1. NAME OF THE MEDICINAL PRODUCT

Spikevax XBB.1.5
Spikevax XBB.1.5 50 micrograms dispersion for injection
COVID-19 mRNA Vaccine (nucleoside modified)

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 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).

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 disease caused by SARS-CoV-2 in individuals 12 years of age and older (see sections 4.2 and 5.2).

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
Individuals 12 years of age and older	One dose of 0.5 mL, given intramuscularly	Spikevax XBB.1.5 should be administered in accordance with official recommendations.

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

Paediatric population
The safety and efficacy of Spikevax XBB.1.5 in children less than 6 months of age have not yet been established. No data are available.

Elderly population
No dosage 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 medicaltreatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Individuals should be observed by a healthcare professional post-vaccination in accordance with the local official recommendations.

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 more often after the second dose compared to the first dose, and more often, but not exclusively in younger males (see section 4.8). There have been reports in females.

Available data indicate that most cases are typically mild and individuals tend to recover within a short time following standard treatment and rest. Some cases required intensive care support. Although causality has not been established, fatal events have been very rarely reported. Local cases of myocarditis with severe outcomes have been rarely reported with strenuous physical activity following vaccination.

Post-authorization data also indicate that myocarditis and pericarditis following vaccination is generally of shorter duration and less severe than infectious myocarditis or pericarditis. Information is not yet available about potential long-term sequelae.

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. Non-specific symptoms of myocarditis and pericarditis also include fatigue, nausea and vomiting, abdominal pain, dizziness or syncope, oedema and cough.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. Please refer to the national vaccination guidances for local recommendations.

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.

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.

Immunocompromised individuals

The effectiveness and immunogenicity of the vaccine have been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy and may be lower (see sections 4.8 and 5.1).
The recommendation to consider an additional dose in severely immunocompromised individuals (see section 4.2) is based on serological evidence with individuals who are immunocompromised after solid organ transplantation (see sections 4.8 and 5.1).

Additional doses may be administered to individuals who are severely immunocompromised in accordance with official recommendations.

Duration of protection

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

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 0.5 mL dose, that is to say essentially‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Other vaccines

Influenza vaccines can be concomitantly administered with Spikevax (including variant formulations) (see section 5.1).

The herpes zoster (shingles) vaccine can be concomitantly administered with Spikevax (including variant formulations) (see section 5.1).

4.6 Fertility, pregnancy and lactation

Pregnancy

No data are available yet regarding the use of Spikevax XBB.1.5 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).

Breast-feeding

No data are available yet regarding the use of Spikevax XBB.1.5 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.

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 XBB.1.5 has no or negligible influence on the ability to drive and use machines. However, some ofthe 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

Participants 18 years of age and older

The safety of Spikevax was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical trial 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 and7,520 (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 conducted in the United States involving 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%).

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 trial conducted in the United States and Canada (NCT04796896) that included data in 4,002 participants 6 through 11 years of age who received at least one dose (50 micrograms) of Spikevax (n=3,007) or placebo (n=995). As of the data cut-off date of 10 November 2021, the median duration of blinded follow-up for safety was 51 days after Dose 2, and 1,284 participants had been followed for at least 2 months after Dose 2 (vaccine=1,006, placebo=218). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

The most frequent adverse reactions in participants 6 through 11 years of age following administration of the primary series 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%).

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 effectiveness 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 through 11 years; 2 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=4,792) or placebo (n=1,596). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

In this clinical study, the adverse reactions in participants 6 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%).

In participants 6 months through 23 months of age who received the vaccine, a 1-year-old female experienced serious adverse events of a grade 3 fever 6 hours after dose 1 and a febrile convulsion 1 day after dose 1. These events were considered related to vaccination.

In a clinical study, 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%).

In a clinical study, 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 participants 12 through 17 years of age;
- 4,002 participants 6 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 trials and post authorisation experience in 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	Rare	Anaphylaxis
	Not known	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
	Not known	Cerebral venous thrombosis
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Uncommon	Abdominal pain****
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Acute and delayed urticaria*****
	Not known	Erythema multiforme Mechanical urticaria Chronic urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
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********

*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site.
** 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.
***** Includes both acute and delayed urticaria; the frequency category was rare.
****** 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.

Participants 18 years of age and older (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 (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 (50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (50 micrograms) was similar to that after the second dose in the primary series.

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 (XBB.1.5 / Omicron 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. There were no Grade 4 local or systemic reactions and no fatal events or serious adverse events in this interim analysis. 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).

Spikevax (original) as a three-dose primary series and fourth (booster) dose was well tolerated with an acceptable safety profile in SOT recipients. 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.

Adverse Event Reporting to HSA

Healthcare professionals are required to report any suspected serious adverse events observed with the use of Spikevax to HSA as soon as possible. All fatal and life-threatening events are to be reported as soon as possible, within 24 hours. Please report the adverse events to the Vigilance and Compliance Branch at Tel: 6866 1111 or report online at https://www.hsa.gov.sg/adverse-events.

4.9 Overdose

No case of overdose has been reported.

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.

The nucleoside-modified mRNA in Spikevax XBB.1.5 (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.

