▼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 BIVALENT ORIGINAL/OMICRON (ELASOMERAN/IMELASOMERAN) COVID-19 VACCINE

1 NAME OF THE MEDICINE

Elasomeran/imelasomeran

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Concentration	Presentation	Dose(s)	Composition
0.1 mg/mL	Multidose vial	2.5 mL: 5 doses of 0.5 mL each 5 mL: 10 doses of 0.5 mL each	One dose (0.5 mL) contains 25 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles), and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).
	Pre-filled syringe	1 dose of 0.5 mL For single use only.	One dose (0.5 mL) contains 25 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles) and 25 micrograms of imelasomeran, a COVID-19 mRNA Vaccine (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.

Imelasomeran contains mRNA, 5'-capped, encoding a full-length, codon-optimised pre-fusion stabilised conformation variant (K983P and V984P) of the SARSCoV-2 spike (S) glycoprotein (Omicron variant, B.1.1.529).

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 BIVALENT ORIGINAL/OMICRON (elasomeran/imelasomeran) COVID-19 Vaccine has **provisional approval** for the indication below:

As a booster dose for 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 immunogenicity and short-term safety data. Continued approval depends on the evidence of longer term benefits and safety from ongoing clinical trials and post-market assessment.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dose

Refer to Table 1 below for dosing.

Table 1: SPIKEVAX BIVALENT ORIGINAL/OMICRON for booster doses (see sections 4.4 and 5.1)

Age(s)	Dose	Recommendations
Individuals 18 years of age and older	0.5 mL, containing 50 micrograms	SPIKEVAX BIVALENT ORIGINAL/OMICRON may be given at least 3 months following a primary series and /or previous booster dose with SPIKEVAX (original) or another authorised/ approved COVID-19 vaccine, in accordance with official recommendations.

Paediatric population

The safety and efficacy of SPIKEVAX BIVALENT ORIGINAL/OMICRON 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.

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

Do not shake or dilute.

Multidose vials

SPIKEVAX BIVALENT ORIGINAL/OMICRON vials are multidose.

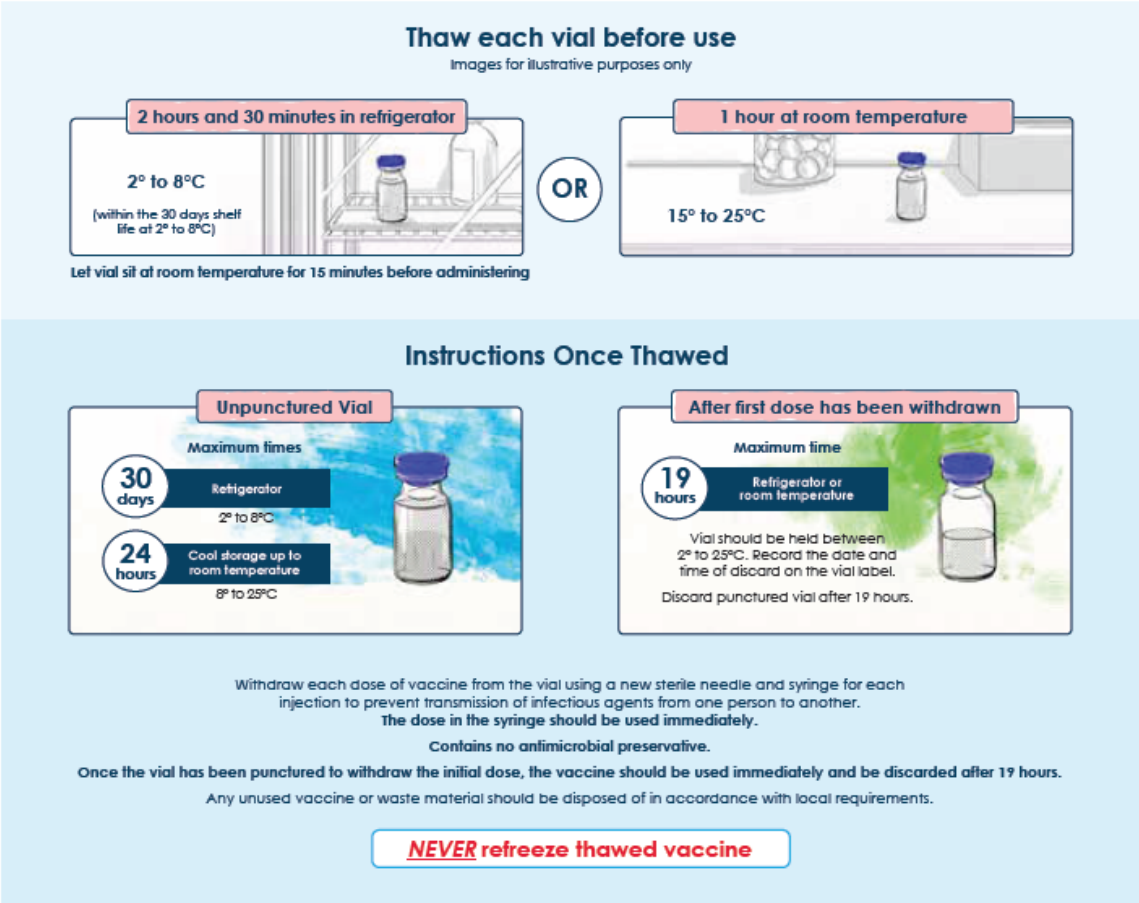
Swirl the vial gently after thawing and before each withdrawal.

