▼ 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 – mNEXSPIKE XBB.1.5 (SARS-CoV-2 spike protein (mRNA) XBB.1.5) COVID-19 VACCINE

1. NAME OF THE MEDICINE

SARS-CoV-2 spike protein (mRNA) XBB.1.5

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Table 1: mNEXSPIKE XBB.1.5 qualitive and quantitative composition

Strength	Container	Dose(s)	Composition per dose
10 micrograms	Pre-filled syringe	1 dose of 0.2 mL For single-use only.	One dose (0.2 mL) contains 10 micrograms of SARS-CoV-2 spike protein (mRNA) XBB.1.5

SARS-CoV-2 spike protein (mRNA) XBB.1.5 is a nucleoside-modified messenger RNA (mRNA) encoding the subdomains of spike receptor binding domain (RBD) and N-terminal domain (NTD) protein of the SARS-CoV-2 circulating variant.

mNEXSPIKE XBB.1.5 does not contain any preservatives, antibiotics, adjuvants, or human- or animal-derived materials. The pre-filled syringe stopper does not contain natural rubber latex.

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

mNEXSPIKE XBB.1.5 (SARS-CoV-2 spike protein (mRNA) XBB.1.5) COVID-19 Vaccine is indicated for:

Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 in individuals 12 years of age and older.

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

4.2 DOSE AND METHOD OF ADMINISTRATION

Dose

Table 2. mNEXSPIKE XBB.1.5 dosage

Age(s)	Dose	Additional recommendations
Individuals 12 years of age and older	One dose of 0.2 mL, given intramuscularly	If previously vaccinated, mNEXSPIKE XBB.1.5 should be administered at least 3 months after a recent dose of a COVID-19 vaccine (see sections 4.4 and 5.1).

The use of this vaccine should be in accordance with clinical recommendations in Australia, made by ATAGI in the Australian Immunisation Handbook.

Paediatric population

The safety and efficacy of mNEXSPIKE XBB.1.5 in children less than 12 years of age have not yet been established. No data are available.

Elderly

No dose adjustment is required in elderly individuals ≥65 years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products. For precautions to be taken before administering the vaccine, see section 4.4 Special Warnings and Precautions for Use.

Preparation

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

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.2 mL can be administered from each pre-filled syringe.

mNEXSPIKE XBB.1.5 is supplied in a single-dose, pre-filled syringe (without needle) containing 0.2 mL (10 micrograms) mRNA and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed outside the carton or in the carton itself, either in the refrigerator or at room temperature (Table 3).

Table 3. Thawing instructions for mNEXSPIKE XBB.1.5 pre-filled syringes and cartons before use

Configuration	Thaw instructions and duration			
	Thaw temperature (in a refrigerator) (°C)	Thaw duration (minutes)	Thaw temperature (at room temperature) (°C)	Thaw duration (minutes)
Carton of 1 or 2 syringes	2 – 8	100	15 – 25	40
Carton of 10 syringes	2 – 8	160	15 – 25	80
One syringe (removed from carton)	2 – 8	100	15 – 25	40

Handling instructions

- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- mNEXSPIKE XBB.1.5 is a white to off-white suspension. Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection.
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- Discard after single use.

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

4.3 CONTRAINDICATIONS

mNEXSPIKE XBB.1.5 is contraindicated in individuals with known severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine or to a previous dose of mNEXSPIKE XBB.1.5.

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

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

Myocarditis and pericarditis

Postmarketing data with authorised or approved COVID-19 vaccines demonstrate increased risks of myocarditis and pericarditis, particularly within the first week following vaccination and the observed risk is highest in males 12 through 24 years of age.

Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. No cases of vaccine-related myocarditis or pericarditis have been reported in clinical studies of mNEXSPIKE XBB.1.5.

Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

Altered immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished immune response to mNEXSPIKE XBB.1.5.

Limitations of vaccine effectiveness

mNEXSPIKE XBB.1.5 may not protect all vaccine recipients.