5.2 Clinical studies

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 mRNA of the Omicron XBB.1.5 spike protein) 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 vaccine (mRNA-1273- P205, Part J). The two groups were randomised 1:1 in an open-label fashion.
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.

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.

Clinical efficacy in adults
The randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) 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). 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 – Per-Protocol Set

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 interimanalysis 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.

Additional efficacy analyses

Subgroup analyses of vaccine efficacy 14 days after Dose 2 can be found in Table 5.

Table 5. Subgroup analyses of vaccine efficacy - COVID-19 14 days after Dose 2 per adjudication committee assessments (primary efficacy analysis set) – per-protocol set

Subgroup	Spikevax	Placebo	% Vaccine

	Participants N	**COVID-19 cases n**	**Incidence rate of COVID-19 per 1,000 person-years**	**Participants N**	**COVID-19 cases n**	**Incidence rate of COVID-19 per 1,000 person-years**	**efficacy (95% CI)****
Overall At risk*	3,206	4	5.227	3,167	43	57.202	90.9 (74.7, 96.7)
At risk 18 to <65	2,155	2	3.947	2,118	35	70.716	94.4 (76.9, 98.7)
Not At risk 18 to <65	8,396	5	2.594	8,403	121	63.054	95.9 (90.0,98.3)
Females	6,768	7	4.364	6,611	98	62.870	93.1 (85.2,96.8)
Males	7,366	4	2.352	7,462	87	50.730	95.4 (87.4,98.3)

* Participants at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease or HIV infection), regardless of age
** VE and 95% CI from the stratified Cox proportional hazard model

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

A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titers 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 titers 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.

Clinical efficacy in children 6 through 11 years of age

The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical trial to evaluate the safety, reactogenicity, and effectiveness of Spikevax in children ages 6 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 4,011 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 (50 micrograms 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 titers 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 titers 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.

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 effectiveness 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 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 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” was 46.4% (95% CI: 19.8, 63.8) for children 2 through 5 years of age and 31.5% (95% CI: -27.7, 62.0) for children 6 months through 23 months of age.

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 “CDC case definition” was 36.8% (95% CI: 12.5, 54.0) for children 2 through 5 years of age and 50.6% (95% CI: 21.4, 68.6) for children 6 months through 23 months of age.

Immunogenicity in children 6 months through 5 years of age

For children aged 23 months 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 adolescents 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 adolescents 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 effectiveness of 25 micrograms to be inferred in both children 2 years through 5 years and infants and toddlers aged 6 months through 23 months.

Immunogenicity in participants 18 years of age and older – after booster dose (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 (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 (50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (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 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 7172.0 (95% CI: 6610.4, 7781.4). 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.

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 in this study and in the P301 study. 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.

Vaccine efficacy evaluating real-world effectiveness of Spikevax (original) and Spikevax bivalent variant-containing formulations.

This study (mRNA-1273-P901) evaluated the effectiveness of Spikevax (original) administered as a two- or three-dose primary series among immunocompromised individuals against symptomatic SARS-CoV-2 infection, COVID-19-associated hospitalisation, and COVID-19-associated death. Incidence of COVID-19-associated outcomes among immunocompromised individuals who received three doses of Spikevax (original) was compared to individuals who received two doses of Spikevax (original) to estimate relative VE (rVE) and absolute VE, respectively. “Immunocompromised” was defined as having a diagnosis of HIV/acquired immunodeficiency syndrome, leukemia, lymphoma, congenital and other rare conditions, organ transplant procedure, or use of immunosuppressant medication prior to receipt of the third dose. There were 21 942 immunocompromised individuals who received a third dose of Spikevax (original) and were matched on age, sex, race/ethnicity, and date of receipt of the third dose to an equal number of individuals who received two doses of Spikevax (original) only. The adjusted rVE of three doses versus two doses of Spikevax (original) was 55.0% (95% CI: 50.8, 58.9), 83.0% (95% CI: 75.4, 88.3), and 87.1% (95% CI: 30.6, 97.6) against SARS-CoV-2 infection, COVID-19-associated hospitalisation, and COVID-19-associated death, respectively.

Following the approval of Spikevax bivalent Original/Omicron BA.4-5, a follow-up analysis in this study also evaluated the VE of Spikevax bivalent Original/Omicron BA.4-5 administered as a booster dose among individuals (including immunocompromised individuals) who previously received two or more doses of any monovalent mRNA COVID-19 vaccine only in preventing COVID-19-associated hospitalisation. Incidence of COVID-19-associated hospitalisation among booster-vaccinated individuals was compared to individuals who received a monovalent mRNA COVID-19 vaccine only or no COVID-19 vaccination (i.e., unvaccinated) to estimate rVE and absolute VE, respectively.

"Immunocompromised" was defined as having a diagnosis of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome, leukemia, lymphoma, congenital and other rare conditions, organ transplant procedure, or use of immunosuppressant medication prior to the date of booster vaccination (or cohort selection for monovalent only and unvaccinated cohorts).

