▼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.

One dose (0.5 mL) contains 100 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 18 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

SPIKEVAX is administered as a course of 2 doses (0.5 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).

There are no data available on the interchangeability of SPIKEVAX with other COVID-19 vaccines to complete the vaccination course. Individuals who have received the first dose of SPIKEVAX should receive the second dose of SPIKEVAX to complete the vaccination course.

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.

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 Ten (10) doses (of 0.5 mL each) can be withdrawn from each vial.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

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

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

Thaw Each Vial Before Use

Vial images for illustrative purposes only

Let vial sit at room temperature for 15 minutes before administering

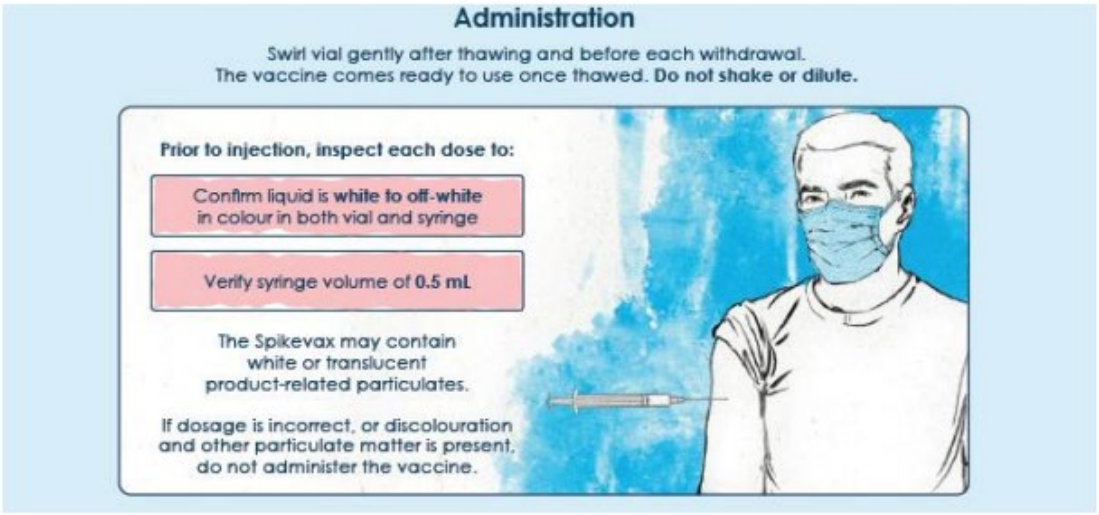
Instructions Once Thawed

Withdraw each 0.5 mL 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.**

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**



Paediatric population

The safety and efficacy of SPIKEVAX in children and adolescents less than 18 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.

For instructions regarding thawing, handling, and 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.

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.

The second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of SPIKEVAX.

Myocarditis and pericarditis

There have been very rare reports of myocarditis and pericarditis occurring after vaccination with SPIKEVAX. These cases have primarily occurred within 14 days following the vaccination, more often after the second dose, and more often in younger men. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general.

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.

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.

Immunocompromised individuals

The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of SPIKEVAX may be lower in immunosuppressed 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 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).

Paediatric use

The safety and efficacy of SPIKEVAX in children and adolescents less than 18 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

There is limited experience with use of SPIKEVAX in pregnant women.

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).

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)

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.

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. Local and systemic adverse reactions were more frequently reported 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: Tabulated list of adverse reactions for SPIKEVAX

MedDRA System Organ Class Frequency Adverse reactions	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.

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

Study 1 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 2.

Table 2: 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.

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.

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 10 doses of 0.5 mL.

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
Phone: 0800 909 630

9 DATE OF FIRST APPROVAL

09 August 2021

10 DATE OF REVISION

Not applicable

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
	New Product Information