▼This vaccine is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – SPIKEVAX (ELASOMERAN) COVID-19 VACCINE

1 NAME OF THE MEDICINE

Elasomeran

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial which contains 10 doses of 0.5 mL each or a maximum of 20 doses of 0.25 mL each.

One dose (0.5 mL) of the primary series contains 100 micrograms of messenger RNA (mRNA) (embedded in SM-102 lipid nanoparticles).

One dose (0.25 mL) of the booster contains 50 micrograms of messenger RNA (mRNA) (embedded in SM-102 lipid nanoparticles).

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.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Suspension for injection.

White to off white suspension.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

SPIKEVAX (elasomeran) COVID-19 Vaccine has **provisional approval** for the indication below:

Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 in individuals 6 years of age and older.

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

The decision has been made on the basis of short-term efficacy and safety data. Continued approval depends on the evidence of longer term efficacy and safety from ongoing clinical trials and post-market assessment.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dose

Primary Series

Individuals 12 years of age and older
SPIKEVAX is administered as a course of 2 doses (0.5 mL each).

Individuals 6 through 11 years of age
SPIKEVAX is administered as a course of 2 doses (0.25 mL each).

It is recommended to administer the second dose 28 days after the first dose (see section 4.4 Special Warnings and Precautions for Use and section 5.1 Pharmacodynamic Properties).

Immunocompromised individuals
A third dose of SPIKEVAX (0.5 mL) administered at least 28 days following the first two doses of this vaccine is authorised foradministration to individuals who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Booster Dose

Individuals 18 years of age and older
SPIKEVAX is administered intramuscularly as a single booster dose (0.25 mL; 50 micrograms) at least 6 months after completing a primary series.

The decision when and for whom to implement a booster (third dose) of SPIKEVAX should be made based on available vaccine safety and effectiveness data (see sections 4.4 Special warning and precautions for use and 5.1 Pharmacodynamic properties), in accordance with official recommendations.

Interchangeability

Primary series
The interchangeability of SPIKEVAX with other COVID-19 vaccines to complete the vaccination course has not been established.

Individuals who have received one dose of SPIKEVAX should receive the second dose of SPIKEVAX to complete the vaccination course.

Booster dose
There are limited data on the interchangeability of SPIKEVAX with other COVID-19 vaccines as a booster dose (0.25 mL; 50 micrograms). See sections 4.8 Adverse Effects (Undesirable Effects) and 5.1 Pharmacodynamic properties.

A single booster dose of SPIKEVAX (0.25 mL; 50 micrograms) may be administered as a homologous (same brand) booster dose following completion of primary vaccination with SPIKEVAX or as a heterologous booster dose following completion of primary vaccination with another authorised or approved COVID-19 vaccine, in accordance with official recommendations.

Paediatric population

The safety and efficacy of SPIKEVAX in children and adolescents less than 6 years 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 Special Warnings and Precautions for Use.

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

The vaccine comes ready to use once thawed.

Do not shake or dilute.

Swirl the vial gently after thawing and before each withdrawal.

Inspect SPIKEVAX vials visually for foreign particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.

SPIKEVAX vials are multidose. Ten (10) doses of 0.5 mL volume each or a maximum of twenty (20) doses of 0.25 mL volume can be withdrawn from each vial. Pierce the stopper preferably at a different site each time.

Thawed vials and filled syringes can be handled in room light conditions.

For practical reasons, if the contents of the vial are to be used within a short period of time, drawing up the content in multiple syringes at once may be considered.

Frozen Storage

Store frozen between –25° to –15°C

Do not store on dry ice or below -50°C

Store in the original carton to protect from light.

Thaw Each Vial Before Use

Vial images for illustrative purposes only

2 hours and 30 minutes in refrigerator

2° to 8°C
(within the 30 days shelf life at 2° to 8°C)

OR

1 hour at room temperature

15° to 25°C

Let vial sit at room temperature for 15 minutes before administering

Instructions Once Thawed

Unpunctured Vial

Maximum times

30 days Refrigerator 2° to 8°C

24 hours Cool storage up to room temperature 8° to 25°C

After first dose has been withdrawn

Maximum time

19 hours Refrigerator or room temperature

Vial should be held between 2° to 25°C. Record the date and time of discard on the vial label.

