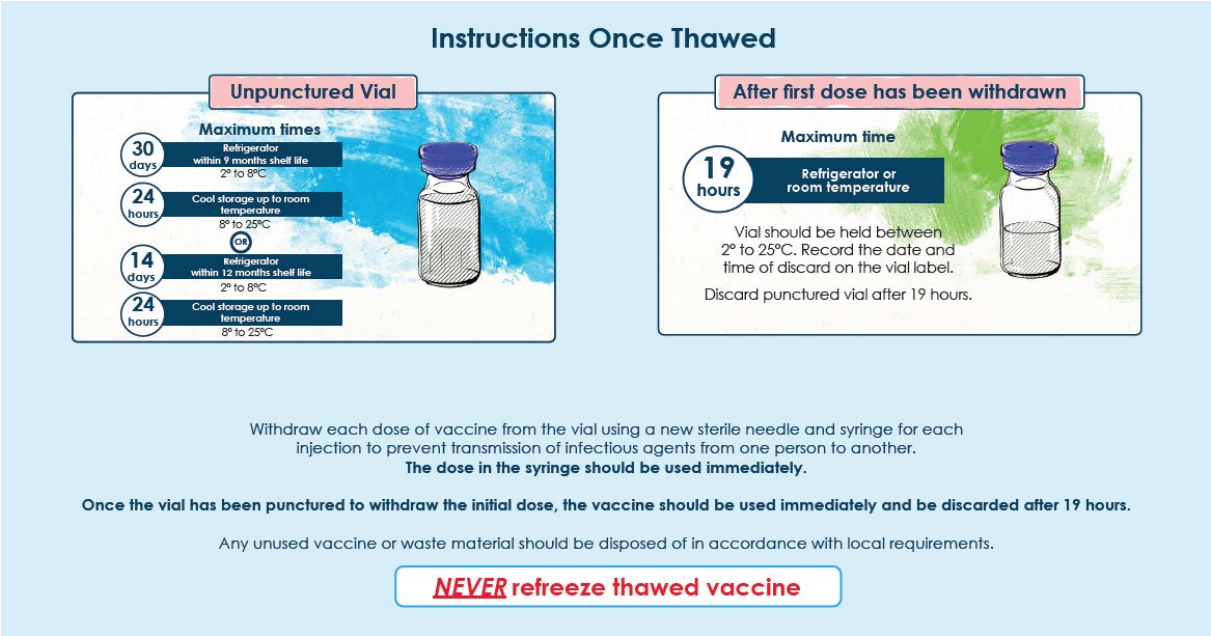
Pierce the stopper preferably at a different site each time.

Verify that the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each multidose vial before use following the instructions below (Table 4).

Table 4. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax 50 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe. Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.

Spikevax is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (50 micrograms) mRNA and must be thawed prior to administration.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 5).

Table 5. Thawing instructions for pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	**Thaw duration (minutes)**	**Thaw temperature (at room temperature) (°C)**	**Thaw duration (minutes)**
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax 50 micrograms. If the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- After thawing, do not refreeze.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosing and schedule

Table 6. Spikevax dosing for primary series, a third dose in severely immunocompromised and booster doses

Vaccination	**Spikevax 0.2 mg/mL dispersion for injection**	**Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe***
Primary series	Individuals 12 years of age and older	Not applicable†

Vaccination	Spikevax 0.2 mg/mL dispersion for injection	Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe*
It is recommended to get the second dose of the same vaccine 28 days after the first dose to complete the vaccination course.	two 0.5 mL injections	
	Children 6 years through 11 years of age two 0.25 mL injections	Children 6 years through 11 years of age two 0.5 mL injections
	Not applicable	Children 6 months through 5 years of age two 0.25 mL injections*
Third dose in severely immunocompromised at least 1 month after the second dose	Individuals 12 years of age and older 0.5 mL	Not applicable‡
	Children 6 years through 11 years of age 0.25 mL	Children 6 years through 11 years of age 0.5 mL
	Not applicable	Children 6 months through 5 years of age 0.25 mL*
Booster dose may be given at least 3 months after the second dose	Individuals 12 years of age and older 0.25 mL	Individuals 12 years of age and older 0.5 mL
	Not applicable	Individuals 6 years of age and older 0.25 mL*

* Do not use the pre-filled syringe to deliver a partial volume of 0.25 mL.
†For primary series for individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.
‡For the third dose in severely immunocompromised individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Spikevax.

Individuals should be observed by a healthcare professional for at least 15 minutes after vaccination.

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

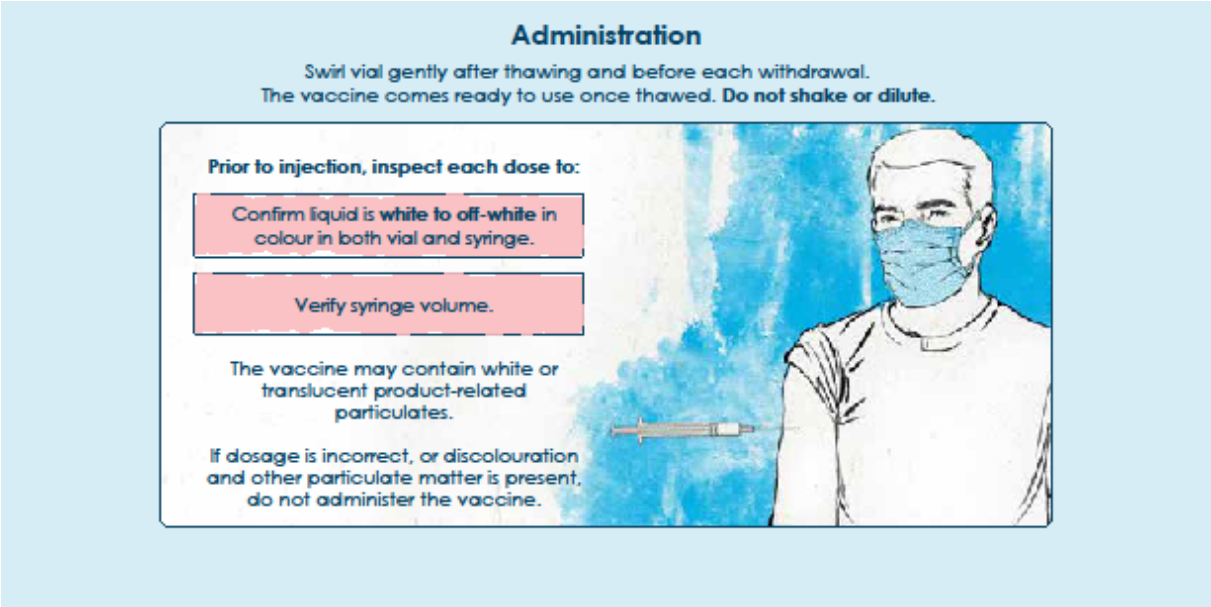
Different injectable vaccines should be given at different injection sites.

Spikevax must not be mixed with other vaccines or medicinal products in the same syringe.

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm or in infants and young children, the anterolateral aspect of the thigh. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Pre-filled syringes

Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner). With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Uncap the needle when ready for administration. Administer the entire dose intramuscularly. Discard syringe after use. For single-use only.

Package leaflet: Information for the user

Spikevax bivalent Original/Omicron BA.1
(50 micrograms/50 micrograms)/mL dispersion for injection
Spikevax bivalent Original/Omicron BA.1
25 micrograms/25 micrograms dispersion for injection
Spikevax bivalent Original/Omicron BA.1
25 micrograms/25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
elasomeran/imelasomeran

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Spikevax bivalent Original/Omicron BA.1 is and what it is used for

Spikevax bivalent Original/Omicron BA.1 is a vaccine used to prevent COVID-19 caused by SARS-CoV-2. It is given to adults and children aged 6 years and older. The active substance in Spikevax bivalent Original/Omicron BA.1 is mRNA encoding the SARS-CoV-2 spike protein. The mRNA is embedded in SM-102 lipid nanoparticles.

Spikevax bivalent Original/Omicron BA.1 is only for individuals who have previously received at least a primary vaccination course against COVID-19.

As Spikevax bivalent Original/Omicron BA.1 does not contain the virus, it cannot give you COVID-19.

How the vaccine works
Spikevax bivalent Original/Omicron BA.1 stimulates the body's natural defences (immune system). The vaccine works by causing the body to produce protection (antibodies) against the virus that causes COVID-19. Spikevax bivalent Original/Omicron BA.1 uses a substance called messenger ribonucleic acid (mRNA) to carry instructions that cells in the body can use to make the spike protein that is also on the virus. The cells then make antibodies against the spike protein to help fight off the virus. This will help to protect you against COVID-19.

2. What you need to know before you are given Spikevax bivalent Original/Omicron BA.1

The vaccine must not be given if you are **allergic** to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Spikevax bivalent Original/Omicron BA.1 if:

- you have previously had a severe, life-threatening **allergic** reaction after any other vaccine injection or after you were given Spikevax (original) in the past.
- you have a very weak or compromised immune system
- you have ever fainted following any needle injection.
- you have a bleeding disorder
- you have a high fever or severe infection; however, you can have your vaccination if you have a mild fever or upper airway infection like a cold
- you have any serious illness
- if you have anxiety related to injections

There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) after vaccination with Spikevax (see section 4).

These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose.

Most cases of myocarditis and pericarditis recover. Some cases required intensive care support and fatal cases have been seen.

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Spikevax bivalent Original/Omicron BA.1.

Capillary leak syndrome (CLS) flare-ups
A few cases of capillary leak syndrome flare-ups (causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint, low blood pressure) have been reported following vaccination with Spikevax (original). If you have previously had episodes of CLS, talk to a doctor before you are given Spikevax bivalent Original/Omicron BA.1.

Duration of protection
As with any vaccine, the third dose of Spikevax bivalent Original/Omicron BA.1 may not fully protect all those who receive it and it is not known how long you will be protected.

Children
Spikevax bivalent Original/Omicron BA.1 is not recommended for children aged under 6 years.

Other medicines and Spikevax bivalent Original/Omicron BA.1
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Spikevax bivalent Original/Omicron BA.1 may affect the way other medicines work, and other medicines may affect how Spikevax bivalent Original/Omicron BA.1 works.

Immunocompromised individuals

The efficacy of Spikevax bivalent Original/Omicron BA.1 may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Pregnancy and breast-feeding
If you are pregnant or think you may be pregnant, tell your doctor, nurse or pharmacist before you receive this vaccine. No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.1 during pregnancy. However, a large amount of information from pregnant women vaccinated with Spikevax (original) during the second and third trimester have not shown negative effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no increased risk for miscarriage has been seen. Since differences between the two products are only related to the spike protein in the vaccine, and there are no clinically meaningful differences, Spikevax bivalent Original/Omicron BA.1 can be used during pregnancy.

No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.1 during breast feeding.

However, no effects on the breastfed newborn/infant are anticipated. Data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax bivalent Original/Omicron BA.1 can be given during breastfeeding.