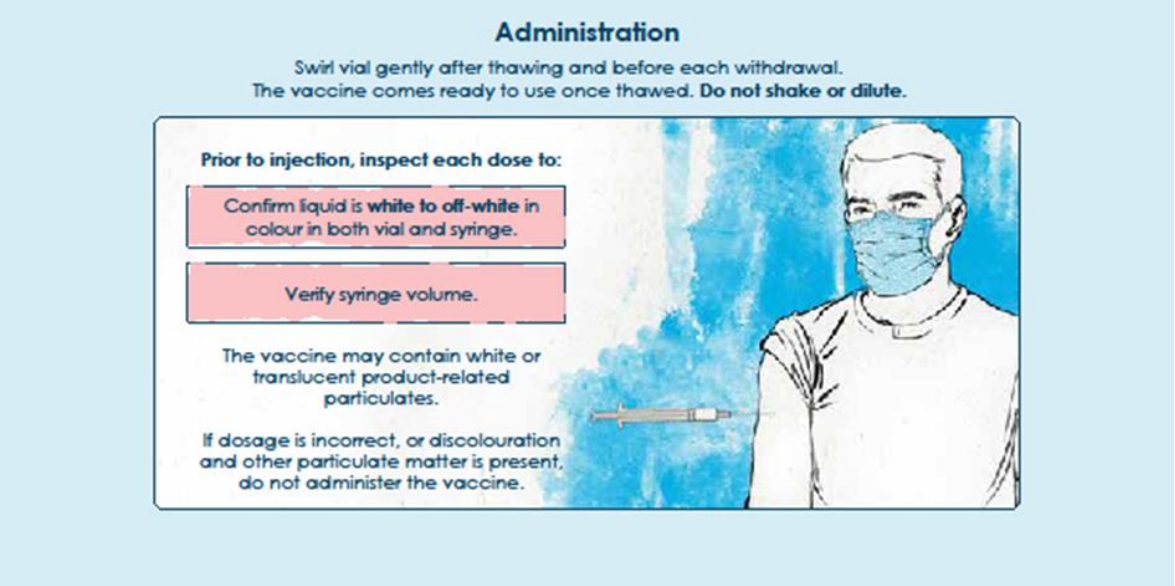
Inspect the vials visually for foreign particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.

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.

Five (5) doses (of 0.5 mL volume each) can be withdrawn from each 2.5 mL vial.

Ten (10) doses (of 0.5 mL volume each) can be withdrawn from each 5 mL vial.





Pre-filled syringe

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

Thaw each pre-filled syringe before use following the instructions below.

Thaw in refrigerator	**Thaw at room temperature**
Thaw between 2°C to 8°C for 2 hours. Let each syringe stand at room temperature (15°C to 25°C) for 15 minutes before administering.	Alternatively, thaw between 15°C to 25°C for 1 hour.

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 (original) or SPIKEVAX BIVALENT ORIGINAL/OMICRON.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Traceability

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

Hypersensitivity and anaphylaxis

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

Close observation 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 (original) or SPIKEVAX BIVALENT ORIGINAL/OMICRON, see Section 4.3 Contraindications.

Myocarditis and pericarditis

There is an increased risk for myocarditis and pericarditis following vaccination with SPIKEVAX (original) or SPIKEVAX BIVALENT ORIGINAL/OMICRON.

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, but not exclusively, in adolescent and young adult males. There have also been reports in females.

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, however, severe outcomes, including death, have been rarely reported and information on long-term sequelae is lacking.