Discard punctured vial after 19 hours.

Withdraw each dose of vaccine from the vial using a new sterile needle and syringe for each injection to prevent transmission of infectious agents from one person to another.
The dose in the syringe should be used immediately.

Contains no antimicrobial preservative.

Once the vial has been punctured to withdraw the initial dose, the vaccine should be used immediately and be discarded after 19 hours.

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

NEVER **refreeze thawed vaccine**

Administration

Swirl vial gently after thawing and before each withdrawal.
The vaccine comes ready to use once thawed. **Do not shake or dilute.**

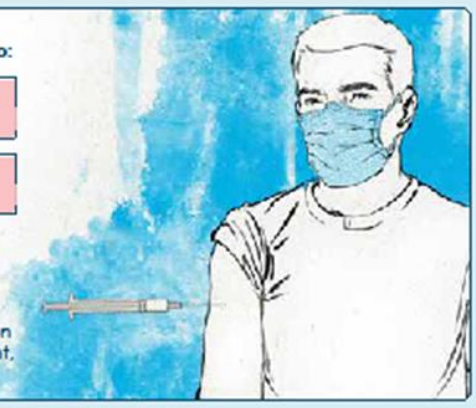
Prior to injection, inspect each dose to:

Confirm liquid is **white to off-white** in colour in both vial and syringe.

Verify syringe volume.

The vaccine may contain white or translucent product-related particulates.

If dosage is incorrect, or discolouration and other particulate matter is present, do not administer the vaccine.



For instructions on disposal of the vaccine, see section 6.6 Special Precautions for Disposal.

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 List of Excipients or in individuals with known severe allergic reactions (e.g., anaphylaxis) to a previous dose of SPIKEVAX.

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 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.

Subsequent doses of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of SPIKEVAX, see Section 4.3 Contraindications.

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 after the second dose, and more often in adolescent and young adult males.

Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general. Available short-term follow-up data suggest that the symptoms resolve in most individuals, but information on long-term sequelae is lacking.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis.

Vaccine recipients 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.

For further details, please refer to the relevant clinical guidelines developed by the Australian Technical Advisory Group on Immunisation.

Altered immunocompetence

If SPIKEVAX is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response to the vaccine may be diminished.

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.

Some individuals may have stress-related responses associated with the process of vaccination itself. Stress-related responses are temporary and resolve on their own. They may include dizziness, fainting, palpitations, increases in heart rate, alterations in blood pressure, feeling short of breath, tingling sensations, sweating and/or anxiety. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation and precautions should be 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.

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

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 vaccine contains less than 1 mmol sodium (23 mg) per 0.5 mL dose, that is to say, essentially ‘sodium-free’.

Use in the elderly

SPIKEVAX was assessed in individuals 12 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 (12-64 years).

Paediatric use

The safety and efficacy of SPIKEVAX in children less than 6 years of age have not yet been established. No data are available.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No interaction studies have been performed. Concomitant administration of SPIKEVAX with other vaccines has not been studied.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity in females.

In a combined fertility and developmental toxicity study, 100 micrograms of mRNA (elasomeran) 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 dams from prior to mating to the end of the study on lactation day 21 as well as in fetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryofetal or offspring development or postnatal development. No data are available on SPIKEVAX vaccine placental transfer or excretion in milk. The effect on male fertility has not been determined.

Use in pregnancy – Pregnancy Category B1

No adequate and well-controlled studies of SPIKEVAX use in pregnant women have been conducted. Available data on SPIKEVAX administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A combined fertility and development toxicity study in rats did not show vaccine-related harmful effects on embryofetal development (see Effects on fertility).

Administration of SPIKEVAX in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

Use in lactation

It is unknown whether SPIKEVAX is excreted in human milk. A combined fertility and developmental toxicity study in rats did not show harmful effects on offspring development before weaning (see Effects of fertility). Data are not available to assess the effects of SPIKEVAX on the breastfed infant or

on milk production/excretion. Therefore, use of SPIKEVAX is not recommended in breastfeeding mothers.