Driving and using machines
Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Spikevax bivalent Original/Omicron BA.1 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How you will be given Spikevax bivalent Original/Omicron BA.1

Individuals 12 years of age and older
The dose of Spikevax bivalent Original/Omicron BA.1 is 0.5 mL, given at least 3 months after the last prior dose of a COVID-19 vaccine.

Children 6 years through 11 years of age
The dose of Spikevax bivalent Original/Omicron BA.1 is 0.25 mL, given at least 3 months after the last prior dose of a COVID-19 vaccine.

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.

After each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least **15 minutes** to monitor for signs of an allergic reaction.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.

Spikevax bivalent Original/Omicron BA.1 is only for individuals who have previously received at least a primary vaccination course against COVID-19.

For details on the primary vaccination course in individuals 6 years of age and older, see the Package Leaflet for Spikevax 0.2 mg/mL.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:
- feeling faint or light-headed;
- changes in your heartbeat;
- shortness of breath;
- wheezing;
- swelling of your lips, face, or throat;
- hives or rash;
- nausea or vomiting;
- stomach pain.

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common (may affect more than 1 in 10 people):
- swelling/tenderness in the underarm
- decreased appetite (observed in 6 month to 5 year olds)
- irritability/crying (observed in 6 month to 5 year olds)
- headache
- sleepiness (observed in 6 month to 5 year olds)
- nausea
- vomiting
- muscle ache, joint aches, and stiffness
- pain or swelling at the injection site
- redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)
- feeling very tired
- chills
- fever

Common (may affect up to 1 in 10 people):
- diarrhoea
- rash
- rash or hives at the injection site (some of which may occur approximately 9 to 11 days after the injection)

Uncommon (may affect up to 1 in 100 people):
- itchiness at the injection site
- dizziness
- stomach pain
- raised, itchy rash (urticaria) (which may occur from the time of injection and up to approximately two weeks after the injection)

Rare (may affect up to 1 in 1 000 people)
- temporary one-sided facial drooping (Bell's palsy)
- swelling of the face (swelling of the face may occur in individuals who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

Very rare (may affect up to 1 in 10 000 people)

- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain

Frequency not known
- severe allergic reactions with breathing difficulties (anaphylaxis)
- reaction of increased sensitivity or intolerance by the immune system (hypersensitivity)
- a skin reaction that causes red spots or patches on the skin that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme)
- extensive swelling of the vaccinated limb
- heavy menstrual bleeding (most cases appeared to be non-serious and temporary in nature)
- rash elicited by external stimulus such as firm stroking, scratching, or pressure to the skin (mechanical urticaria)
- raised, itchy rash with a duration of more than six weeks (chronic urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this vaccine.

5. How to store Spikevax bivalent Original/Omicron BA.1

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Information about storage, expiry, and use and handling are described in the section intended for healthcare professionals at the end of the package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Spikevax bivalent Original/Omicron BA.1 contains

Table 1. Composition by container type

Strength	Container	Dose(s)	Composition
Spikevax bivalent Original/Omicron BA.1 (50 mcg/50 mcg)/mL dispersion for injection	Multidose 2.5 mL vial	5 doses of 0.5 mL each or 10 doses of 0.25 mL each	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles). One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside
	Multidose 5 mL vial	10 doses of 0.5 mL each or 20 doses of 0.25 mL each	

Strength	Container	Dose(s)	Composition
			modified) (embedded in SM-102 lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.1 25 mcg/25 mcg dispersion for injection	Single-dose 0.5 mL vial	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.1 25 mcg/25 mcg dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	

Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (original).

Imelasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding a full-length, codon-optimised pre-fusion stabilised conformation variant (K983P and V984P) of the SARS-CoV-2 spike (S) glycoprotein (Omicron variant, BA.1).

The other ingredients are SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate), cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

What Spikevax bivalent Original/Omicron BA.1 looks like and contents of the pack

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection

Spikevax bivalent Original/Omicron BA.1 is a white to off white dispersion supplied in a 2.5 mL or 5 mL glass multidose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size:
10 multidose vials. Each vial contains 2.5 mL.
10 multidose vials. Each vial contains 5 mL.

Not all pack sizes may be marketed.

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection

Spikevax bivalent Original/Omicron BA.1 is a white to off white dispersion supplied in a 0.5 mL glass single-dose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 single-dose vials

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Spikevax bivalent Original/Omicron BA.1 is a white to off white dispersion supplied in a pre-filled syringe (cyclic olefin polymer) with plunger stopper and a tip cap (without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack size: 10 pre-filled syringes

Marketing Authorisation Holder

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Norge
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Österreich
Tel: 0800 909636

Polska
Tel: 800 702 406

Portugal
Tel: 800 210 256

România
Tel: 0800 400 625

Slovenija
Tel: 080 083082

Slovenská republika
Tel: 0800 191 647

Suomi/Finland
Puh/Tel: 0800 774198

Sverige
Tel: 020 10 92 13

This leaflet was last revised in

Scan the code with a mobile device to get the package leaflet in different languages.

Or visit the URL https://www.ModernaCovid19Global.com

Detailed information on this vaccine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Spikevax bivalent Original/Omicron BA.1 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials with a blue flip-off cap)

Spikevax bivalent Original/Omicron BA.1 should be administered by a trained healthcare professional.

The vaccine comes ready to use once thawed.

Do not shake or dilute.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration.

Spikevax bivalent Original/Omicron BA.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.

Vials are stored in a freezer at -50ºC to -15ºC.

Five (5) or ten (10) doses (of 0.5 mL each) can be withdrawn from each multidose vial, depending on vial size. Ten (10) or twenty (20) doses (of 0.25 mL each) can be withdrawn from each multidose vial, depending on vial size.

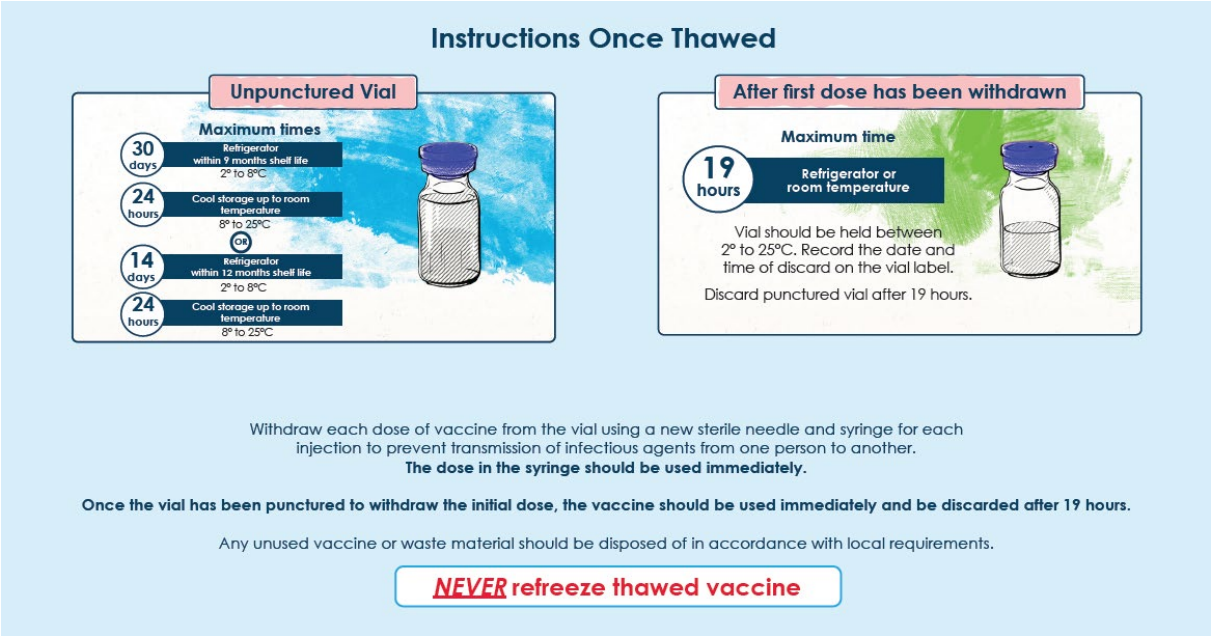
Pierce the stopper preferably at a different site each time.

Verify that the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each multidose vial before use following the instructions below (Table 2).

Table 2. Thawing instructions for multidose vials before use

Configuration	**Thaw instructions and duration**			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection (single-dose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal. Thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 10 vials may be thawed either in the refrigerator or at room temperature (Table 3).

Table 3. Thawing instructions for single-dose vials and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

Spikevax bivalent Original/Omicron BA.1 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax bivalent Original/Omicron BA.1 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (25 micrograms of elasomeran and 25 micrograms of imelasomeran) mRNA and must be thawed prior to administration.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 4).

Table 4. Thawing instructions for Spikevax bivalent Original/Omicron BA.1 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax bivalent Original/Omicron BA.1. If the product name is Spikevax 50 micrograms or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax bivalent Original/Omicron BA.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- After thawing, do not refreeze.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosing and schedule

Individuals 12 years of age and older
The dose of Spikevax bivalent Original/Omicron BA.1 is 0.5 mL, given at least 3 months after the last prior dose of a COVID-19 vaccine.

Children 6 years through 11 years of age

The dose of Spikevax bivalent Original/Omicron BA.1 is 0.25 mL, given at least 3 months after the last prior dose of a COVID-19 vaccine.

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Spikevax bivalent Original/Omicron BA.1.

Individuals should be observed by a healthcare professional for at least 15 minutes after vaccination.

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

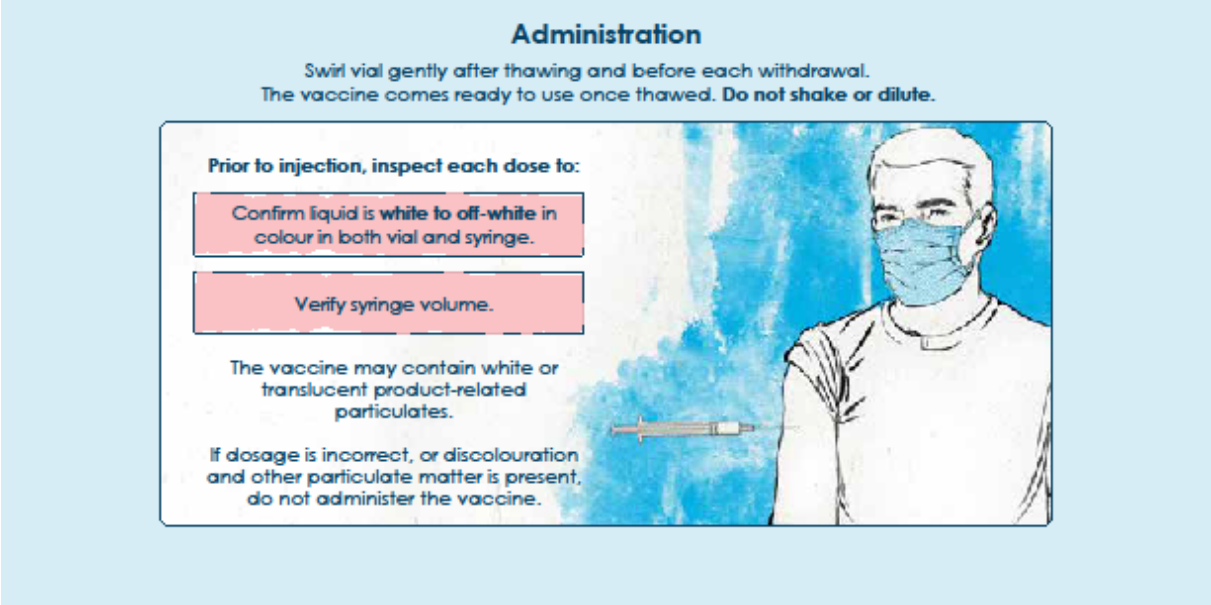
Different injectable vaccines should be given at different injection sites.