Use in the elderly

Clinical studies of mNEXSPIKE XBB.1.5 included approximately 1634 participants 65 years of age and older and 322 participants 75 years of age and older (see sections 4.8 and 5.1).

Some local and systemic adverse reactions were reported in a lower proportion of participants 65 years of age and older compared to participants 12 years through 64 years of age (see section 4.8).

Relative vaccine efficacy was similar between participants 65 years of age and older and participants 18 years through 64 years (see section 5.1).

Paediatric use

The safety and efficacy of mNEXSPIKE XBB.1.5 in children less than 12 years of age have not yet been established. No data are available.

Effects on laboratory tests

No data are available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

mNEXSPIKE XBB.1.5 can be concomitantly administered with influenza vaccines (standard and high-dose).

Different injectable vaccines should be given at different injection sites.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data are available on fertility in humans with use of mNEXSPIKE XBB.1.5.
In a combined fertility and developmental toxicity study, mRNA-1283 vaccine was administered to female rats at 80 µg/dose by the intramuscular route (4 doses spanning between pre-mating day 28 and gestation day 13). Anti-SARS-CoV-2 spike NTD and RBD antibodies were present in serum of maternal animals from prior to mating to the end of the study on lactation day 21. There were no vaccine-related adverse effects on female fertility and pregnancy rate. The effect of mNEXSPIKE XBB.1.5 on male fertility has not been determined.

Use in pregnancy – Pregnancy Category B1

No adequate and well-controlled studies of mNEXSPIKE XBB.1.5 use in pregnant women have been conducted.
Available clinical data on mNEXSPIKE XBB.1.5 administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

Pregnant individuals infected with SARS-CoV-2 are at increased risk of severe COVID-19 compared with non-pregnant individuals.

A combined fertility and developmental toxicity study in female rats, administered 80 µg/dose of mRNA-1283 vaccine twice prior to mating and twice during gestation, revealed no evidence of vaccine-related harmful effects on maternal health, pregnancy outcome, embryofetal development, or neonatal development (see Effects on Fertility). Anti-SARS-CoV-2 spike NTD and RBD antibodies were present in serum of maternal animals from prior to mating to the end of the study on lactation day 21, as well as in fetuses and offspring.

Use in lactation

In a combined fertility and developmental toxicity study in rats (see Effects on Fertility), anti-SARS-CoV-2 spike NTD and RBD antibodies were detected in milk in lactating rats (at approximately 10% of the antibody titres in maternal serum) and in serum of their nursing pups (approximately the same antibody titres as in maternal serum).

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to mNEXSPIKE XBB.1.5 is negligible. Observational data from women who were breastfeeding after vaccination with SPIKEVAX (elasomeran) and its variants have not shown a risk for adverse effects in breastfed newborns/infants.

mNEXSPIKE XBB.1.5 can be used during breast-feeding.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects of mNEXSPIKE XBB.1.5 on the ability to drive and use machines have been performed. Some of the effects mentioned under section 4.8 Adverse Effects (Undesirable Effects) may affect the ability to drive or use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Study 1 Evaluated Efficacy and Immunogenicity of Single Dose mNEXSPIKE (Bivalent Original and Omicron BA.4/BA.5)

The safety of mNEXSPIKE was evaluated in a Phase 3 randomised, observer-blind, active-controlled clinical study. Study 1 (NCT05815498) was conducted in the United States, United Kingdom, and Canada involving 11 417 participants 12 years of age and older who received a single dose of mNEXSPIKE (10 micrograms mRNA; n=5 706) or Spikevax bivalent Original/Omicron BA.4-5 (50 micrograms mRNA; n=5 711) (hereafter referred to as

comparator vaccine). The vaccine formula of both mNEXSPIKE and comparator vaccine administered in the study encoded the SARS-CoV-2 Wuhan-Hu 1 strain (Original) and Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5). The median duration of follow-up for safety was 8.8 months.