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 Adverse Effects (Undesirable Effects) may temporarily affect the ability to drive or use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Participants 18 years of age and older

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) (Study P301, 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.

Solicited adverse reactions were reported more frequently among vaccine participants than placebo. 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.

Delayed injection site reactions that began >7 days after vaccination were reported in 1.2% of vaccine recipients and 0.4% of placebo recipients. Delayed injection site reactions included pain, erythema, and swelling, and are likely related to vaccination.

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. Grade 3 solicited local adverse reactions were more frequently reported after Dose 2 than after Dose 1. Systemic adverse reactions were reported more frequently by vaccine participants after Dose 2 than after Dose 1. Grade 3 systemic adverse reactions (fatigue, myalgia, arthralgia, and headache) were reported more frequently after Dose 2 than after Dose 1.

The safety profile presented below is based on data generated in a placebo-controlled clinical study on 30,351 adults ≥ 18 years of age.

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 1).

Table 1: Tabulated list of adverse reactions for SPIKEVAX

MedDRA System Organ Class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Immune system disorders	Not known	Anaphylaxis Hypersensitivity
Nervous system disorders	Very common	Headache
	Rare	Acute peripheral facial paralysis**
Cardiac disorders	Not known	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/Vomiting
Skin and subcutaneous tissue disorders	Common	Rash
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
	Common	Injection site erythema 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.

**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.

***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.

**** Delayed injection site reactions included pain, erythema and swelling.

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

Adolescents 12 -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) (Study P203, NCT04649151). Overall, 51.4% were male, 48.6% were female, 11.6% were Hispanic or Latino, 83.9% were White, 3.4% were African American, 5.9% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 1.0% were other races, and 4.5% were multiracial. Demographic characteristics were similar among participants who received SPIKEVAX and those who received placebo.

In the SPIKEVAX group and the placebo group, the median follow-up time after the second injection was 53 days and 51 days, respectively.

In a clinical study, 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%).

Adverse reactions reported are listed in Table 2 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 listed according to frequency

MedDRA system organ class	**Frequency**	**Adverse reaction(s)**
Nervous system disorders	Very common	Headache
Gastrointestinal disorders	Very common	Nausea/vomiting
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills Axillary swelling/tenderness

		Injection site swelling Injection site erythema Pyrexia

Immunocompromised participants 18 years of age and older

From an independent report (*Hall VG, Ferreira VH, Ku T et al. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. N Engl J Med*) in 60 participants who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years previously (range 1.99-6.75 years) who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported.

Children 6 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). Part 1 is an open-label phase of the trial for safety, dose selection, and immunogenicity and included 380 participants 6 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 4,002 participants 6 through 11 years of age who received at least one dose (0.25 mL) of SPIKEVAX (n=3,007) or placebo (n=995). In Part 2, the median follow-up duration was 82 days after dose 1 and 51 days after dose 2. A total of 2981 (99.1%) subjects in the mRNA-1273 group and 966 (97.1%) in the placebo group have been followed for 28 days or more after dose 2. A total of 1,066 (35.3%) subjects in the mRNA-1273 group and 218 (21.9%) in the placebo group have been followed for 56 days or more after dose 2.

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 children 6 through 11 years of age following administration of the primary series were injection site pain (94.8%), fatigue (64.5%), headache (54.3%), chills (30.3%), myalgia (28.2%), nausea/vomiting (24%), fever (23.9%), injection site erythema (18.7%), axillary swelling/tenderness (18%), injection site swelling (17%), and arthralgia (16.1%). While fever rates were observed to be higher among children 6 to < 12 years old (23.9%) when compared to 18 to <25 year olds (18.1%), they were found to be generally of short duration (<24 hours). No febrile seizure and no grade 4 fevers are reported.

Booster dose participants

Study 3 is an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study to evaluate the safety, reactogenicity, and immunogenicity of SPIKEVAX in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL 1 month apart) of SPIKEVAX (primary series). In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose was similar to that after the second dose in the primary series.