Spikevax bivalent Original/Omicron BA.1 must not be mixed with other vaccines or medicinal products in the same syringe.

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Pre-filled syringes

Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner). With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Uncap the needle when ready for administration. Administer the entire dose intramuscularly. Discard syringe after use. For single-use only.

Package leaflet: Information for the user

Spikevax bivalent Original/Omicron BA.4-5
(50 micrograms/50 micrograms)/mL dispersion for injection
Spikevax bivalent Original/Omicron BA.4-5
25 micrograms/25 micrograms dispersion for injection
Spikevax bivalent Original/Omicron BA.4-5
25 micrograms/25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
elasomeran/davesomeran

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Spikevax bivalent Original/Omicron BA.4-5 is and what it is used for

Spikevax bivalent Original/Omicron BA.4-5 is a vaccine used to prevent COVID-19 caused by SARS-CoV-2. It is given to adults and children aged 6 months and older. The active substance in Spikevax bivalent Original/Omicron BA.4-5 is mRNA encoding the SARS-CoV-2 spike protein. The mRNA is embedded in SM-102 lipid nanoparticles.

As Spikevax bivalent Original/Omicron BA.4-5 does not contain the virus, it cannot give you COVID-19.

How the vaccine works
Spikevax bivalent Original/Omicron BA.4-5 stimulates the body's natural defences (immune system). The vaccine works by causing the body to produce protection (antibodies) against the virus that causes COVID-19. Spikevax bivalent Original/Omicron BA.4-5 uses a substance called messenger ribonucleic acid (mRNA) to carry instructions that cells in the body can use to make the spike protein that is also on the virus. The cells then make antibodies against the spike protein to help fight off the virus. This will help to protect you against COVID-19.

2. What you need to know before you are given Spikevax bivalent Original/Omicron BA.4-5

The vaccine must not be given if you are **allergic** to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Spikevax bivalent Original/Omicron BA.4-5 if:

- you have previously had a severe, life-threatening **allergic** reaction after any other vaccine injection or after you were given Spikevax (original) in the past.
- you have a very weak or compromised immune system
- you have ever fainted following any needle injection.
- you have a bleeding disorder
- you have a high fever or severe infection; however, you can have your vaccination if you have a mild fever or upper airway infection like a cold
- you have any serious illness
- if you have anxiety related to injections

There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) after vaccination with Spikevax (see section 4).

These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose.

Most cases of myocarditis and pericarditis recover. Some cases required intensive care support and fatal cases have been seen.

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Spikevax bivalent Original/Omicron BA.4-5.

Capillary leak syndrome (CLS) flare-ups
A few cases of capillary leak syndrome flare-ups (causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint, low blood pressure) have been reported following vaccination with Spikevax (original). If you have previously had episodes of CLS, talk to a doctor before you are given Spikevax bivalent Original/Omicron BA.4-5.

Duration of protection
As with any vaccine, the third dose of Spikevax bivalent Original/Omicron BA.4-5 may not fully protect all those who receive it and it is not known how long you will be protected.

Children
Spikevax bivalent Original/Omicron BA.4-5 is not recommended for children aged under 6 months.

Other medicines and Spikevax bivalent Original/Omicron BA.4-5
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Spikevax bivalent Original/Omicron BA.4-5 may affect the way other medicines work, and other medicines may affect how Spikevax bivalent Original/Omicron BA.4-5 works.

Immunocompromised individuals
The efficacy of Spikevax bivalent Original/Omicron BA.4-5 may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Pregnancy and breast-feeding
If you are pregnant or think you may be pregnant, tell your doctor, nurse or pharmacist before you receive this vaccine. No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.4-5 during pregnancy. However, a large amount of information from pregnant women vaccinated with Spikevax (original) during the second and third trimester have not shown negative effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no increased risk for miscarriage has been seen. Since differences between the two products are only related to the spike protein in the vaccine, and there are no clinically meaningful differences, Spikevax bivalent Original/Omicron BA.4-5 can be used during pregnancy.

No data are available yet regarding the use of Spikevax bivalent Original/Omicron BA.4-5 during breast feeding.

However, no effects on the breastfed newborn/infant are anticipated. Data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax bivalent Original/Omicron BA.4-5 can be given during breastfeeding.

Driving and using machines
Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Spikevax bivalent Original/Omicron BA.4-5 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How you will be given Spikevax bivalent Original/Omicron BA.4-5

Table 1. Spikevax bivalent Original/Omicron BA.4-5 posology

Age(s)	Dose	Additional recommendations
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of Spikevax, one dose of Spikevax bivalent Original/Omicron BA.4-5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax bivalent Original/Omicron BA.4-5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

Age(s)	Dose	Additional recommendations
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 2. Spikevax bivalent Original/Omicron BA.4-5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.

After each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least **15 minutes** to monitor for signs of an allergic reaction.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:
- feeling faint or light-headed;
- changes in your heartbeat;
- shortness of breath;
- wheezing;
- swelling of your lips, face, or throat;
- hives or rash;

- nausea or vomiting;
- stomach pain.

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common (may affect more than 1 in 10 people):
- swelling/tenderness in the underarm
- decreased appetite (observed in 6 month to 5 year olds)
- irritability/crying (observed in 6 month to 5 year olds)
- headache
- sleepiness (observed in 6 month to 5 year olds)
- nausea
- vomiting
- muscle ache, joint aches, and stiffness
- pain or swelling at the injection site
- redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)
- feeling very tired
- chills
- fever

Common (may affect up to 1 in 10 people):
- diarrhoea
- rash
- rash or hives at the injection site (some of which may occur approximately 9 to 11 days after the injection)

Uncommon (may affect up to 1 in 100 people):
- itchiness at the injection site
- dizziness
- stomach pain
- raised, itchy rash (urticaria) (which may occur from the time of injection and up to approximately two weeks after the injection)

Rare (may affect up to 1 in 1 000 people)
- temporary one-sided facial drooping (Bell's palsy)
- swelling of the face (swelling of the face may occur in individuals who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

Very rare (may affect up to 1 in 10 000 people)
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain

Frequency not known
- severe allergic reactions with breathing difficulties (anaphylaxis)
- reaction of increased sensitivity or intolerance by the immune system (hypersensitivity)
- a skin reaction that causes red spots or patches on the skin that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme)
- extensive swelling of the vaccinated limb
- heavy menstrual bleeding (most cases appeared to be non-serious and temporary in nature)
- rash elicited by external stimulus such as firm stroking, scratching, or pressure to the skin (mechanical urticaria)
- raised, itchy rash with a duration of more than six weeks (chronic urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this vaccine.

5. How to store Spikevax bivalent Original/Omicron BA.4-5

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Information about storage, expiry, and use and handling are described in the section intended for healthcare professionals at the end of the package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Spikevax bivalent Original/Omicron BA.4-5 contains

Table 3. Composition by container type

Strength	Container	Dose(s)	Composition
Spikevax bivalent Original/Omicron BA.4-5 (50 mcg/50 mcg)/mL dispersion for injection	Multidose 2.5 mL vial	5 doses of 0.5 mL each or a maximum of 10 doses of 0.25 mL each	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles). One dose (0.25 mL) contains 12.5 micrograms of elasomeran and 12.5 micrograms of daveasomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax bivalent Original/Omicron BA.4-5 25 mcg/25 mcg dispersion for injection	Single-dose 0.5 mL vial	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).

Strength	Container	Dose(s)	Composition
Spikevax bivalent Original/Omicron BA.4-5 25 mcg/25 mcg dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran and 25 micrograms of davesomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).

Elasomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (original).

Davesomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 Omicron variant lineages BA.4 and BA.5. The S proteins of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 are identical.

The other ingredients are SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate), cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

What Spikevax bivalent Original/Omicron BA.4-5 looks like and contents of the pack

Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection

Spikevax bivalent Original/Omicron BA.4-5 is a white to off white dispersion supplied in a glass multidose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection

Spikevax bivalent Original/Omicron BA.4-5 is a white to off white dispersion supplied in a glass single-dose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 single-dose vials. Each vial contains 0.5 mL.

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Spikevax bivalent Original/Omicron BA.4-5 is a white to off white dispersion supplied in a pre-filled syringe (cyclic olefin polymer) with plunger stopper and a tip cap (without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack size: 10 pre-filled syringes

Marketing Authorisation Holder

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Manufacturers

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Nederland
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Österreich
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Polska
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France
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Hrvatska
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Ísland
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Portugal
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România
Tel: 0800 400 625

Slovenija
Tel: 080 083082

Slovenská republika
Tel: 0800 191 647

Suomi/Finland
Puh/Tel: 0800 774198

Sverige
Tel: 020 10 92 13

This leaflet was last revised in

Scan the code with a mobile device to get the package leaflet in different languages.

Or visit the URL https://www.ModernaCovid19Global.com

Detailed information on this vaccine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms/50 micrograms)/mL dispersion for injection (multidose vials with a blue flip-off cap)

Spikevax bivalent Original/Omicron BA.4-5 should be administered by a trained healthcare professional.

The vaccine comes ready to use once thawed.

Do not shake or dilute.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration.

Spikevax bivalent Original/Omicron BA.4-5 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.

Vials are stored in a freezer at -50ºC to -15ºC.

Five (5) doses (of 0.5 mL each) or a maximum of ten (10) doses (0.25 mL each) can be withdrawn from each multidose vial.