In Study 1, the median age of the population was 56 years (range 12-96); 8.7% of participants were 12 years through 17 years, 62.6% were 18 years through 64 years, and 28.7% were 65 years and older. Overall, 45.7% of the participants were male, 54.3% were female, 13.2% were Hispanic or Latino, 82.2% were White, 11.2% were Black or African American, 3.6% were Asian, 0.4% were American Indian or Alaska Native, 0.1% were Native Hawaiian or Pacific Islander, 0.4% were other races, and 1.5% were Multiracial. Demographic characteristics were similar between participants who received mNEXSPIKE and those who received comparator vaccine.

The most commonly (≥10%) reported adverse reactions following administration mNEXSPIKE were injection site pain (68.5%), fatigue (50.4%), headache (44.2%), myalgia (38.2%), arthralgia (29.7%), chills (22.7%), axillary swelling or tenderness (19.7 %) and nausea/vomiting (12.1%).

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of adverse reactions was higher in individuals aged 12 to < 65 years than in those aged 65 years and above.

Participants 12 years through 17 years of age: pain at the injection site (68.8%), headache (54.5%), fatigue (47.3%), myalgia (39.2%), axillary swelling/tenderness (34.6%), chills (31.6%), arthralgia (23.9%), and nausea/vomiting (16.1%).

Participants 18 years through 64 years of age: pain at the injection site (74.8%), fatigue (54.3%), headache (47.8%), myalgia (41.6%), arthralgia, (32.4%), chills (24.3%), axillary swelling/tenderness (21.7%), and nausea/vomiting (13.8%).

Participants 65 years of age and older: pain at the injection site (54.6%), fatigue (43.0%), headache (33.1%), myalgia (30.5%), arthralgia, (25.6%), chills (16.5%), and axillary swelling/tenderness (10.7%).

Solicited local and systemic adverse reactions reported following vaccine administration had a median duration of 2 days for mNEXSPIKE and 2 to 3 days for comparator vaccine.

Tabulated list of adverse reactions

The safety profile and the frequencies of adverse reactions presented below are based on data of 5 706 individuals aged 12 years and older who received a single dose of mNEXSPIKE in Study 1 (see section 5.1).

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 frequency (Table 4).

Table 4. Adverse reactions from mNEXSPIKE clinical studies experience in individuals 12 years of age and older

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Very common	Lymphadenopathy*
Nervous system disorders	Very common	Headache
Gastrointestinal disorders	Very common	Nausea/vomiting
Skin and subcutaneous tissue disorders	Very rare	Rash
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
General disorders and administration site conditions	Very common	Injection site pain Fatigue Chills
	Common	Pyrexia Injection site swelling Injection site erythema

*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.

mNEXSPIKE's safety and reactogenicity profile was consistent with the known safety profile of the comparator vaccine. In the overall study population, the incidence of any solicited adverse reactions was lower for the mNEXSPIKE group compared to the comparator group within 7 days after vaccination. Solicited local and systemic adverse reactions reported following vaccine administration had a median duration of 2 days for mNEXSPIKE and 2 to 3 days for the comparator vaccine. Local reactions trended lower, systemic reactions were similar.

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

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

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: Vaccines, COVID-19 vaccines, ATC code: J07BN01

Mechanism of action

The nucleoside-modified mRNA in mNEXSPIKE XBB.1.5 is formulated in lipid particles, which encodes the membrane-bound, linked N-terminal domain (NTD) and receptor-binding domain (RBD) of the spike (S) glycoprotein from SARS-CoV-2 strains, which are known to be the immuno-dominant epitopes for protective immune responses. The vaccine elicits an immune response to the NTD and RBD of the S antigen, which may contribute to protection against COVID-19.