Booster dose following primary vaccination with another authorised or approved COVID-19 vaccine

The safety of a SPIKEVAX (0.25 mL) booster dose in individuals who completed primary vaccination with another authorised or approved COVID-19 Vaccine (heterologous booster dose) is inferred from

the safety of a SPIKEVAX (0.25 mL) booster dose administered following completion of a Moderna COVID-19 Vaccine primary series (homologous booster dose) and from data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose (0.5 mL) of SPIKEVAX. In this study, adults who had completed primary vaccination with a SPIKEVAX 2-dose series (N=151), a COVID-19 Vaccine Janssen single dose (N=156), or a COMIRNATY 2-dose series (N=151) at least 12 weeks prior to enrolment and who reported no history of SARS-CoV-2 infection were randomised 1:1:1 to receive a booster dose of one of three vaccines: SPIKEVAX (0.5 mL), COVID-19 Vaccine Janssen, or COMIRNATY. Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the SPIKEVAX, heterologous booster dose (0.5 mL) did not identify any new safety concerns, as compared with adverse reactions reported following SPIKEVAX primary series doses or homologous booster dose (0.25 mL).

Post-marketing experience

Although the events listed in Table 3 were not observed in the clinical trials, they are considered adverse drug reactions for SPIKEVAX as they were reported in the post-marketing experience. Unless otherwise noted in Table 3, these reactions were derived from spontaneous reports, the frequencies could not be determined and are thus considered as not known.

Table 3: Adverse reactions from SPIKEVAX post marketing experience

System Organ Class	Frequency	Adverse Drug Reaction
Immune system disorders	Not known	Anaphylaxis Hypersensitivity reactions (e.g. erythema multiforme)
Cardiac disorders	Very rare	Myocarditis* Pericarditis*
Nervous system disorders	Rare	Paraesthesia
	Rare	Hypoaesthesia

*The frequency of myocarditis and pericarditis is unknown in the 6 through 11 year old age group, as there is currently no post marketing experience.

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 suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

No case of overdose has been reported.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Vaccine, other viral vaccines, ATC code: J07BX03

Mechanism of action

SPIKEVAX 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 spike protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is nonreplicating, 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 trials

Clinical efficacy in adults

Study P301 was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or who 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.

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.

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 – per-protocol set

Age group (years)	SPIKEVAX			Placebo			% Vaccine efficacy (95% CI)*
	Subjects N	COVID-19 cases N	Incidence rate of COVID-19 per 1000 person-years	Subjects N	COVIV-19 cases N	Incidence rate of COVID-19 per 1000 person-years	
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% (48.6, 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% confidence interval 88.5, 96.4%).

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.

Clinical efficacy in adolescents 12 through 17 years of age

Study P203 is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study (NCT04649151) to evaluate the safety, reactogenicity, and effectiveness of SPIKEVAX in adolescents ages 12 to 17 years in the United States. 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. Participants will be followed for efficacy and safety until 1 year after the second dose.

A secondary efficacy analysis was performed in 3,236 participants who received at least Dose 1 of either SPIKEVAX (n=2,163) or placebo (n=1,073), and had a negative baseline SARS-CoV-2 status (referred to as the modified Intent-to-Treat Set). In the mITT set, 48.5% were female, 11.2% were Hispanic or Latino, 83.9% were White, 2.8% were African American, 6.3% were Asian, and 0.9% other races. 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 the presence of at least one symptom from a list of COVID-19 symptoms occurring at least 14 days after Dose 1 and a positive nasopharyngeal (NP) swab or saliva sample for SARS-CoV-2 by RT-PCR (reverse transcription-polymerase chain reaction). Listed symptoms were fever (temperature > 38ºC/≥ 100.4ºF), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, or vomiting or diarrhoea.

There were 2 COVID-19 cases in the SPIKEVAX group and 13 cases in the placebo group, with a vaccine efficacy of 92.7% (95% confidence interval of 67.8% to 99.2%).

