New Zealand Data sheet

1 PRODUCT NAME

NUVAXOVID COVID-19 Vaccine 5 micrograms adjuvanted, suspension for injection [SARS-CoV-2 rS (NVX-CoV2373)]

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

These are multidose vials which contain 5 doses or 10 doses of 0.5 mL per vial (see section 6.5).

One dose (0.5 mL) contains 5 micrograms of SARS-CoV-2 spike protein* and is adjuvanted with Matrix-M.

Adjuvant Matrix-M contains, per 0.5 mL dose: Quillaja Saponaria saponins fraction A (42.5 micrograms) and Quillaja Saponaria saponins fraction C (7.5 micrograms), see section 6.5.

*produced by recombinant DNA technology using baculovirus expressions system in an insect cell line that is derived from Sf9 cells from the *Spodoptera frugiperda* species.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection.

NUVAXOVID is colourless to slightly yellow, clear to mildly opalescent.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

NUVAXOVID has provisional consent (see Section 5.1) for the indication:

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

Dosage

Primary series

NUVAXOVID is administered intramuscularly as a course of 2 doses of 0.5 mL each. It is recommended that the second dose is to be administered 3 weeks after the first dose, see section 5.1.

Booster Dose

Individuals 12 years of age and older

A booster dose of NUVAXOVID (0.5 mL) may be administered intramuscularly at least 6 months after completion of the second dose of the primary series in adults 18 years of age and older and at least 5 months after completion of the second dose of the primary series in adolescents 12 to 17 years of age. NUVAXOVID may be administered as a homologous booster dose following completion of a primary series with NUVAXOVID or as a heterologous booster dose following completion of a primary series with another approved COVID-19 vaccine, in accordance with official recommendations.

The decision when and for whom to implement a booster dose of NUVAXOVID should be made based on available vaccine safety and effectiveness data (see sections 4.8 and 5.1), in accordance with official recommendations.

Interchangeability

There are no data available on the interchangeability of NUVAXOVID with other COVID-19 vaccines to complete the primary vaccination course. Individuals who have received a first dose of NUVAXOVID should receive the second dose of NUVAXOVID to complete the vaccination course, see section 4.4.

For precautions for administering the vaccine, see section 4.4.

Method of Administration

NUVAXOVID is for intramuscular injection only, preferably into the deltoid muscle of the upper arm.

Do not inject the vaccine intravascularly, subcutaneously, or intradermally.

This vaccine should be handled by a healthcare professional using aseptic techniques to ensure the sterility of each dose. The vaccine contains no antimicrobial preservative.

The vaccine comes ready to use. Do not dilute.

Inspect the vial:

- Gently swirl the multidose vial before and in between each dose withdrawal. Do not shake.
    - Each multidose vial contains a colourless to slightly yellow, clear to mildly opalescent suspension free from visible particles.
    - Visually inspect the contents of the vial for visible particulate matter and/or discolouration prior to administration. Do not administer the vaccine if either are present.

Administer the vaccine:

- An overfill is included per vial to ensure that a maximum of five doses (vial of 2.5 mL) or ten doses (vial of 5 mL) of 0.5 mL each can be extracted.
- Each 0.5 mL dose is withdrawn into a sterile needle and sterile syringe to be administered by intramuscular injection, preferably in the deltoid muscle of the upper arm.
- Use a separate sterile needle and syringe for each individual dose, prior to use in a vaccination session.
    - Do not mix the vaccine in the same syringe with any other vaccines or medicinal products.
    - Do not pool excess vaccine from multiple vials.

Storage after first needle puncture:

- NUVAXOVID t contains no antimicrobial preservative. Store the opened vial between 2°C to 25°C for up to 12 hours after first puncture, see section 6.3.
- Record the date and time of discard on the vial label.

Discard:

- Discard this vaccine if not used within 12 hours after first puncture of the vial, see section 6.3.

For instructions regarding disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special Warnings and Precautions for Use

Hypersensitivity and Anaphylaxis

Events of anaphylaxis have been reported with COVID-19 vaccines including NUVAXOVID. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of NUVAXOVID.

Myocarditis and Pericarditis

Myocarditis and pericarditis have been reported in male and female adults within 14 days of administering NUVAXOVID (see section 4.8 Undesirable Effects).

Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general.

Available data cannot determine a causal association with NUVAXOVID.

Vaccinated individuals, parents and caregivers 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.

The risk of myocarditis and pericarditis after a third dose of NUVAXOVID has not yet been characterized.