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

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. Additionally, non-specific symptoms such as fatigue, nausea and vomiting, abdominal pain, dizziness or syncope, oedema and cough have been reported in some recipients with myocarditis or pericarditis. 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.

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.

Capillary leak syndrome flare-ups

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

Immunocompromised individuals

The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of SPIKEVAX BIVALENT ORIGINAL/OMICRON may be lower in immunocompromised 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 BIVALENT ORIGINAL/OMICRON 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

Use of SPIKEVAX BIVALENT ORIGINAL/OMICRON and SPIKEVAX (original) in the elderly is described in Section 5.1 Pharmacodynamic Properties.

Paediatric use

The safety and efficacy of SPIKEVAX BIVALENT ORIGINAL/OMICRON 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 (ORIGINAL) or SPIKEVAX BIVALENT ORIGINAL/OMICRON 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 (original) was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. SARS-CoV-2 antibody responses were present in 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 (original) or SPIKEVAX BIVALENT ORIGINAL/OMICRON vaccine placental transfer or excretion in milk. The effect on male fertility has not been determined.

Use in pregnancy – Pregnancy Category B1

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

Use in lactation

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

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

SPIKEVAX BIVALENT ORIGINAL/OMICRON 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)

Summary of the Safety Profile

SPIKEVAX BIVALENT ORIGINAL/OMICRON booster dose

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

The SPIKEVAX BIVALENT ORIGINAL/OMICRON booster had a reactogenicity profile similar to that of the SPIKEVAX original booster given as a second booster dose. The frequency of adverse reactions after immunisation with SPIKEVAX BIVALENT ORIGINAL/OMICRON was also similar or lower relative to that of a first booster dose of SPIKEVAX original (50 micrograms) and relative to the second dose of the SPIKEVAX (original) primary series (100 micrograms). No new safety signals were identified.

SPIKEVAX (original)

Participants 18 years of age and older

The safety of SPIKEVAX (original) was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30,351 participants 18 years of age and older who received at least one dose of SPIKEVAX (original) (n=15,185) or placebo (n=15,166) (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. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Tabulated list of adverse reactions from clinical studies and post-authorisation experience in individuals 18 years of age and older

The safety profile presented below is based on data generated in a placebo-controlled clinical study in 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 2).

Table 2: Adverse reactions from SPIKEVAX (original) clinical trials and post authorisation experience in individuals 18 years of age and older

MedDRA system organ class	Frequency	Adverse reaction(s)
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‡ Hypoaesthesia Paraesthesia
Cardiac disorders	Very rare	Myocarditis Pericarditis
Gastrointestinal disorders	Very common	Nausea/vomiting
Skin and subcutaneous tissue disorders	Common	Rash
	Rare	Acute and delayed 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
	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. 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 adult participants in the vaccine group and one adult participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.

^ 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 adult vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported 1 and 2 days, respectively, after vaccination.

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

Participants 18 years of age and older (SPIKEVAX (original) booster dose)

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

Description of selected adverse reactions

Myocarditis

SPIKEVAX BIVALENT ORIGINAL/OMICRON

The risk of myocarditis after a booster dose (50 microgram) of SPIKEVAX BIVALENT ORIGINAL/OMICRON has not yet been fully characterised, however myocarditis and pericarditis have been reported following booster doses of SPIKEVAX.

SPIKEVAX (original)

The increased risk of myocarditis after vaccination with SPIKEVAX (original) is highest in younger males (see section 4.4). There have also been reports in females.

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

Myocarditis and pericarditis have been reported following booster doses of SPIKEVAX.

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

Elasomeran and imelasomeran contain mRNA encapsulated in lipid nanoparticles.

The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral 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

SPIKEVAX BIVALENT ORIGINAL/OMICRON

Immunogenicity in participants 18 years of age and older – after SPIKEVAX BIVALENT ORIGINAL/OMICRON booster dose (0.5 mL, 50 micrograms)

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

Study P205 Part G evaluated the safety, reactogenicity and immunogenicity of the SPIKEVAX BIVALENT ORIGINAL/OMICRON vaccine when administered as a second booster dose to adults who previously received 2 doses of SPIKEVAX (original) (100 microgram) as a primary series and a booster dose of SPIKEVAX (original) (50 micrograms) at least 3 months prior to enrollment. In P205 Part F, study participants received SPIKEVAX BIVALENT ORIGINAL/OMICRON (50 micrograms) as a second

booster dose and the Part F group serves as a within-study, non-contemporaneous comparator group to the SPIKEVAX BIVALENT ORIGINAL/OMICRON group.