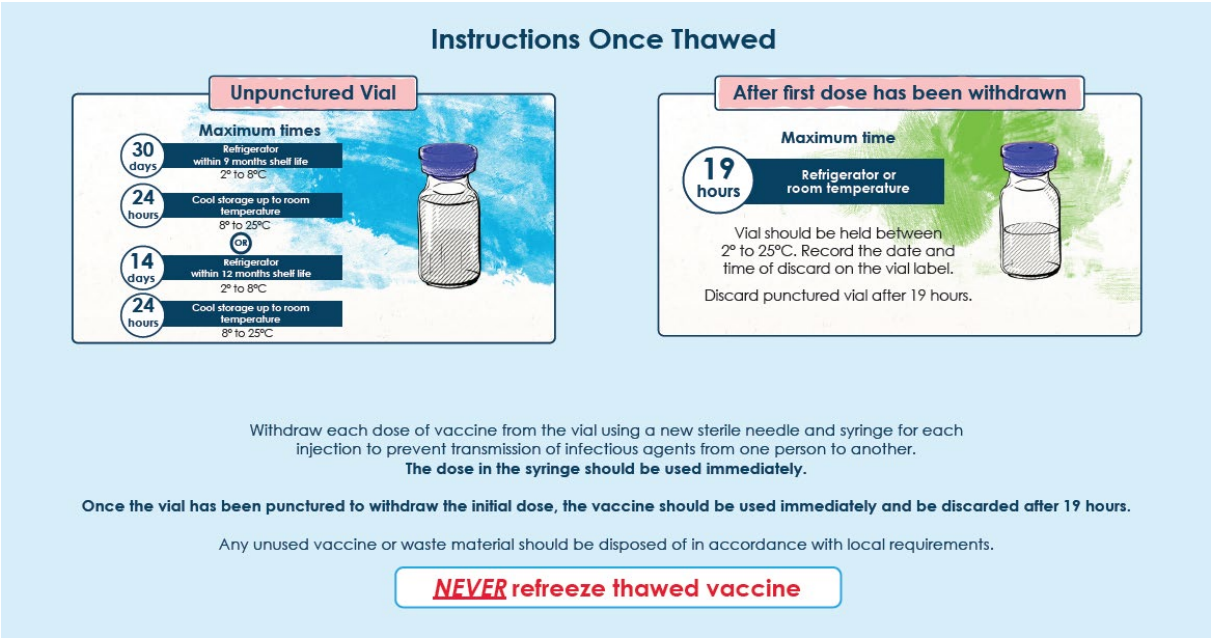
Pierce the stopper preferably at a different site each time.

Verify that the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.4-5. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL or Spikevax bivalent Original/Omicron BA.1, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each multidose vial before use following the instructions below (Table 4).

Table 4. Thawing instructions for multidose vials before use

Configuration	**Thaw instructions and duration**			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour



Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection (single-dose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.4-5. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1, please make reference to the Summary of Product Characteristics for that formulation.

Thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 10 vials may be thawed either in the refrigerator or at room temperature (Table 5).

Table 5. Thawing instructions for single-dose vials and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

Spikevax bivalent Original/Omicron BA.4-5 25 micrograms/25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax bivalent Original/Omicron BA.4-5 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (25 micrograms of elasomeran and 25 micrograms of davesomeran) mRNA and must be thawed prior to administration.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 6).

Table 6. Thawing instructions for Spikevax bivalent Original/Omicron BA.4-5 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

Verify that the product name of the pre-filled syringe is Spikevax bivalent Original/Omicron BA.4-5. If the product name is Spikevax 50 micrograms, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax bivalent Original/Omicron BA.4-5 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- After thawing, do not refreeze.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosing and schedule

Table 7. Spikevax bivalent Original/Omicron BA.4-5 dosing

Age(s)	**Dose**	**Additional recommendations**
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of Spikevax, one dose of Spikevax bivalent Original/Omicron BA.4-5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax bivalent Original/Omicron BA.4-5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	

Age(s)	Dose	Additional recommendations
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 8. Spikevax bivalent Original/Omicron BA.4-5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Spikevax bivalent Original/Omicron BA.4-5.

Individuals should be observed by a healthcare professional for at least 15 minutes after vaccination.

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

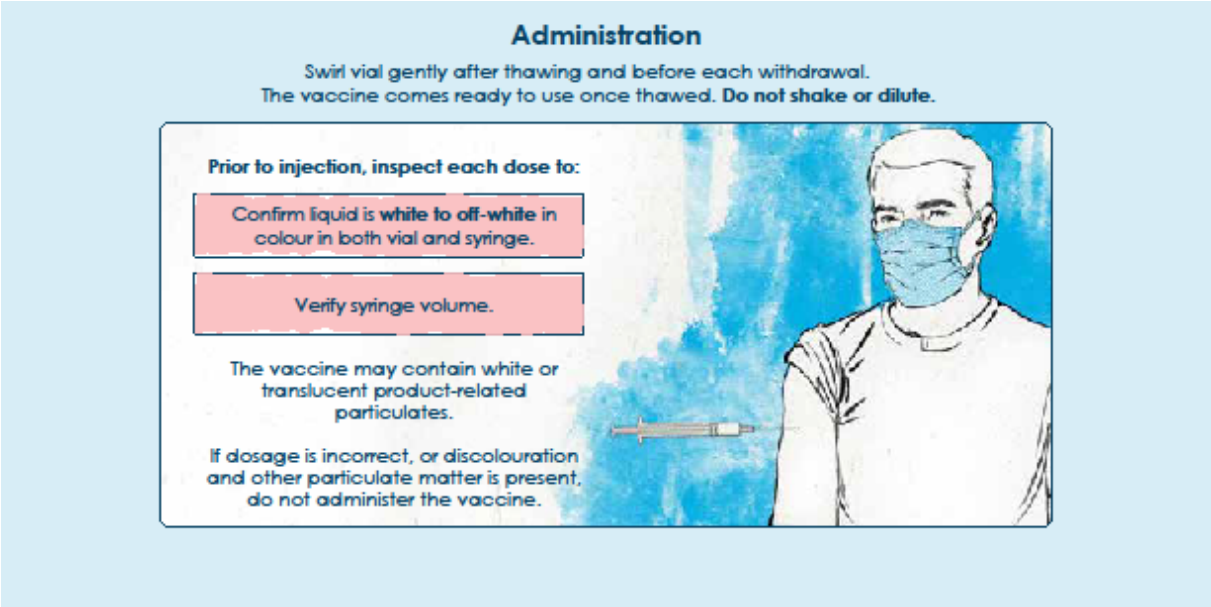
Different injectable vaccines should be given at different injection sites.

Spikevax bivalent Original/Omicron BA.4-5 must not be mixed with other vaccines or medicinal products in the same syringe.

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Pre-filled syringes

Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner). With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Uncap the needle when ready for administration. Administer the entire dose intramuscularly. Discard syringe after use. For single-use only.

Package leaflet: Information for the user

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection
Spikevax XBB.1.5 50 micrograms dispersion for injection
Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe
Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine
andusomeran

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Spikevax XBB.1.5 is and what it is used for

Spikevax XBB.1.5 is a vaccine used to prevent COVID-19 caused by SARS-CoV-2. It is given to adults and children aged 6 months and older. The active substance in Spikevax XBB.1.5 is mRNA encoding the SARS-CoV-2 spike protein. The mRNA is embedded in SM-102 lipid nanoparticles.

As Spikevax XBB.1.5 does not contain the virus, it cannot give you COVID-19.

How the vaccine works
Spikevax XBB.1.5 stimulates the body's natural defences (immune system). The vaccine works by causing the body to produce protection (antibodies) against the virus that causes COVID-19. Spikevax XBB.1.5 uses a substance called messenger ribonucleic acid (mRNA) to carry instructions that cells in the body can use to make the spike protein that is also on the virus. The cells then make antibodies against the spike protein to help fight off the virus. This will help to protect you against COVID-19.

2. What you need to know before you are given Spikevax XBB.1.5

The vaccine must not be given if you are **allergic** to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Spikevax XBB.1.5 if:

- you have previously had a severe, life-threatening **allergic** reaction after any other vaccine injection or after you were given Spikevax (original) in the past.
- you have a very weak or compromised immune system
- you have ever fainted following any needle injection.
- you have a bleeding disorder
- you have a high fever or severe infection; however, you can have your vaccination if you have a mild fever or upper airway infection like a cold
- you have any serious illness
- if you have anxiety related to injections

There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) after vaccination with Spikevax (see section 4).

These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose.

Most cases of myocarditis and pericarditis recover. Some cases required intensive care support and fatal cases have been seen.

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Spikevax XBB.1.5.

Capillary leak syndrome (CLS) flare-ups
A few cases of capillary leak syndrome flare-ups (causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint, low blood pressure) have been reported following vaccination with Spikevax (original). If you have previously had episodes of CLS, talk to a doctor before you are given Spikevax XBB.1.5.

Duration of protection
As with any vaccine, the additional dose of Spikevax XBB.1.5 may not fully protect all those who receive it and it is not known how long you will be protected.

Children
Spikevax XBB.1.5 is not recommended for children aged under 6 months.

Other medicines and Spikevax XBB.1.5
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Spikevax XBB.1.5 may affect the way other medicines work, and other medicines may affect how Spikevax XBB.1.5 works.

Immunocompromised individuals
The efficacy of Spikevax XBB.1.5 may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Pregnancy and breast-feeding
If you are pregnant or think you may be pregnant, tell your doctor, nurse or pharmacist before you receive this vaccine. No data are available yet regarding the use of Spikevax XBB.1.5 during pregnancy. However, a large amount of information from pregnant women vaccinated with Spikevax (original) during the second and third trimester have not shown negative effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination

during the first trimester is limited, no increased risk for miscarriage has been seen. Since differences between the two products are only related to the spike protein in the vaccine, and there are no clinically meaningful differences, Spikevax XBB.1.5 can be used during pregnancy.

No data are available yet regarding the use of Spikevax XBB.1.5 during breast feeding.

However, no effects on the breastfed newborn/infant are anticipated. Data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax XBB.1.5 can be given during breastfeeding.

Driving and using machines
Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Spikevax XBB.1.5 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How you will be given Spikevax XBB.1.5

Table 1. Spikevax XBB.1.5 posology

Age(s)	Dose	Additional recommendations
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of any Spikevax vaccine, one dose of Spikevax XBB.1.5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax XBB.1.5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the 0.5 mL single-dose vial or 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 2. Spikevax XBB.1.5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the 0.5 mL single-dose vial or 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.

After each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least **15 minutes** to monitor for signs of an allergic reaction.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:
- feeling faint or light-headed;
- changes in your heartbeat;
- shortness of breath;
- wheezing;
- swelling of your lips, face, or throat;
- hives or rash;
- nausea or vomiting;
- stomach pain.

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common (may affect more than 1 in 10 people):
- swelling/tenderness in the underarm
- decreased appetite (observed in 6 month to 5 year olds)
- irritability/crying (observed in 6 month to 5 year olds)
- headache
- sleepiness (observed in 6 month to 5 year olds)

- nausea
- vomiting
- muscle ache, joint aches, and stiffness
- pain or swelling at the injection site
- redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)
- feeling very tired
- chills
- fever

Common (may affect up to 1 in 10 people):
- diarrhoea
- rash
- rash or hives at the injection site (some of which may occur approximately 9 to 11 days after the injection)

Uncommon (may affect up to 1 in 100 people):
- itchiness at the injection site
- dizziness
- stomach pain
- raised, itchy rash (urticaria) (which may occur from the time of injection and up to approximately two weeks after the injection)

Rare (may affect up to 1 in 1 000 people)
- temporary one-sided facial drooping (Bell's palsy)
- swelling of the face (swelling of the face may occur in individuals who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

Very rare (may affect up to 1 in 10 000 people)
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain

Frequency not known
- severe allergic reactions with breathing difficulties (anaphylaxis)
- reaction of increased sensitivity or intolerance by the immune system (hypersensitivity)
- a skin reaction that causes red spots or patches on the skin that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme)
- extensive swelling of the vaccinated limb
- heavy menstrual bleeding (most cases appeared to be non-serious and temporary in nature)
- rash elicited by external stimulus such as firm stroking, scratching, or pressure to the skin (mechanical urticaria)
- raised, itchy rash with a duration of more than six weeks (chronic urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this vaccine.

