1. NAME OF THE MEDICINAL PRODUCT

Spikevax 0.2 mg/mL dispersion for injection
elasomeran 1.26 mg/vial
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).

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 18 years 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 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 18 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. A dosing window of 3 to 6 weeks for administration of the second dose can be allowed in special cases (see sections 4.4 and 5.1). There are limited data available on the interchangeability of Spikevax with other COVID-19 vaccines to complete the primary vaccination course. Individuals who have received the first dose of Spikevax should receive the second dose of Spikevax to complete the primary vaccination course.
	Third dose in severely immuno-compromised	Individuals 18 years of age and older who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.	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 (see sections 4.48 and 5.1).

	Booster dose	Individuals 18 years of age and older	1 (one) dose of 0.25 mL, containing 50 micrograms mRNA	Spikevax may be used to boost individuals 18 years of age and older who have received a primary series with Spikevax at least 6 months after completion of the primary series (see section 5.1).

Paediatric population
Spikevax is not indicated for patients below 18 years of age.

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. 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. In cases of hypersensitivity reactions (excluding

anaphylaxis) following first dose of the vaccine, a consultation with allergy expert should be considered and close observation is recommended following vaccination as follows:

30 minutes:

- People with a history of an immediate allergic reaction of any severity to another vaccine or injectable therapy.
- People with a history of anaphylaxis due to any cause.

15 minutes:

- All other persons.

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 medical 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

High-dose quadrivalent influenza vaccine can be concomitantly administered with Spikevax.

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.

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 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 individuals 18 years 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
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
	Common	Diarrhoea
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria¶
	Not known	Erythema multiforme Mechanical 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.
‡ 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.

¶ 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

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).

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 18 years 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).

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

Sucrose
SM-102 (lipid nanoparticles):
- SM-102
- Cholesterol
- DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine)
- PEG2000 DMG (1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000)

Trometamol hydrochloride (Tris-HCl)
Trometamol (Tris)
Sodium acetate trihydrate
Acetic acid (Glacial)
Water for injections

6.2. Incompatibilities

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

6.3. Shelf life

Unopened vial

The expiry date of the product is indicated on the packaging materials.

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).

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 vial

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 at 2°C to 8ºC and 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.

6.4. Special precautions for storage

Store in a freezer at -25ºC to -15ºC.
Keep the vial in the outer carton in order to protect from light.
Do not store on dry ice or below -50ºC.
For storage conditions after thawing and first opening see section 6.3.

Transportation of thawed 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 shelf life 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.

6.5. Nature and contents of container

5 mL dispersion in a type 1 glass or type 1 equivalent glass 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.

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 -25˚C to -15˚C.

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.

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).

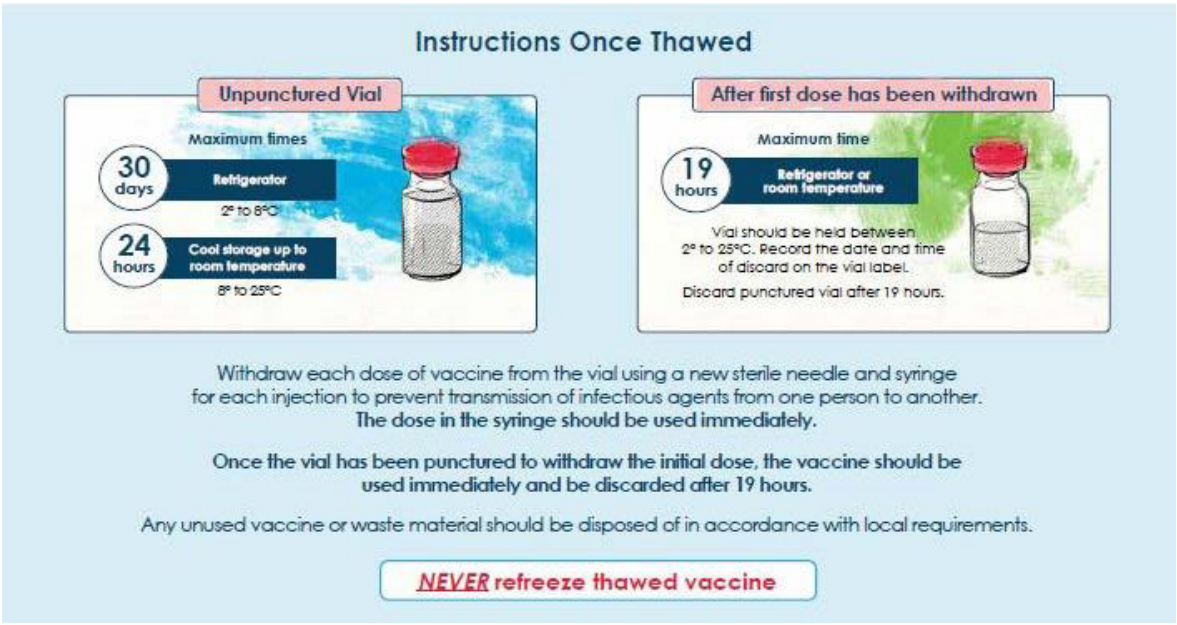
Pierce the stopper preferably at a different site each time. Do not puncture the vial more than 20 times.