Clinical Trials

Study 1: Evaluated efficacy and immunogenicity of single-dose mNEXSPIKE (Bivalent Original and Omicron BA.4/BA.5)

Study 1

Study 1 was a Phase 3 randomised, observer-blind, active-controlled clinical trial that evaluated the relative vaccine efficacy, safety and immunogenicity of mNEXSPIKE in participants 12 years of age and older in the United States, United Kingdom, and Canada. Randomisation was stratified by age: 12 years through 17 years, 18 through 64 years, and 65 years of age and older. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalisation for worsening disease during the 2 months before enrolment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 11 454 participants were randomised in a 1:1 ratio to receive mNEXSPIKE (10 micrograms mRNA; n=5 728), a vaccine formulation targeting Original and Omicron BA.4/BA.5 strains, or Spikevax bivalent Original/Omicron BA.4-5, the comparator vaccine (50 micrograms mRNA; n=5 726). All participants except one in the mNEXSPIKE group had previously received at least one dose of a COVID-19 vaccine prior to the study with a median time of 9.8 months since the last dose. Participants will be followed for efficacy and safety for one year.

The primary efficacy analysis population (referred to as the Per-Protocol Set for Efficacy) included 11 366 participants who received either mNEXSPIKE (n=5 679) or Spikevax bivalent Original/Omicron BA.4-5 (n=5 687). In the Per-Protocol Set for Efficacy, 45.7% of participants were male, 54.3% were female, 13.1% were Hispanic or Latino; 82.2% were White, 11.1% were African American, 3.6% were Asian, 0.4% were American Indian or Alaska Native, 0.1% were Native Hawaiian or Pacific Islander, 0.3% were other races, and 1.5% were Multiracial. The median age of participants was 56 years (range 12-96) and 28.7% of participants were 65 years of age and older. There were no notable differences in demographics between participants who received mNEXSPIKE and those who received comparator vaccine.

The population for the relative vaccine efficacy analysis included participants 12 years of age and older who were enrolled from 28 March 2023, and followed for the development of COVID-19 through 31 January 2024. The median length of follow-up was 8.8 months.

The primary efficacy hypothesis in this study was to demonstrate the non-inferior vaccine efficacy against COVID-19 starting 14 days after mNEXSPIKE to Spikevax bivalent Original/Omicron BA.4-5. The statistical criterion to demonstrate non-inferiority required that the lower bound of the 99.4% CI be >-10%; this hypothesis was successfully met (Table 5).

Table 5. Relative vaccine efficacy against COVID-19* in participants 12 years of age and older starting 14 days after a single dose of mNEXSPIKE or comparator mRNA vaccine – Per-Protocol Set for efficacy

Age	mNEXSPIKE[a]			Comparator[b]			% Relative vaccine efficacy (99.4% CI)[c]
	Participants (N)	COVID-19 cases (n)	Incidence rate of COVID-19 per 100 person-months	Participants (N)	COVID-19 cases (n)	Incidence rate of COVID-19 per 100 person-months	
All participants	5 679	560	1.4	5 687	617	1.5	9.3 (-6.6, 22.8)

* Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab for SARS-CoV-2 by RT-PCR. Listed symptoms were fever (temperature >38°C / ≥100.4°F), 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.

[a] Dosing was a single dose (10 micrograms mRNA).

[b] Dosing was a single dose (50 micrograms mRNA).

[c] Relative Vaccine Efficacy (rVE) = 1-hazard ratio (mNEXSPIKE vs. Spikevax bivalent Original/Omicron BA.4-5). Hazard ratio and CI are estimated using a stratified Cox proportional hazard model (stratified by age group per randomisation) with Efron's method of tie handling and with the treatment group as a fixed effect. Alpha-adjusted 2-sided (99.4%) CI for CDC-defined COVID-19 is calculated using Lan-DeMets O'Brien-Fleming approximation spending function (nominal one-sided alpha = 0.0028). It is based on 1177 CDC-defined COVID-19 events, representing 56.4% information fraction of target total number of events (N=2087, target rVE of 3% [mRNA-1283 vs mRNA-1273]).