Immunogenicity in adolescents 12 through 17 years of age

In Study P203 (NCT04649151), an analysis was conducted of SARS-CoV-2 50% neutralising titers and seroresponse rates 28 days after Dose 2 in a subset of adolescents aged 12 through 17 in Study P203 and in participants aged 18 through 25 in Study P301 who had no immunologic or virologic evidence of prior COVID-19 at baseline. Noninferior immune responses and seroresponse rates were demonstrated in a comparison of adolescents aged 12 through 17 years to participants aged 18 through 25 (Table 5).

Table 5: Summary of geometric mean titer and seroresponse rate – comparison of adolescents 12 through 17 years of age to participants 18 through 25 years of age – per-protocol immunogenicity subset

Assay	Time point	SPIKEVAX		12-17 years/18-25 years	
		12 – 17 years N=340	18-25 years N=305		
		GLSM (95% CI)*	GLSM (95% CI)*	GMR (95% CI)**	Met noninferiority objective (Y/N)***
SARS-CoV-2 neutralisation assay – ID50 (titer)****	28 days after Dose 2	1401.7 (1276.3, 1539.4)	1301.3 (1177.0, 1438.8)	1.08 (0.94, 1.24)	Y
		Seroresponse % (95% CI)* 98.8 (97.0, 99.7) ¶	**Seroresponse %** (95% CI)* 98.6 (96.6, 99.6) ¶	**Difference in seroresponse rate %** (95% CI) # 0.2 (-1.8, 2.4)	

GLSM = Geometric least squares mean
GMR = Geometric mean ratio
n = Number of subjects with non-missing data at the corresponding timepoint
* 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.
** The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (adolescents in Study P203 and young adults in Study P301) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
*** Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%.
**** SARS-CoV-2 50% inhibitory dose (ID50) neutralisation titers were determined using a SARS-CoV-2 Spike-Pseudotyped Virus Neutralisation Assay. Quantification of SARS-CoV-2 neutralising antibodies utilises lentivirus particles expressing SARS-CoV-2 Spike protein on their surface and contains a firefly luciferase (Luc) reporter gene for quantitative measurements of infection by relative luminescence units (RLU). Neutralisation is measured as the serum dilution at which RLU is reduced by 50% (ID50) relative to mean RLU in virus control wells virus but after subtraction of mean RLU in cell control wells.
¶ Seroresponse due to vaccination specific to pseudovirus neutralising antibody ID50 titer at a subject level is defined as a change from below LLOQ to equal or above LLOQ, or at least a 3.3-fold rise if baseline is equal to or above LLOQ.
# Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

<u>Clinical efficacy in children 6 through 11 years of age</u>

The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical trial to evaluate the safety, reactogenicity, and effectiveness of the 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. Participants will be followed for effectiveness and safety until 1 year after the second dose.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of November 10, 2021 was performed in 3,583 participants who received two doses (0.25 mL at 0 and 1 month) of either SPIKEVAX (n=2,701) or placebo (n=882), and had a negative baseline SARS-CoV-2 status (referred to as the modified Intent-to-Treat Set [mITT]). Between participants who received SPIKEVAX and those who received placebo, there were no notable differences in demographics.

In Part 2, the median follow up duration was 82 days after dose 1 and 51 days after dose 2. A total of 2981 (99.1%) subjects in the mRNA-1273 group and 966 (97.1%) in the placebo group have been followed for 28 days or more after dose 2. A total of 1,066 (35.3%) subjects in the mRNA-1273 group and 218 (21.9%) in the placebo group have been followed for 56 days or more after dose 2.

Immunogenicity in children 6 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 subset of children aged 6 through 11 (n=134) in the paediatric study and in participants aged 18 through 25 (n=295) in the adult study (NCT04796896). 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 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 immunocompromised recipients

From an independent report (*Hall VG, Ferreira VH, Ku T et al. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. N Engl J Med*), a separate randomised controlled study has been conducted in 120 participants who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years previously (range 1.99-6.75 years). A third dose (0.5 mL) of SPIKEVAX was administered to 60 participants approximately 2 months after they had received a second dose; saline placebo was given to 60 individuals for comparison (NCT04885907). Significant increases in levels of SARS-CoV-2 antibodies occurred four weeks after the third dose in 55.0% of participants in the SPIKEVAX group (33 of 60) and 17.5% of participants in the placebo group (10 of 57).