5. How to store Spikevax XBB.1.5

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Information about storage, expiry, and use and handling are described in the section intended for healthcare professionals at the end of the package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Spikevax XBB.1.5 contains

Table 3. Composition by container type

Strength	Container	Dose(s)	Composition
Spikevax XBB.1.5 0.1 mg/mL dispersion for injection	Multidose 2.5 mL vial	5 doses of 0.5 mL each or a maximum of 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax XBB.1.5 50 mcg dispersion for injection	Single-dose 0.5 mL vial	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax XBB.1.5 50 mcg dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax XBB.1.5 25 mcg dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.25 mL For single-use only.	One dose (0.25 mL) contains 25 micrograms of andusomeran, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).

Andusomeran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron XBB.1.5).

The other ingredients are SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate), cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

What Spikevax XBB.1.5 looks like and contents of the pack

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection

Spikevax XBB.1.5 is a white to off white dispersion supplied in a glass multidose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax XBB.1.5 50 micrograms dispersion for injection

Spikevax XBB.1.5 is a white to off white dispersion supplied in a glass single-dose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack sizes:
1 single-dose vial
10 single-dose vials
Each vial contains 0.5 mL.

Not all pack sizes may be marketed.

Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe and Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe

Spikevax XBB.1.5 is a white to off white dispersion supplied in a pre-filled syringe (cyclic olefin copolymer) with plunger stopper and a tip cap (without needle).

The pre-filled syringe is packaged in a paper inner tray within a carton or in 1 clear blister containing 1 pre-filled syringe or 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack sizes:
1 pre-filled syringe
10 pre-filled syringes

Not all pack sizes may be marketed.

Marketing Authorisation Holder

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

Manufacturers

Rovi Pharma Industrial Services, S.A.

Paseo de Europa, 50
28703. San Sebastián de los Reyes
Madrid
Spain

Moderna Biotech Spain S.L.
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28037 Madrid
Spain

Rovi Pharma Industrial Services, S.A.
Calle Julián Camarillo n°35
28037 Madrid
Spain

Patheon Italia S.p.A.
2 Trav. SX Via Morolense 5
03013 Ferentino (FR)
Italy

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Ireland
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Lietuva
Tel: 88 003 1114

Luxembourg/Luxemburg
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Magyarország
Tel: 06 809 87488

Malta
Tel: 8006 5066

Nederland
Tel: 0800 409 0001

Norge
Tlf: 800 31 401

Österreich
Tel: 0800 909636

Polska
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Portugal
Tel: 800 210 256

România
Tel: 0800 400 625

Slovenija
Tel: 080 083082

Slovenská republika

Sími: 800 4382

Italia
Tel: 800 928 007

Κύπρος
Τηλ: 80091080

Latvija
Tel: 80 005 898

Tel: 0800 191 647

Suomi/Finland
Puh/Tel: 0800 774198

Sverige
Tel: 020 10 92 13

This leaflet was last revised in

Scan the code with a mobile device to get the package leaflet in different languages.

Or visit the URL https://www.ModernaCovid19Global.com

Detailed information on this vaccine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Spikevax XBB.1.5 should be administered by a trained healthcare professional.

The vaccine comes ready to use once thawed.

Do not shake or dilute.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration.

Spikevax XBB.1.5 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.

Frozen vaccine
Vials are stored in a freezer at -50ºC to -15ºC.

Spikevax XBB.1.5 0.1 mg/mL dispersion for injection (multidose vials with a blue flip-off cap)

Five (5) doses (of 0.5 mL each) or a maximum of ten (10) doses (0.25 mL each) can be withdrawn from each multidose vial.

Pierce the stopper preferably at a different site each time.

Verify that the vial has a blue flip-off cap and the product name is Spikevax XBB.1.5. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL, Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

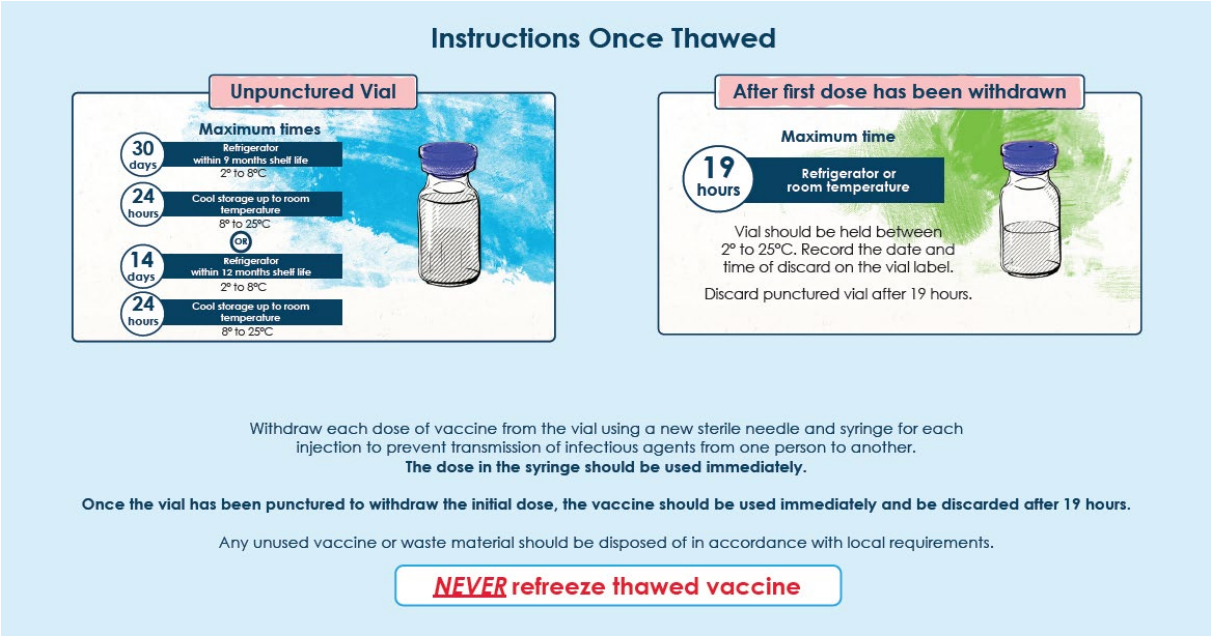
Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each multidose vial before use following the instructions below (Table 4).

Table 4. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C.



<u>Spikevax XBB.1.5 50 micrograms dispersion for injection (single-dose vials)</u>

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax XBB.1.5. If the vial has a

blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 1 or 10 vials may be thawed either in the refrigerator or at room temperature (Table 5).

Table 5. Thawing instructions for single-dose vials and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C.

Spikevax XBB.1.5 50 micrograms dispersion for injection in pre-filled syringe and Spikevax XBB.1.5 25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.25 mL or 0.5 mL can be administered from each pre-filled syringe, depending on labelled syringe volume. Do not use the 0.5 mL pre-filled syringe to administer a 0.25 mL dose.

Spikevax XBB.1.5 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.25 mL (25 micrograms of andusomeran) or 0.5 mL (50 micrograms of andusomeran) mRNA and must be thawed prior to administration.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 1 or 2 pre-filled syringes, depending on pack size) or in the carton itself, either in the refrigerator or at room temperature (Table 6).

Table 6. Thawing instructions for Spikevax XBB.1.5 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Pre-filled syringe transport duration is limited by the shipper qualification duration.

Verify that the product name of the pre-filled syringe is Spikevax XBB.1.5. If the product name is Spikevax 50 micrograms, Spikevax bivalent Original/Omicron BA.1 or Spikevax bivalent Original/Omicron BA.4-5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax XBB.1.5 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- After thawing, do not refreeze.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosing and schedule

Table 7. Spikevax XBB.1.5 dosing

Age(s)	Dose	Additional recommendations
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of Spikevax, one dose of Spikevax XBB.1.5 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax XBB.1.5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the 0.5 mL single-dose vial or 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 8. Spikevax XBB.1.5 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the 0.5 mL single-dose vial or 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Spikevax XBB.1.5.

Individuals should be observed by a healthcare professional for at least 15 minutes after vaccination.

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

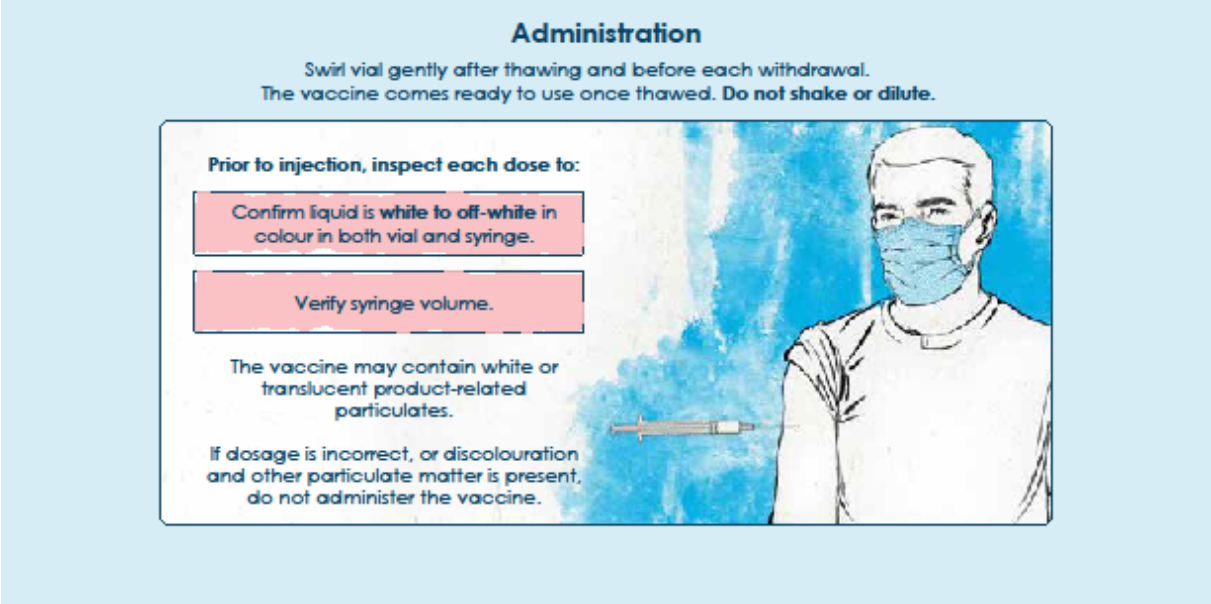
Different injectable vaccines should be given at different injection sites.

Spikevax XBB.1.5 must not be mixed with other vaccines or medicinal products in the same syringe.

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Pre-filled syringes

Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner). With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Uncap the needle when ready for administration. Administer the entire dose intramuscularly. Discard syringe after use. For single-use only.