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 an 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 been assessed in a limited number of immunocompromised individuals. The efficacy of NUVAXOVID 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 7 days after their second dose. As with all vaccines, vaccination with NUVAXOVID may not protect all vaccine recipients.

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.

Use in the Elderly

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

Paediatric Use

The safety and efficacy of NUVAXOVID in children less than 12 years of age have not yet been established. Limited data are available.

Effects on Laboratory Tests

No data available.

4.5 Interaction with Other Medicines and Other Forms of Interaction

No interaction studies have been performed.

Co-administration of NUVAXOVID with inactivated influenza vaccines has been evaluated in a limited number of adult participants in an exploratory clinical trial sub-study (2019nCoV-302), see section 4.8 and section 5.1.

The binding antibody response to SARS-CoV-2 was lower when NUVAXOVID was given concomitantly with inactivated influenza vaccine. The seroconversion rates of these participants, given NUVAXOVID and flu vaccine concomitantly, were similar to the seroconversion rates of the participants in the main study who received NUVAXOVID alone. The clinical significance of this is unknown.

Concomitant administration of NUVAXOVID 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.

A developmental and reproductive toxicity study was performed in female rats administered four intramuscular doses (2 prior to mating; 2 during gestation) of 5 micrograms SARS-CoV-2 rS protein (approximately 200-fold excess relative to the human dose of 5 micrograms on a body surface-adjusted basis) with 10 micrograms Matrix-M adjuvant (approximately 7-fold excess relative to the human dose of 50 micrograms on a body surface-adjusted basis). No vaccine-

related adverse effects on female fertility, pregnancy/lactation, or development of the embryo/fetus and offspring through post-natal Day 21 were observed. The study did not evaluate effects on male fertility.

Use in Pregnancy – Pregnancy Category B1

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

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

Administration of NUVAXOVID 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 NUVAXOVID is excreted in human milk.

4.7 Effects on Ability to Drive and Use Machines

NUVAXOVID has no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable Effects

Summary of Safety Profile

Participants 18 years of age and older – after 2-dose primary series

The safety of NUVAXOVID was evaluated from an interim analysis of pooled data from 5 ongoing clinical trials conducted in Australia, South Africa, the United Kingdom, and the United States and Mexico. At the time of the analysis, a total of 49,950 participants age 18 years and older received at least 1 dose of NUVAXOVID (n=30,058) or placebo (n=19,892). At the time of vaccination, the median age was 48 years (range 18 to 95 years). The median duration of follow-up was 70 days post-Dose 2, with 32,993 (66%) participants completing more than 2 months follow-up post-Dose 2.

Of the pooled reactogenicity data, which includes participants aged 18 and older enrolled in the 2 Phase 3 studies who received any dose of NUVAXOVID (n=20,055) or placebo (n=10,561), the most frequent adverse reactions were injection site tenderness (75%), injection site pain (62%), fatigue (53%), myalgia (51%), headache (50%), malaise (41%), arthralgia (24%) and nausea or vomiting (15%). Adverse reactions were usually mild to moderate in severity with a median duration of less than or equal to 2 days for local events and less than or equal to 1 day for systemic events following vaccination.

Overall, there was a higher incidence of adverse reactions in younger age groups: the incidence of injection site tenderness, injection site pain, fatigue, myalgia, headache, malaise, arthralgia, and nausea or vomiting was higher in adults aged 18 to less than 65 years than those aged 65 years and above.

Local and systemic adverse reactions were more frequently reported after Dose 2 than Dose 1.

Licensed inactivated seasonal influenza vaccines were co-administered on the same day as the Dose 1 of NUVAXOVID (n=217) or placebo (n=214) in the opposite deltoid muscle of the arm in 431 participants enrolled in an exploratory Phase 3 (2019nCoV-302) sub-study. The frequency of local and systemic adverse reactions in the influenza sub-study population was higher than in the main study population following Dose 1 in both NUVAXOVID and placebo recipients. Frequencies of solicited local and systemic adverse reactions were similar between the sub-study and main study populations following Dose 2 of NUVAXOVID alone.

Overall, a lower frequency of reactogenicity events was associated with greater age across the 5 main studies and seasonal influenza vaccine sub-study.

Adolescents 12 to 17 years of age – after 2-dose primary series

The safety of NUVAXOVID in adolescents was evaluated in an interim analysis of the paediatric expansion portion of an ongoing Phase 3 multicentre, randomised, observer-blinded, placebo-controlled study (Study 2019nCoV-301).

Safety data were collected in 2,232 participants 12 to 17 years of age, with and without evidence of prior SARS CoV-2 infection, in United States who received at least 1 dose of NUVAXOVID (n=1,487) or placebo (n=745).