Immunogenicity in participants 18 years of age and older – after booster dose (0.25 mL, 50 micrograms)

Study 3 is an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study to evaluate the safety, reactogenicity, and immunogenicity of SPIKEVAX in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL 1 month apart) of SPIKEVAX (primary series). In an open-label phase, 149 of those participants (Per-Protocol Set) received a single booster dose (0.25 mL) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL) 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 or approved COVID-19 vaccine in adults 18 years of age and older

Effectiveness of a SPIKEVAX (0.25 mL) booster dose in individuals who completed primary vaccination with another authorised or approved COVID-19 Vaccine (heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a SPIKEVAX (0.25 mL) booster dose administered following completion of a SPIKEVAX primary series and from immunogenicity data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose (0.5 mL) of SPIKEVAX. In this study, adults who had completed primary vaccination with a SPIKEVAX 2-dose series (N=151), a COVID-19 Vaccine Janssen single dose (N=156), or a COMIRNATY 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: SPIKEVAX, COVID-19 Vaccine Janssen, or COMIRNATY. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to SPIKEVAX (0.5 mL) was demonstrated regardless of primary vaccination.

5.2 PHARMACOKINETIC PROPERTIES

Not applicable

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

The novel lipid components SM-102 and PEG-2000-DMG of the vaccine were negative in the bacterial reverse mutation Ames test and in vitro micronucleus test in human peripheral blood lymphocytes. A luciferase mRNA in SM102-containing lipid nanoparticles was negative in a rat bone marrow micronucleus assay (IV dose of SM-102 28.5 mg/kg, PEG-2000-DMG 2.8 mg/kg), whilst a surrogate ZIKA mRNA-based vaccine formulated in SM-102-containing lipid nanoparticles induced micronuclei in male rats, but not in females (IV dose of SM-102 60 mg/kg, PEG-2000-DMG 6 mg/kg). The weight of evidence suggests the genotoxicity potential of the novel lipid components SM-102 and PEG-2000-DMG is very low. The other components of SPIKEVAX (other lipids and mRNA) are not expected to be genotoxic.

Carcinogenicity

Carcinogenicity studies were not performed. The components of the vaccine (lipids and mRNA) are not expected to have carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Heptadecan-9-yl 8-[2-hydroxyethyl-(6-oxo-6-undecoxyhexyl)amino]octanoate
Cholesterol
Distearoylphosphatidylcholine

1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000
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

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Unopened vial:

The unopened vaccine may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days. Once thawed the vaccine should not be re-frozen.

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 25°C after initial puncture (within the allowed use period of 30 days at 2°C to 8°C and 24 hours at 8°C to 25°C). Contains no antimicrobial preservative. From a microbiological point of view, the product should be used immediately. Do not refreeze.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store frozen between -25°C to -15°C.

Store in the original carton to protect from light.

Do not store on dry ice or below -50°C.

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 suspension in a vial (type 1 or type 1 equivalent glass) with a stopper (chlorobutyl rubber) and a flip-off plastic cap with seal (aluminium seal).

Each vial contains 5 mL of SPIKEVAX (elasomeran) COVID-19 Vaccine.

Pack size: 10 multidose vials

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

CAS number

2457298-05-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription only medicine (Schedule 4)

8 SPONSOR

Moderna Australia Pty Ltd
Level 6, 60 Martin Place
Sydney
NSW, 2000
www.modernacovid19global.com/au/
Phone: 1800 344 018
Email address: apacmedinfo@modernatx.com

9 DATE OF FIRST APPROVAL

09 August 2021

10 DATE OF REVISION

18 February 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.1	Change indication to include individuals 6 through 11 years of age
4.2	Add dose information for individuals 6 through 11 years of age
4.4	Remove precaution for individuals 6 through 11 years of age
4.8	Add adverse effect information for individuals 6 through 11 years of age

5.1	Add efficacy & immunogenicity information for individuals 6 through 11 years of age