Package leaflet: Information for the user

Spikevax JN.1 0.1 mg/mL dispersion for injection
Spikevax JN.1 50 micrograms dispersion for injection
Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Spikevax JN.1 is and what it is used for

Spikevax JN.1 is a vaccine used to prevent COVID-19 caused by SARS-CoV-2. It is given to adults and children aged 6 months and older. The active substance in Spikevax JN.1 is mRNA encoding the SARS-CoV-2 spike protein. The mRNA is embedded in SM-102 lipid nanoparticles.

As Spikevax JN.1 does not contain the virus, it cannot give you COVID-19.

How the vaccine works
Spikevax JN.1 stimulates the body's natural defences (immune system). The vaccine works by causing the body to produce protection (antibodies) against the virus that causes COVID-19. Spikevax JN.1 uses a substance called messenger ribonucleic acid (mRNA) to carry instructions that cells in the body can use to make the spike protein that is also on the virus. The cells then make antibodies against the spike protein to help fight off the virus. This will help to protect you against COVID-19.

2. What you need to know before you are given Spikevax JN.1

The vaccine must not be given if you are **allergic** to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Spikevax JN.1 if:

- you have previously had a severe, life-threatening **allergic** reaction after any other vaccine injection or after you were given Spikevax (original) in the past.
- you have a very weak or compromised immune system

- you have ever fainted following any needle injection.
- you have a bleeding disorder
- you have a high fever or severe infection; however, you can have your vaccination if you have a mild fever or upper airway infection like a cold
- you have any serious illness
- if you have anxiety related to injections

There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) after vaccination with Spikevax (see section 4).

These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose.

Most cases of myocarditis and pericarditis recover. Some cases required intensive care support and fatal cases have been seen.

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Spikevax JN.1.

Capillary leak syndrome (CLS) flare-ups
A few cases of capillary leak syndrome flare-ups (causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint, low blood pressure) have been reported following vaccination with Spikevax (original). If you have previously had episodes of CLS, talk to a doctor before you are given Spikevax JN.1.

Duration of protection
As with any vaccine, the additional dose of Spikevax JN.1 may not fully protect all those who receive it and it is not known how long you will be protected.

Children
Spikevax JN.1 is not recommended for children aged under 6 months.

Other medicines and Spikevax JN.1
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Spikevax JN.1 may affect the way other medicines work, and other medicines may affect how Spikevax JN.1 works.

Immunocompromised individuals
The efficacy of Spikevax JN.1 may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Pregnancy and breast-feeding
If you are pregnant or think you may be pregnant, tell your doctor, nurse or pharmacist before you receive this vaccine. No data are available yet regarding the use of Spikevax JN.1 during pregnancy. However, a large amount of information from pregnant women vaccinated with Spikevax (original) during the second and third trimester have not shown negative effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no increased risk for miscarriage has been seen. Since differences between the two products are only related to the spike protein in the vaccine, and there are no clinically meaningful differences, Spikevax JN.1 can be used during pregnancy.

No data are available yet regarding the use of Spikevax JN.1 during breast feeding.

However, no effects on the breastfed newborn/infant are anticipated. Data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax JN.1 can be given during breastfeeding.

Driving and using machines
Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Spikevax JN.1 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How you will be given Spikevax JN.1

Table 1. Spikevax JN.1 posology

Age(s)	Dose	Additional recommendations
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of any Spikevax vaccine, one dose of Spikevax JN.1 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax JN.1 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 2. Spikevax JN.1 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations

Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.

After each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least **15 minutes** to monitor for signs of an allergic reaction.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:
- feeling faint or light-headed;
- changes in your heartbeat;
- shortness of breath;
- wheezing;
- swelling of your lips, face, or throat;
- hives or rash;
- nausea or vomiting;
- stomach pain.

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common (may affect more than 1 in 10 people):
- swelling/tenderness in the underarm
- decreased appetite (observed in 6 month to 5 year olds)
- irritability/crying (observed in 6 month to 5 year olds)
- headache
- sleepiness (observed in 6 month to 5 year olds)
- nausea
- vomiting
- muscle ache, joint aches, and stiffness

- pain or swelling at the injection site
- redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)
- feeling very tired
- chills
- fever

Common (may affect up to 1 in 10 people):
- diarrhoea
- rash
- rash or hives at the injection site (some of which may occur approximately 9 to 11 days after the injection)

Uncommon (may affect up to 1 in 100 people):
- itchiness at the injection site
- dizziness
- stomach pain
- raised, itchy rash (urticaria) (which may occur from the time of injection and up to approximately two weeks after the injection)

Rare (may affect up to 1 in 1 000 people)
- temporary one-sided facial drooping (Bell's palsy)
- swelling of the face (swelling of the face may occur in individuals who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

Very rare (may affect up to 1 in 10 000 people)
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain

Frequency not known
- severe allergic reactions with breathing difficulties (anaphylaxis)
- reaction of increased sensitivity or intolerance by the immune system (hypersensitivity)
- a skin reaction that causes red spots or patches on the skin that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme)
- extensive swelling of the vaccinated limb
- heavy menstrual bleeding (most cases appeared to be non-serious and temporary in nature)
- rash elicited by external stimulus such as firm stroking, scratching, or pressure to the skin (mechanical urticaria)
- raised, itchy rash with a duration of more than six weeks (chronic urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this vaccine.

5. How to store Spikevax JN.1

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Information about storage, expiry, and use and handling are described in the section intended for healthcare professionals at the end of the package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Spikevax JN.1 contains

Table 3. Composition by container type

Strength	Container	Dose(s)	Composition
Spikevax JN.1 0.1 mg/mL dispersion for injection	Multidose 2.5 mL vial	5 doses of 0.5 mL each or a maximum of 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 JN.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of SARS-CoV-2 JN.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax JN.1 50 mcg dispersion for injection	Single-dose 0.5 mL vial	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 JN.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).

SARS-CoV-2 JN.1 mRNA is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (JN.1).

The other ingredients are SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate), cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

What Spikevax JN.1 looks like and contents of the pack

Spikevax JN.1 0.1 mg/mL dispersion for injection

Spikevax JN.1 is a white to off white dispersion supplied in a glass multidose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax JN.1 50 micrograms dispersion for injection

Spikevax JN.1 is a white to off white dispersion supplied in a glass single-dose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack sizes:
1 single-dose vial
10 single-dose vials
Each vial contains 0.5 mL.

Not all pack sizes may be marketed.

Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe

Spikevax JN.1 is a white to off white dispersion supplied in a pre-filled syringe (cyclic olefin copolymer) with plunger stopper and a tip cap (without needle).

The pre-filled syringe is packaged in a paper inner tray within a carton or in 1 clear blister containing 1 pre-filled syringe or 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack sizes:
1 pre-filled syringe
10 pre-filled syringes

Not all pack sizes may be marketed.

Marketing Authorisation Holder

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

Manufacturers

Rovi Pharma Industrial Services, S.A.
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Moderna Biotech Spain S.L.
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Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Latvija
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Lietuva
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Luxembourg/Luxemburg
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Malta
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Nederland
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Norge
Tlf: 800 31 401

Österreich
Tel: 0800 909636

Polska
Tel: 800 702 406

Portugal
Tel: 800 210 256

România
Tel: 0800 400 625

Slovenija
Tel: 080 083082

Slovenská republika
Tel: 0800 191 647

Suomi/Finland
Puh/Tel: 0800 774198

Sverige
Tel: 020 10 92 13

This leaflet was last revised in

Scan the code with a mobile device to get the package leaflet in different languages.

Or visit the URL https://www.ModernaCovid19Global.com

Detailed information on this vaccine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Spikevax JN.1 should be administered by a trained healthcare professional.

The vaccine comes ready to use once thawed.

Do not shake or dilute.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration.

Spikevax JN.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.

Frozen vaccine
Vials are stored in a freezer at -50ºC to -15ºC.

Spikevax JN.1 0.1 mg/mL dispersion for injection (multidose vials with a blue flip-off cap)

Five (5) doses (of 0.5 mL each) or a maximum of ten (10) doses (0.25 mL each) can be withdrawn from each multidose vial.

Pierce the stopper preferably at a different site each time.

Verify that the vial has a blue flip-off cap and the product name is Spikevax JN.1. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 or Spikevax XBB.1.5, please make reference to the Summary of Product Characteristics for that formulation.

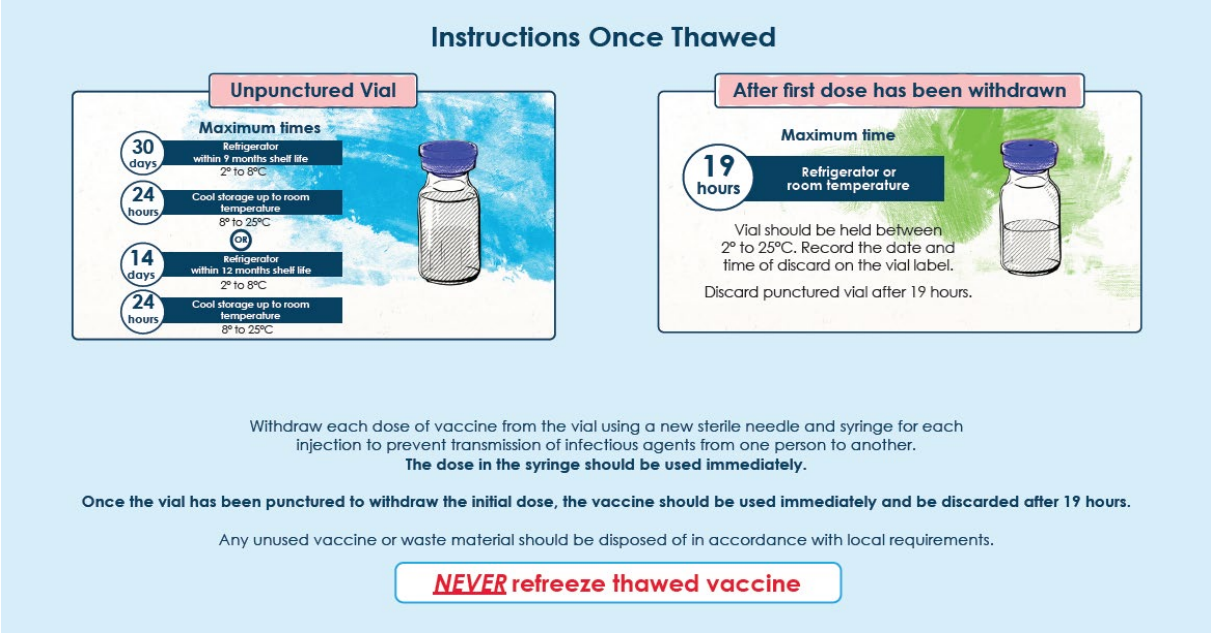
Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each multidose vial before use following the instructions below (Table 4).

Table 4. Thawing instructions for multidose vials before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C.



Spikevax JN.1 50 micrograms dispersion for injection (single-dose vials)

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before withdrawal.