In this study, the primary immunogenicity analysis was based on the primary immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster) (Table 3).

Table 3: Ancestral SARS-CoV-2 (D614G) and Omicron (BA.1) neutralising antibody titres (ID50) - SPIKEVAX BIVALENT Original/Omicron 50 µg and SPIKEVAX (original) 50 µg administered as second booster doses

	Omicron variant		Ancestral SARS-CoV-2	
	P205 Part G	**P205 Part F**	**P205 Part G**	**P205 Part F**
Antibody: PsVNA nAb ID_{50} titres	**SPIKEVAX BIVALENT ORIGINAL / OMICRON 50 µg (N=334)**	**SPIKEVAX (original) 50 µg (N=260)**	**SPIKEVAX BIVALENT ORIGINAL / OMICRON 50 µg (N=334)**	**SPIKEVAX (original) 50 µg (N=260)**
Pre-booster, n	334	260	334	260
Observed GMT (95% CI)[a]	298.1 (258.8, 343.5)	332.0 (282.0, 390.9)	1266.7 (1120.2, 1432.5)	1521.0 (1352.8, 1710.2)
Day 29, n	334	260	334	260
Observed GMT (95% CI)[a]	2372.4 (2070.6, 2718.2)	1473.5 (1270.8, 1708.4)	5977.3 (5321.9, 6713.3)	5649.3 (5056.8, 6311.2)
Observed GMFR (95% CI)[a]	8.0 (7.2, 8.8)	4.4 (4.0, 5.0)	4.7 (4.4, 5.1)	3.7 (3.4, 4.0)
GLSM [estimated GMT] (95% CI)[b]	2479.9 (2264.5, 2715.8)	1421.2 (1283.0, 1574.4)	6422.3 (5990.1, 6885.7)	5286.6 (4887.1, 5718.9)
GMR (97.5% CI)[b]	**1.7 (1.5, 2.0)**		**1.2 (1.1, 1.4)**	

Abbreviations: CI = confidence interval; GLSM = geometric least squares mean; GMFR = geometric mean fold-rise; GMR = geometric mean ratio; GMT = geometric mean titre; ID_{50} = 50% inhibitory dilution; LLOQ = lower limit of quantification; nAb = neutralising antibodies; PsVNA = pseudotyped virus neutralisation assay; SARS-CoV-2 = severe acute respiratory syndrome-2; n = number of participants with non-missing data at the corresponding timepoint.

[a] 95% CI is calculated based on the t-distribution of the log-transformed values or the difference in the log-transformed values for GM value and GM fold-rise, respectively, then back transformed to the original scale for presentation.

[b] Based on ANCOVA modeling; the model includes adjustment for treatment group, pre-booster antibody titres, and age groups.

Observed neutralising antibody titres for Omicron subvariants BA.4/5 after the SPIKEVAX BIVALENT ORIGINAL/OMICRON booster dose

Table 4 presents the summary of the observed neutralising antibody GMTs and GMFRs against Omicron BA.4/BA.5 for participants who received either the SPIKEVAX BIVALENT

ORIGINAL/OMICRON 50 microgram booster vaccine (Part G) or the SPIKEVAX (original) 50 microgram booster vaccine (Part F) as a second booster dose (4th dose). This exploratory analysis was conducted in the immunogenicity set which includes participants with no evidence of SARS-CoV-2 infection at baseline (pre-booster).

Table 4: Summary of neutralising antibody geometric mean titres for the Omicron BA.4/BA.5 variant - comparison between SPIKEVAX BIVALENT ORIGINAL/OMICRON 50 µg and SPIKEVAX (original) 50 µg booster doses

	PPSI - Neg	
	P205 Part G	**P205 Part F**
Antibody: PsVNA nAb ID_{50} titres	**SPIKEVAX BIVALENT ORIGINAL/ OMICRON 50 µg (N=334)**	**SPIKEVAX (original) 50 µg (N=260)**
Pre-booster, n[a]	334	260
Observed GMT (95% CI)[a,b]	115.6	139.7
	(98.5, 135.6)	(119.5, 163.3)
Day 29, n[a]	333	260
Observed GMT (95% CI)[a,b]	727.4	492.1
	(632.8, 836.1)	(431.1, 561.9)
Observed GMFR (95% CI)[a,b]	6.3	3.5
	(5.7, 6.9)	(3.2, 3.9)
GLSM [Estimated GMT] (95% CI)[b]	776.4 (719.5, 837.9)	458.3 (420.6, 499.3)
GMR (95% CI)[b]	**1.7 (1.5, 1.9)**	