There were 12 338 immunocompromised individuals who received two or more doses of any monovalent mRNA COVID-19 vaccine followed by a booster dose of Spikevax bivalent Original/Omicron BA.4-5; 19 991 immunocompromised individuals received two or more doses of monovalent mRNA COVID-19 vaccine but no booster dose; and 4 788 immunocompromised individuals did not receive any COVID-19 vaccine (unvaccinated). The rVE (compared to individuals who received a monovalent mRNA COVID-19 vaccine only or were unvaccinated) against COVID-19-associated hospitalisation was 64.7% (95% CI: 44.0, 77.7) in immunocompromised individuals compared to 71.3% (95% CI: 64.5, 76.7) in immunocompetent individuals. The absolute VE was 71.8% (95% CI: 48.8, 84.5) in immunocompromised individuals and 84.1% (95% CI: 80.1, 87.4) in immunocompetent individuals.

Concomitant administration of Spikevax and Fluarix quadrivalent influenza vaccine

In an open-label, randomised clinical trial (NCT05047770, Study 217670), 988 adults aged 18 years and older received doses of Spikevax (original) (50 micrograms) and standard quadrivalent flu vaccine either concomitantly (n=498) or sequentially (n=497), administered two weeks apart. The antibody responses to each vaccine were similar, whether administered concomitantly or sequentially. Furthermore, immunological non-inferiority between concomitant and sequential administration was demonstrated for the Spikevax (original) (50 micrograms) in terms of anti-S protein antibody GMC and for all four strains included in Fluarix quadrivalent in terms of hemagglutination inhibition (HI) antibody GMTs.

Concomitant administration of Spikevax and Shingrix herpes zoster (shingles) vaccine

In an open-label, randomised clinical trial (NCT0504770, Study 217670), 515 adults aged ≥50 years received Spikevax (original) (50 micrograms) and two doses of Shingrix (56 days apart). Spikevax was either co-administered with the first dose of Shingrix (n=257) or sequentially administered two weeks apart (n=258). The antibody response to each vaccine was similar, whether co-administered or provided sequentially. Furthermore, immunological non-inferiority between sequential and co-administration was demonstrated for both the anti-S protein antibody GMC for Spikevax (50 micrograms) and the anti-glycoprotein E antibody GMC for Shingrix.

Elderly population

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 in elderly (≥65 years) was 86.4% (95% confidence interval 61.4%, 95.2%). In a subset of these vaccinated elderly subjects with comorbidities (n=1051), efficacy was 75.2% (95% confidence interval -16.9%, 94.7%).

5.3 Pharmacokinetic properties

Not applicable.

5.4 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 mRNA- 1273 vaccineplacental 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 single-dose vial (Spikevax XBB.1.5 50 micrograms dispersion for injection
12 months at -50ºC to -15ºC.

Within the period of 12 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).

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.

6.4 Special precautions for storage

Spikevax XBB.1.5 50 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.

6.5 Nature and contents of container

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.

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 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.

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 6).

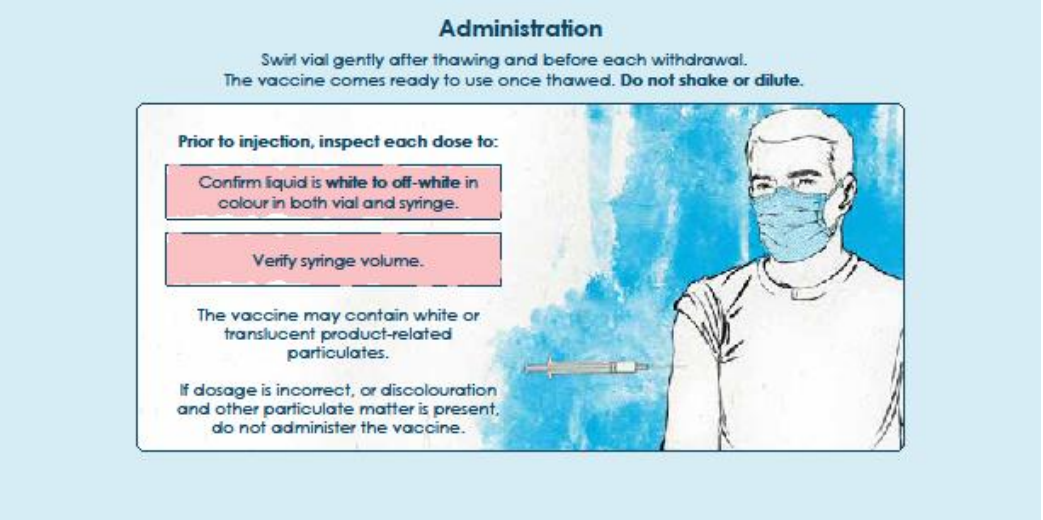
Table 6. Thawing instructions for single-dose vials and carton before use

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

If vials are thawed at 2°C to 8°C, let each vial stand at room temperature (15°C to 25°C) for approximately 15 minutes before administering.

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.



Disposal

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

7. PRODUCT OWNER

MODERNA BIOTECH SPAIN, S.L.
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28037 Madrid
Spain

8. DATE OF TEXT

23 September 2024