Verify that the vial has a blue flip-off cap and the product name is Spikevax JN.1. If the vial has a blue flip-off cap and the product name is Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 or Spikevax XBB.1.5, please make reference to the Summary of Product Characteristics for that formulation.

Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each single-dose vial before use following the instructions below. Each single-dose vial or the carton containing 1 or 10 vials may be thawed either in the refrigerator or at room temperature (Table 5).

Table 5. Thawing instructions for single-dose vials and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Single-dose vial	2°C to 8°C	45 minutes	15°C to 25°C	15 minutes

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator)	Thaw duration	Thaw temperature (at room temperature)	Thaw duration
Carton	2°C to 8°C	1 hour 45 minutes	15°C to 25°C	45 minutes

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C.

Spikevax JN.1 50 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax JN.1 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (50 micrograms of SARS-CoV-2 JN.1 mRNA) and must be thawed prior to administration.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 1 or 2 pre-filled syringes, depending on pack size) or in the carton itself, either in the refrigerator or at room temperature (Table 6).

Table 6. Thawing instructions for Spikevax JN.1 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Pre-filled syringe transport duration is limited by the shipper qualification duration.

Verify that the product name of the pre-filled syringe is Spikevax JN.1. If the product name is Spikevax 50 micrograms, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5 or Spikevax XBB.1.5, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the pre-filled syringes
- Do not shake.

- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax JN.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- After thawing, do not refreeze.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosing and schedule

Table 7. Spikevax JN.1 dosing

Age(s)	**Dose**	**Additional recommendations**
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of Spikevax, one dose of Spikevax JN.1 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax JN.1 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

Age(s)	Dose	Additional recommendations
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 8. Spikevax JN.1 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the single-dose vial or pre-filled syringe to deliver a partial volume of 0.25 mL.

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Spikevax JN.1.

Individuals should be observed by a healthcare professional for at least 15 minutes after vaccination.

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

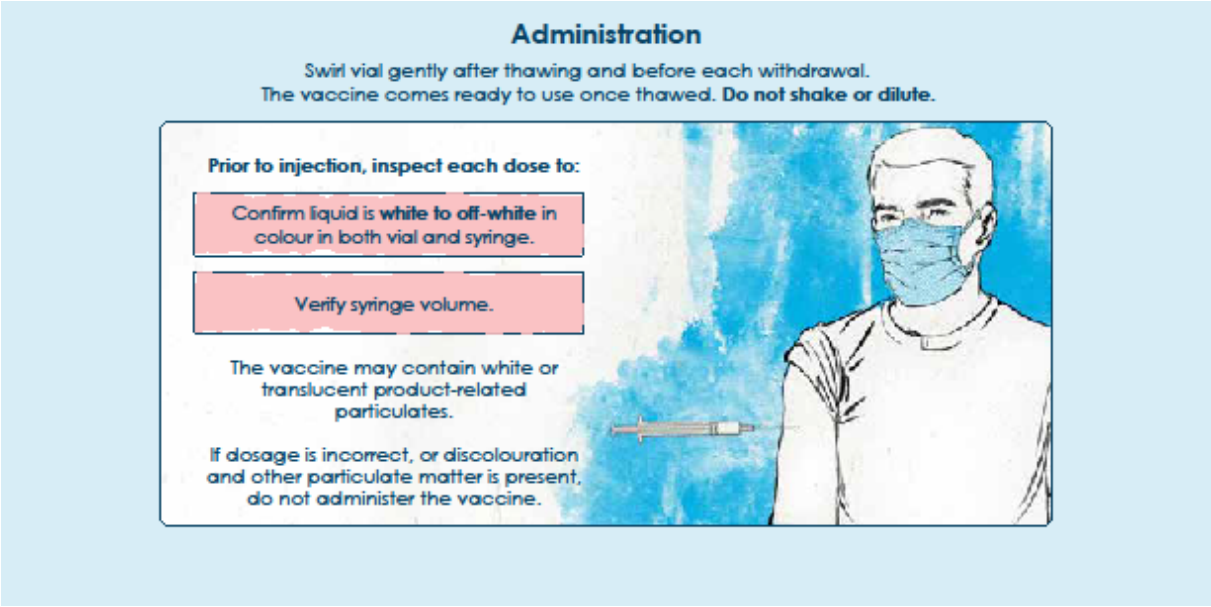
Different injectable vaccines should be given at different injection sites.

Spikevax JN.1 must not be mixed with other vaccines or medicinal products in the same syringe.

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Pre-filled syringes

Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner). With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Uncap the needle when ready for administration. Administer the entire dose intramuscularly. Discard syringe after use. For single-use only.

Package leaflet: Information for the user

Spikevax LP.8.1 0.1 mg/mL dispersion for injection
Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe
Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe
COVID-19 mRNA Vaccine

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Spikevax LP.8.1 is and what it is used for

Spikevax LP.8.1 is a vaccine used to prevent COVID-19 caused by SARS-CoV-2. It is given to adults and children aged 6 months and older. The active substance in Spikevax LP.8.1 is mRNA encoding the SARS-CoV-2 spike protein. The mRNA is embedded in SM-102 lipid nanoparticles.

As Spikevax LP.8.1 does not contain the virus, it cannot give you COVID-19.

How the vaccine works
Spikevax LP.8.1 stimulates the body's natural defences (immune system). The vaccine works by causing the body to produce protection (antibodies) against the virus that causes COVID-19. Spikevax LP.8.1 uses a substance called messenger ribonucleic acid (mRNA) to carry instructions that cells in the body can use to make the spike protein that is also on the virus. The cells then make antibodies against the spike protein to help fight off the virus. This will help to protect you against COVID-19.

2. What you need to know before you are given Spikevax LP.8.1

The vaccine must not be given if you are **allergic** to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Spikevax LP.8.1 if:

- you have previously had a severe, life-threatening **allergic** reaction after any other vaccine injection or after you were given Spikevax (original) in the past.
- you have a very weak or compromised immune system

- you have ever fainted following any needle injection.
- you have a bleeding disorder
- you have a high fever or severe infection; however, you can have your vaccination if you have a mild fever or upper airway infection like a cold
- you have any serious illness
- if you have anxiety related to injections

There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) after vaccination with Spikevax (see section 4).

These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often in younger males, and more often after the second dose compared to the first dose.

Most cases of myocarditis and pericarditis recover. Some cases required intensive care support and fatal cases have been seen.

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Spikevax LP.8.1.

Capillary leak syndrome (CLS) flare-ups
A few cases of capillary leak syndrome flare-ups (causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint, low blood pressure) have been reported following vaccination with Spikevax (original). If you have previously had episodes of CLS, talk to a doctor before you are given Spikevax LP.8.1.

Duration of protection
As with any vaccine, the additional dose of Spikevax LP.8.1 may not fully protect all those who receive it and it is not known how long you will be protected.

Children
Spikevax LP.8.1 is not recommended for children aged under 6 months.

Other medicines and Spikevax LP.8.1
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Spikevax LP.8.1 may affect the way other medicines work, and other medicines may affect how Spikevax LP.8.1 works.

Immunocompromised individuals
The efficacy of Spikevax LP.8.1 may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

Pregnancy and breast-feeding
If you are pregnant or think you may be pregnant, tell your doctor, nurse or pharmacist before you receive this vaccine. No data are available yet regarding the use of Spikevax LP.8.1 during pregnancy. However, a large amount of information from pregnant women vaccinated with Spikevax (original) during the second and third trimester have not shown negative effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no increased risk for miscarriage has been seen. Since differences between the two products are only related to the spike protein in the vaccine, and there are no clinically meaningful differences, Spikevax LP.8.1 can be used during pregnancy.

No data are available yet regarding the use of Spikevax LP.8.1 during breast feeding.

However, no effects on the breastfed newborn/infant are anticipated. Data from women who were breastfeeding after vaccination with Spikevax (original) have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax LP.8.1 can be given during breastfeeding.

Driving and using machines
Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Spikevax LP.8.1 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How you will be given Spikevax LP.8.1

Table 1. Spikevax LP.8.1 posology

Age(s)	Dose	Additional recommendations
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of any Spikevax vaccine, one dose of Spikevax LP.8.1 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	Spikevax LP.8.1 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 2. Spikevax LP.8.1 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations

Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.

After each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least **15 minutes** to monitor for signs of an allergic reaction.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:
- feeling faint or light-headed;
- changes in your heartbeat;
- shortness of breath;
- wheezing;
- swelling of your lips, face, or throat;
- hives or rash;
- nausea or vomiting;
- stomach pain.

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common (may affect more than 1 in 10 people):
- swelling/tenderness in the underarm
- decreased appetite (observed in 6 month to 5 year olds)
- irritability/crying (observed in 6 month to 5 year olds)
- headache
- sleepiness (observed in 6 month to 5 year olds)
- nausea
- vomiting
- muscle ache, joint aches, and stiffness
- pain or swelling at the injection site

- redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)
- feeling very tired
- chills
- fever

Common (may affect up to 1 in 10 people):
- diarrhoea
- rash
- rash or hives at the injection site (some of which may occur approximately 9 to 11 days after the injection)

Uncommon (may affect up to 1 in 100 people):
- itchiness at the injection site
- dizziness
- stomach pain
- raised, itchy rash (urticaria) (which may occur from the time of injection and up to approximately two weeks after the injection)

Rare (may affect up to 1 in 1 000 people)
- temporary one-sided facial drooping (Bell's palsy)
- swelling of the face (swelling of the face may occur in individuals who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

Very rare (may affect up to 1 in 10 000 people)
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain

Frequency not known
- severe allergic reactions with breathing difficulties (anaphylaxis)
- reaction of increased sensitivity or intolerance by the immune system (hypersensitivity)
- a skin reaction that causes red spots or patches on the skin that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (erythema multiforme)
- extensive swelling of the vaccinated limb
- heavy menstrual bleeding (most cases appeared to be non-serious and temporary in nature)
- rash elicited by external stimulus such as firm stroking, scratching, or pressure to the skin (mechanical urticaria)
- raised, itchy rash with a duration of more than six weeks (chronic urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this vaccine.

5. How to store Spikevax LP.8.1

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Information about storage, expiry, and use and handling are described in the section intended for

healthcare professionals at the end of the package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Spikevax LP.8.1 contains

Table 3. Composition by container type

Strength	Container	Dose(s)	Composition
Spikevax LP.8.1 0.1 mg/mL dispersion for injection	Multidose 2.5 mL vial	5 doses of 0.5 mL each or a maximum of 10 doses of 0.25 mL each	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles). One dose (0.25 mL) contains 25 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax LP.8.1 50 mcg dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.5 mL For single-use only.	One dose (0.5 mL) contains 50 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).
Spikevax LP.8.1 25 mcg dispersion for injection in pre-filled syringe	Pre-filled syringe	1 dose of 0.25 mL For single-use only.	One dose (0.25 mL) contains 25 micrograms of SARS-CoV-2 LP.8.1 mRNA, a COVID-19 mRNA Vaccine (nucleoside modified) (embedded in SM-102 lipid nanoparticles).

SARS-CoV-2 LP.8.1 mRNA is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (LP.8.1).