Abbreviations: CI = confidence interval; GLSM=geometric least squares mean; GMFR = geometric mean fold-rise (post-baseline/baseline titres); GMT = geometric mean titre; ID_{50} = 50% inhibitory dilution; LOD = limit of detection; mRNA = messenger ribonucleic acid; nAb = neutralizing antibody; PPSI = per-protocol set for immunogenicity; PPSI – Neg = per-protocol Set for immunogenicity – SARs-CoV-2 Negative at baseline; PPSI – Pos = per-protocol Set for immunogenicity – SARS-CoV-2 Positive at baseline; PsVNA = pseudotyped virus neutralization assay.

Note: antibody values reported as below the lower limit of detection are replaced by 0.5 x LOD.

[a] Number of subjects with non-missing data at the timepoint (baseline or post-baseline).

[b] 95% CI is calculated based on the t-distribution of the log-transformed values or the difference in the log-transformed values for GM value and GM fold-rise, respectively, then back transformed to the original scale for presentation.

SPIKEVAX (original)

Clinical efficacy of SPIKEVAX (original) 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 (original). Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or SPIKEVAX (original).

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

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

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

Table 5: Vaccine efficacy analysis: confirmed COVID-19# regardless of severity starting 14 days after the 2nd dose – per-protocol set

Age group (years)	SPIKEVAX (original)			Placebo			% Vaccine efficacy (95% CI)*
	Subjects N	COVID-19 cases N	Incidence rate of COVID-19 per 1000 person-years	Subjects N	COVID-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 (original) to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% 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.

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

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

Immunogenicity of a booster dose of SPIKEVAX (original) following primary vaccination with another authorised or approved COVID-19 vaccine in adults 18 years of age and older

Effectiveness of a SPIKEVAX (original) (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 (original) (0.25 mL) booster dose administered following completion of a SPIKEVAX (original) 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 (original). In this study, adults who had completed primary vaccination with a SPIKEVAX (original) 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 (original), 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 (original) (0.5 mL) was demonstrated regardless of primary vaccination.

Elderly population

SPIKEVAX BIVALENT ORIGINAL/OMICRON was assessed in 437 individuals 18 years of age and older (P205 Part G, safety analysis set), including 38 subjects 75 years of age and older. A total of 174 of the 437 participants (39.8%) were ≥ 65 years of age.

SPIKEVAX (original) was assessed in individuals 6 months of age and older, including 3,768 subjects 65 years of age and older. The efficacy of SPIKEVAX (original) was consistent between elderly (≥65 years) and adolescents and younger adult subjects (12-64 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 repeat dose toxicity and reproductive and developmental toxicity. The full relevance of animal studies to human risk with vaccines for COVID-19 remains to be established.

Genotoxicity

The novel lipid components SM-102 and PEG-2000-DMG of SPIKEVAX (original) and SPIKEVAX BIVALENT ORIGINAL/OMICRON 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 (original) or SPIKEVAX BIVALENT ORIGINAL/OMICRON (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 multidose vial and pre-filled syringe:

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

The unopened vial and pre-filled syringe may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

The pre-filled syringe is for single use in one patient only. Discard any residue.

Punctured multidose 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 -50°C to -15°C.

Store in the original carton to protect from light.

Do not store below -50°C.

For storage conditions after thawing and first opening see section 6.3 Shelf life.

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.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C

Pre-filled syringes can be transported at 2°C to 8°C when shipped using shipping containers that have been qualified to maintain 2° to 8°C. Once thawed and transported in liquid state at 2° to 8°C, pre-filled syringes should not be refrozen and should be stored at 2° to 8°C until use.

6.5 NATURE AND CONTENTS OF CONTAINER

2.5 mL multidose vial (0.1 mg/mL)

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

Each vial contains 2.5 mL.

Pack size: 10 multidose vials

5 mL multidose vial (0.1 mg/mL)

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

Each vial contains 5 mL.

Pack size: 10 multidose vials.

Pre-filled syringe (0.1 mg/mL)

0.5 mL suspension in a pre-filled syringe (polymeric) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

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

Each pre-filled syringe contains 0.5 mL.

Pack size: 10 pre-filled syringes.

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 (elasomeran)

2763208-92-8 (imelasomeran)

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

30 August 2022

10 DATE OF REVISION

21 February 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.8	Addition of heavy menstrual bleeding as adverse reaction