A subgroup analysis of COVID-19 vaccine cases by age group was conducted (Table 6).

Table 6. Relative vaccine efficacy against COVID-19* in participants 12 years of age and older by age subgroup starting 14 days after a single dose of mNEXSPIKE or comparator mRNA vaccine – Per-Protocol Set for efficacy

Age subgroup (years)	mNEXSPIKE[a]			Comparator[b]			% Relative vaccine efficacy (95% CI)[c]
	Participants (N)	COVID-19 cases (n)	Incidence rate of COVID-19 per 100 person-months	Participants (N)	COVID-19 cases (n)	Incidence rate of COVID-19 per 100 person-months	
12 to <18	491	29	1.0	490	23	0.8	-29.2 (-123.3, 25.3)
18 to <65	3 558	382	1.4	3 562	422	1.6	9.7 (-3.8, 21.3)
≥65	1 630	149	1.3	1 635	172	1.5	13.5 (-7.7, 30.6)

* Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab for SARS-CoV-2 by RT-PCR. Listed symptoms were fever (temperature >38°C / ≥100.4°F), 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.

[a] Dosing was a single dose (10 mcg mRNA).

[b] Dosing was a single dose (50 mcg mRNA).

[c] Relative vaccine efficacy (rVE) = 1-hazard ratio (mNEXSPIKE vs. Spikevax bivalent Original/Omicron BA.4-5). Hazard ratio and CI are estimated using a Cox proportional hazard model with Efron's method of tie handling and with the treatment group as a fixed effect.

The primary immunogenicity analysis population included 621 participants who received mNEXSPIKE and 568 participants who received comparator vaccine. Among participants assessed for immunogenicity, 45.3% were male, 54.7% were female, 13.5% were Hispanic or Latino, 80.7% were White, 11.9% were African American or Black, 4.0% were Asian, <0.1% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 0.3% were other races, and 2.1% were Multiracial.

A comparison of neutralising antibody concentrations against a pseudovirus expressing SARS-CoV-2 Spike proteins from the original and Omicron BA.4/BA.5 strains was conducted. In the primary immunogenicity analyses of the GMC ratio following mNEXSPIKE compared to after the comparator vaccine, mNEXSPIKE met the pre-specified non-inferiority criterion of the lower bound of the 95% CI >0.667. Analyses of the difference in seroresponse rates also met the pre-specified non-inferiority criterion with the lower bound of the 95% CI of the SRR-difference >-10%. These analyses are summarised in Table 7 and Table 8.

Table 7. Comparison of geometric mean concentration 28 days after a single dose of mNEXSPIKE versus 28 days after a single dose of comparator mRNA vaccine – Per-Protocol immunogenicity subset *

Assay	mNEXSPIKE[a] GMC N=621 (95% CI)[b]	Comparator[c] GMC N=568 (95% CI)[b]	GMC Ratio (mNEXSPIKE / Comparator) (95% CI)[b]
Omicron BA.4/BA.5	2340.9 (2167.0, 2528.8)	1753.8 (1618.2, 1900.7)	1.3 (1.2, 1.5)
Original SARS-CoV-2 (D614G)	10631.9 (9960.2, 11348.9))	8576.5 (8012.5, 9180.1)	1.2 (1.1, 1.4)

N=Number of participants with non-missing data at the corresponding timepoint(s).

* Per-Protocol Immunogenicity Subset included a randomly selected subset of subjects who received study vaccine and did not have a major protocol deviation that impacted immune response and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose).

[a] Dosing was a single dose (10 micrograms mRNA).

[b] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (mNEXSPIKE vs. comparator vaccine) as fixed effect, adjusted by SARS-CoV-2 infection status at baseline, randomisation age group, number of prior COVID-19 boosters (0, 1, 2, >=3), and type of last prior COVID-19 vaccine. Coefficients for Least Square Means use margins by level. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[c] Comparator vaccine dosing was a single dose (50 micrograms mRNA).

Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

Table 8. Comparison of seroresponse rate 28 days after a single dose of mNEXSPIKE versus 28 days after a single dose of comparator mRNA vaccine – Per-Protocol immunogenicity subset*

Assay	mNEXSPIKE[a] Seroresponse rate[b] N=621 % (95% CI)[c]	Comparator[d] Seroresponse rate[b] N=568 % (95% CI)[c]	Difference in seroresponse rate (mNEXSPIKE - comparator) % (95% CI)[e]
Omicron BA.4/BA.5	79.9 (76.5, 83.0)	65.5 (61.4, 69.4)	14.4 (9.3, 19.4)
Original SARS-CoV-2 (D614G)	83.6 (80.4, 86.4)	72.9 (69.0, 76.5)	10.7 (6.0, 15.4)

N=Number of participants with non-missing data at the corresponding timepoint(s).

* Per-Protocol immunogenicity subset included a randomly selected subset of subjects who received study vaccine, and did not have a major protocol deviation that impacted immune response and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose).

[a] mNEXSPIKE dosing was a single dose (10 micrograms mRNA).

[b] Seroresponse is defined as an antibody value change from baseline below the LLOQ to ≥4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ and <4 × LLOQ, or at least a 2-fold rise if baseline is ≥4 × LLOQ, where baseline refers to pre-dose.

[c] 95% CI is calculated using the Clopper-Pearson method.

[d] Comparator dosing was a single dose (50 micrograms mRNA).

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Study 2

Study 2: Evaluated immunogenicity of single-dose mNEXSPIKE (Monovalent XBB.1.5)

Study 2 was a Phase 3 randomised, observer-blind, active-controlled clinical trial that evaluated the immunogenicity and safety of mNEXSPIKE XBB.1.5 in participants 12 years of age and older in Japan. Randomisation was stratified by age: 12 years through 17 years, 18 through 64 years, and 65 years of age and older. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalisation for worsening disease during the two months before enrolment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 692 participants were randomised in a 1:1 ratio to receive mNEXSPIKE XBB.1.5 (10 micrograms mRNA; n=344), a vaccine formulation targeting Omicron XBB.1.5, or comparator vaccine [targeting Omicron XBB.1.5 (50 mcg mRNA; n=348)]. All participants had previously received at least one dose of a COVID-19 vaccine prior to the study with a median time of 16.7 months since the last dose.

The primary immunogenicity analysis population included 334 participants who received mNEXSPIKE XBB.1.5 and 334 participants who received comparator vaccine. Among participants assessed for immunogenicity, 65.0% were male, 35.0% were female, and all participants were Asian. The median age of participants was 52 years (range 12-83) and 20.7% of participants were 65 years of age and older.

A comparison of neutralising antibody concentrations against a pseudovirus expressing Omicron XBB.1.5 strains was conducted. In the primary immunogenicity analyses of the GMC ratio following mNEXSPIKE XBB.1.5 compared to after the comparator vaccine, mNEXSPIKE XBB.1.5 met the pre-specified non-inferiority criterion of the lower bound of the 95% CI >0.667. Analyses of the difference in seroresponse rates also met the pre-specified non-inferiority criterion with the lower bound of the 95% CI of the SRR-difference >-10%. These analyses are summarised in Table 9 and Table 10.

Table 9. Comparison of geometric mean concentration 28 days after a single dose of mNEXSPIKE XBB.1.5 versus 28 days after a single dose of comparator mRNA vaccine – Per-Protocol immunogenicity set*

Assay	mNEXSPIKE XBB.1.5 GMC (95% CI)[a] N=334	Comparator[b] GMC (95% CI)[a] N=334	GMC Ratio (mNEXSPIKE XBB.1.5 / comparator) (95% CI)[a]
Omicron XBB.1.5	1757.2 (1580.1, 1954.3)	1470.4 (1322.4, 1635.0)	1.20 (1.03, 1.39)

N=Number of participants with non-missing data at baseline and the corresponding timepoint(s).