The other ingredients are SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate), cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), trometamol, trometamol hydrochloride, acetic acid, sodium acetate trihydrate, sucrose, water for injections.

What Spikevax LP.8.1 looks like and contents of the pack

Spikevax LP.8.1 0.1 mg/mL dispersion for injection

Spikevax LP.8.1 is a white to off white dispersion supplied in a glass multidose vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials. Each vial contains 2.5 mL.

Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe and Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe

Spikevax LP.8.1 is a white to off white dispersion supplied in a pre-filled syringe (cyclic olefin copolymer) with plunger stopper and a tip cap (without needle).

The pre-filled syringe is packaged in a paper inner tray within a carton or in 1 clear blister containing 1 pre-filled syringe or 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack sizes:
1 pre-filled syringe
10 pre-filled syringes

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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This leaflet was last revised in

Scan the code with a mobile device to get the package leaflet in different languages.

Or visit the URL https://www.ModernaCovid19Global.com

Detailed information on this vaccine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Spikevax LP.8.1 should be administered by a trained healthcare professional.

The vaccine comes ready to use once thawed.

Do not shake or dilute.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration.

Spikevax LP.8.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.

Frozen vaccine
Vials are stored in a freezer at -50ºC to -15ºC.

Spikevax LP.8.1 0.1 mg/mL dispersion for injection (multidose vials with a blue flip-off cap)

Five (5) doses (of 0.5 mL each) or a maximum of ten (10) doses (0.25 mL each) can be withdrawn from each multidose vial.

Pierce the stopper preferably at a different site each time.

Verify that the vial has a blue flip-off cap and the product name is Spikevax LP.8.1. If the vial has a blue flip-off cap and the product name is Spikevax 0.1 mg/mL, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, Spikevax XBB.1.5 or Spikevax JN.1, please make reference to the Summary of Product Characteristics for that formulation.

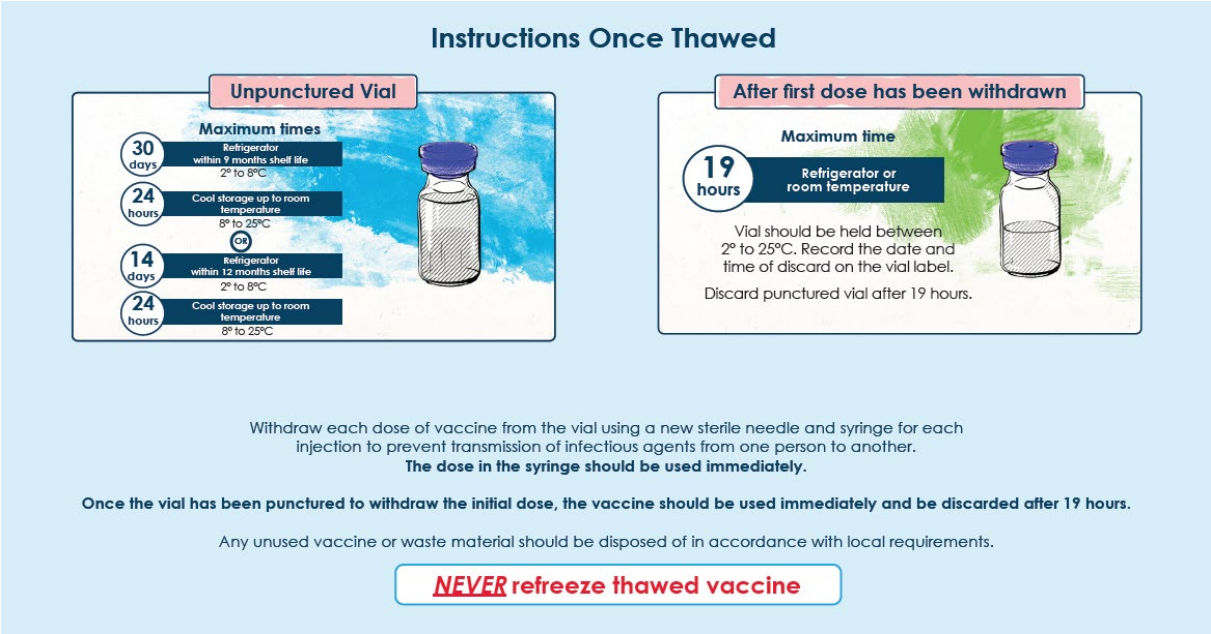
Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each multidose vial before use following the instructions below (Table 4).

Table 4. Thawing instructions for multidose vials before use

Configuration	**Thaw instructions and duration**			
	Thaw temperature (in a refrigerator)	**Thaw duration**	**Thaw temperature (at room temperature)**	**Thaw duration**
Multidose vial	2° – 8°C	2 hours and 30 minutes	15°C – 25°C	1 hour

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Within this period, up to 36 hours may be used for transportation at 2°C to 8°C.



Spikevax LP.8.1 50 micrograms dispersion for injection in pre-filled syringe and Spikevax LP.8.1 25 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.25 mL or 0.5 mL can be administered from each pre-filled syringe, depending on labelled syringe volume. Do not use the 0.5 mL pre-filled syringe to administer a 0.25 mL dose.

Spikevax LP.8.1 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.25 mL (25 micrograms of SARS-CoV-2 LP.8.1 mRNA) or 0.5 mL (50 micrograms of SARS-CoV-2 LP.8.1 mRNA) and must be thawed prior to administration.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thawed vaccine
The vaccine is shipped and supplied frozen or thawed. If the vaccine is frozen, thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 1 or 2 pre-filled syringes, depending on pack size) or in the carton itself, either in the refrigerator or at room temperature (Table 5).

Table 5. Thawing instructions for Spikevax LP.8.1 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Pre-filled syringe in blister pack	2 – 8	55	15 – 25	45
Carton	2 – 8	155	15 – 25	140

If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been marked with the new discard date at 2°C to 8°C.

Pre-filled syringe transport duration is limited by the shipper qualification duration.

Verify that the product name of the pre-filled syringe is Spikevax LP.8.1. If the product name is Spikevax 50 micrograms, Spikevax bivalent Original/Omicron BA.1, Spikevax bivalent Original/Omicron BA.4-5, Spikevax XBB.1.5 or Spikevax JN.1, please make reference to the Summary of Product Characteristics for that formulation.

Handling instructions for the pre-filled syringes

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Spikevax LP.8.1 is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- After thawing, do not refreeze.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosing and schedule

Table 6. Spikevax LP.8.1 dosing

Age(s)	**Dose**	**Additional recommendations**
Children 6 months through 4 years of age, without prior vaccination and no known history of SARS-CoV-2 infection	Two doses of 0.25 mL each, given intramuscularly*	Administer the second dose 28 days after the first dose. If a child has received one prior dose of Spikevax, one dose of Spikevax LP.8.1 should be administered to complete the two-dose series.
Children 6 months through 4 years of age, with prior vaccination or known history of SARS-CoV-2 infection	One dose of 0.25 mL, given intramuscularly*	

Age(s)	Dose	Additional recommendations
Children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	Spikevax LP.8.1 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.
Individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	
Individuals 65 years of age and older	One dose of 0.5 mL, given intramuscularly	One additional dose may be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

* Do not use the 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

Table 7. Spikevax LP.8.1 posology for immunocompromised individuals

Age(s)	Dose	Additional recommendations
Immunocompromised children 6 months through 4 years of age, without prior vaccination	Two doses of 0.25 mL, given intramuscularly*	A third dose in severely immunocompromised may be given at least 28 days after the second dose.
Immunocompromised children 6 months through 4 years of age, with prior vaccination	One dose of 0.25 mL, given intramuscularly*	Additional age-appropriate dose(s) may be administered in severely immunocompromised at least 2 months following the most recent dose of a COVID-19 vaccine at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.
Immunocompromised children 5 years through 11 years of age, with or without prior vaccination	One dose of 0.25 mL, given intramuscularly*	
Immunocompromised individuals 12 years of age and older, with or without prior vaccination	One dose of 0.5 mL, given intramuscularly	

* Do not use the 0.5 mL pre-filled syringe to deliver a partial volume of 0.25 mL.

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Spikevax LP.8.1.

Individuals should be observed by a healthcare professional for at least 15 minutes after vaccination.

Spikevax (including variant formulations) can be concomitantly administered with influenza vaccines (standard and high-dose) and with herpes zoster (shingles) subunit vaccine.

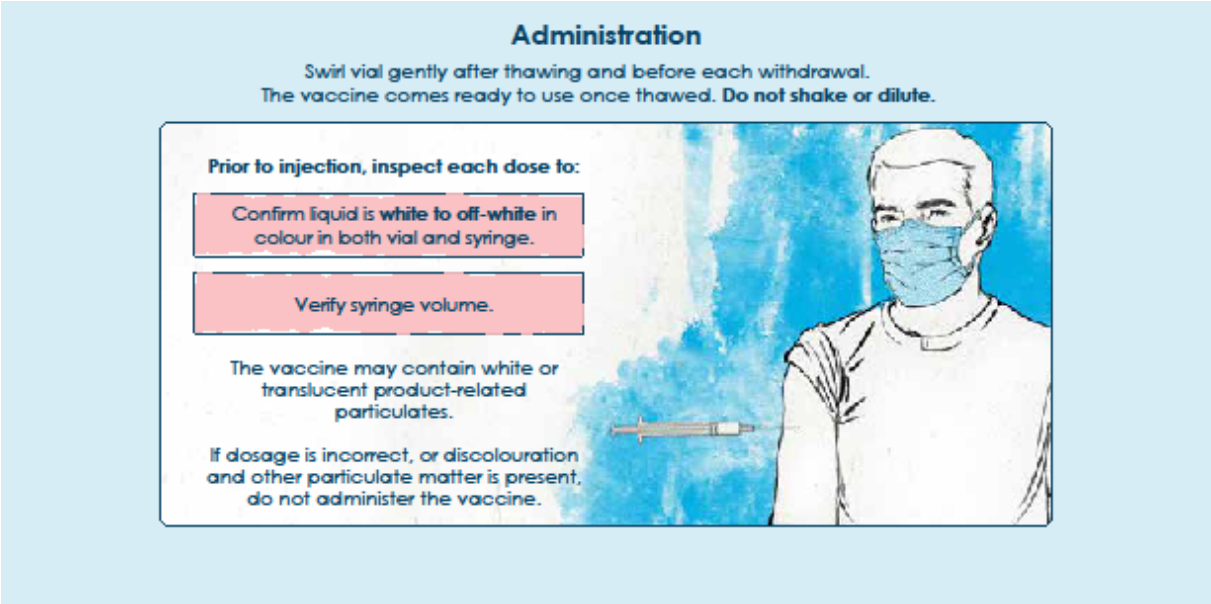
Different injectable vaccines should be given at different injection sites.

Spikevax LP.8.1 must not be mixed with other vaccines or medicinal products in the same syringe.

Administration

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

Multidose vials



Pre-filled syringes

Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner). With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Uncap the needle when ready for administration. Administer the entire dose intramuscularly. Discard syringe after use. For single-use only.