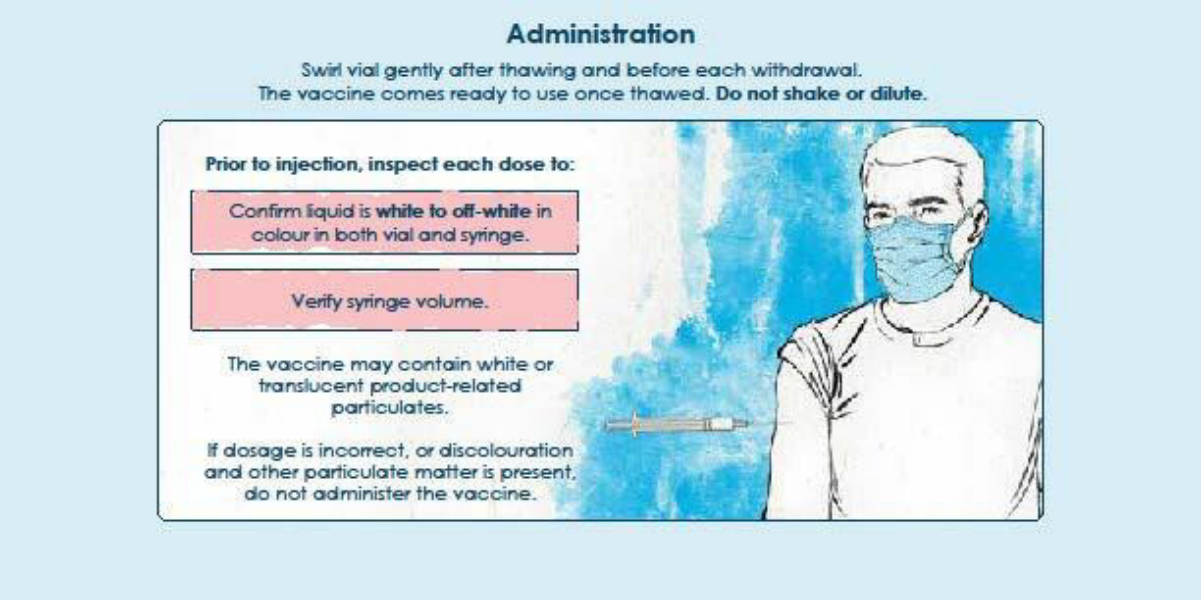
An additional overfill is included in each vial to ensure that a maximum of 10 doses of 0.5 mL or a maximum of 20 doses of 0.25 mL can be delivered.

Thaw each multidose vial before use following the instructions below (Table 5).
When the vial is thawed in the refrigerator, let it sit at room temperature for 15 minutes before administering.

Table 5. 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





Disposal

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

7. MANUFACTURER

MODERNA BIOTECH SPAIN, S.L.
Calle del Príncipe de Vergara 132 Plt
12 Madrid 28002
Spain

8. LICENSE HOLDER

Medison Pharma Ltd.
10 Hashiloach St.,
POB 7090 Petach Tikva
Israel

Registration no. 168-86-36765

Revised in February 2024.

Spikevax-SPC-0224-V1