* Per-Protocol immunogenicity set included subjects who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose).

[a] The log-transformed antibody levels are analysed using an analysis of covariance (ANCOVA) model with the group variable (mNEXSPIKE XBB.1.5 vs. comparator vaccine) as fixed effect, adjusted by SARS-CoV-2 infection status at baseline, randomization age group, number of prior COVID-19 boosters (0, 1, 2, >=3), and type of last prior COVID-19 vaccine. LS means are based on observed margin. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[b] Comparator vaccine dosing was a single dose (SPIKEVAX 2024-2025 Formula 50 mcg mRNA). Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

Table 10. Comparison of seroresponse rate 28 days after a single dose of mNEXSPIKE XBB.1.5 versus 28 days after a single dose of comparator mRNA vaccine – Per-Protocol immunogenicity set*

Assay	mNEXSPIKE XBB.1.5 Seroresponse rate[a] % (95% CI)[b] N=334	Comparator Seroresponse rate[a] % (95% CI)[b] N=334	Difference in seroresponse rate (mNEXSPIKE XBB.1.5 - comparator) % (95% CI)[c]
Omicron XBB.1.5	92.2 (88.8, 94.9)	86.8 (82.7, 90.3)	5.4 (0.8, 10.2)

N=Number of participants with non-missing data at baseline and the corresponding timepoint(s).

* Per-Protocol immunogenicity set included subjects who received study vaccine, did not have a major protocol deviation that impacted immune response, and had both pre-dose and post-dose immunogenicity assessment at timepoint of primary interest (28 days post-dose).

[a] Seroresponse is defined as an antibody value change from baseline below the LLOQ to ≥4 × LLOQ, or at least a 4-fold rise if baseline is ≥ LLOQ and <4 × LLOQ, or at least a 2-fold rise if baseline is ≥4 × LLOQ, where baseline refers to pre-dose.

[b] 95% CI is calculated using the Clopper-Pearson method.

[c] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

5.2 PHARMACOKINETIC PROPERTIES

Not applicable.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

The 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 SM-102-containing lipid nanoparticles was negative in a rat bone marrow micronucleus assay (IV dose of SM-102 32.7

mg/kg, PEG-2000-DMG 5.4 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 lipid components SM-102 and PEG-2000-DMG is very low. The other components of mNEXSPIKE XBB.1.5 (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
Sucrose

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

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.

9 months at -40°C to -15°C.

Within the period of 9 months, after removal from the freezer, pre-filled syringes may be stored refrigerated at 2°C to 8°C, protected from light, for 30 days (see section 6.4).

Once thawed, the vaccine should not be refrozen.

Pre-filled syringes may be stored at 23°Cto 27°Cup to 24 hours after removal from refrigerated conditions.

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

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store in a freezer at -40°C to -15°C.

Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

For storage conditions after thawing, see section 6.3.

Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C
If transport at -40°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C. Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use. Pre-filled syringe transport duration is limited by the shipper qualification.

6.5 NATURE AND CONTENTS OF CONTAINER

0.2 mL suspension in a pre-filled syringe (cyclic olefin copolymer) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in either a blister pack or a paper inner tray within a carton containing 1, or 10 pre-filled syringes.

Pack sizes:

1 pre-filled syringe

10 pre-filled syringes

Each pre-filled syringe contains 0.2 mL.

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

6.7 PHYSICOCHEMICAL PROPERTIES

CAS number
3004805-96-0

7. MEDICINE SCHEDULE (POISONS STANDARD)

Prescription only medicine (Schedule 4)

8. SPONSOR

Moderna Australia Pty Ltd
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www.modernacovid19global.com/au/
Phone: 1800 344 018

Email address: wecare@modernatx.com

9. DATE OF FIRST APPROVAL

18 December 2025