Demographic characteristics were similar among participants who received NUVAXOVID and those who received placebo.

The most frequent adverse reactions were injection site tenderness (71%), injection site pain (67%), headache (63%), myalgia (57%), fatigue (54%), malaise (43%), nausea or vomiting (23%), arthralgia (19%) and pyrexia (17%). Fever was observed more frequently in adolescents 12 to 17 years of age compare with adults, with the frequency being very common after the second dose in adolescents. Adverse reactions were usually mild to moderate in severity with a median duration of less than or equal to 2 days for local events and less than or equal to 1 day for systemic events following vaccination.

Tabulated List of Adverse Reactions

Adverse reactions observed in individuals 12 years and older during clinical studies are listed below according to the following frequency categories:

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).

Table 1: Adverse Reactions from Clinical Trials in Individuals 12 Years of Age and Older

MedDRA System Organ Class	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)
Blood and lymphatic system disorders			Lymphadenopathy		
Nervous system disorders	Headache				
Vascular disorders			Hypertension[d]		
Gastrointestinal disorders	Nausea or vomiting[a]				
Skin and subcutaneous tissue disorders			Rash Erythema Pruritus Urticaria		
Musculoskeletal and connective tissue disorders	Myalgia[a], Arthralgia[a]				
General disorders and administration site conditions	Injection site tenderness[a], Injection site pain[a], Fatigue[a], Malaise[a,b]	Injection site redness[a,c], Injection site swelling[a], Pyrexia[e], Chills, Pain in extremity	Injection site pruritus		

[a] Higher frequencies of these events were observed after the second dose.
[b] This term included events recorded as influenza-like illness
[c] This term includes both injection site redness and injection site erythema (common)
[d] Hypertension was not reported in the adolescent population in the clinical study
[e] Pyrexia was observed more frequently in adolescents 12 to 17 years compared with adults, with the frequency being very common after the second dose in adolescents.

Participants 18 Years of Age and Older – After Booster Dose

The safety and immunogenicity of a booster dose of Nuvaxovid was evaluated in an ongoing Phase 2 randomised, placebo-controlled, observer-blinded clinical study (Study 2019nCoV-101, Part 2) conducted in participants aged 18 to 84 years of age. A total of 254 participants received 2 doses of NUVAXOVID (0.5 mL 3 weeks apart) as the primary vaccination series. A subset of 105 participants (Safety Analysis Set) were randomised to receive a booster dose of NUVAXOVID approximately 6 months after receiving Dose 2 of the primary series; 104 of the 105 participants received NUVAXOVID. The most frequent solicited adverse reactions were injection site tenderness (81%), fatigue (63%), injection site pain (55%), muscle pain (51%), malaise (47%) and headache (46%), joint pain (29%), and fever (17%) with a median duration of 1 to 3 days following vaccination.

In a second ongoing Phase 2a/b randomised, placebo-controlled, observer-blinded clinical study conducted in South Africa (Study 2019nCoV-501), the immunogenicity and safety of a booster dose of NUVAXOVID was evaluated in healthy HIV-negative participants aged 18 to 84 years of age (Cohort 1) and medically stable people living with HIV (PLWH) aged 18 to 64 years of age (Cohort 2). Overall, 1,898 participants (Safety Analysis Set) received a booster dose of NUVAXOVID approximately 6 months after receiving the second dose of a 2-dose primary series. Solicited adverse reactions were not collected following the booster dose. The unsolicited adverse reaction profile for the booster dose was similar to that of the primary series presented in Table 1.

The safety and immunogenicity of a booster dose of NUVAXOVID was evaluated in an ongoing Phase 3, multicentre, randomized, observer-blinded, placebo-controlled study (Study 2019nCoV-301). Overall, 12,777 participants received a booster dose of NUVAXOVID at least 6 months after the two-dose primary series (median of 11 months between completion of primary series and booster dose). Of the 12,777 participants who received a booster dose, 39 participants did not receive NUVAXOVID for all three doses. The safety analyses included evaluation of solicited local and systemic adverse reactions within 7 days after a booster dose for participants who completed the electronic diary (n=10,137). The most frequent solicited adverse reactions were injection site pain/tenderness (78.5%), fatigue/malaise (58.2%), muscle pain (51.4%), headache (45.4%), and joint pain (26.1%).

Adolescents 12 to 17 Years of Age– After Booster Dose

The safety of a booster dose of NUVAXOVID was evaluated in an interim analysis of the paediatric expansion portion of an ongoing Phase 3 multicentre, randomized, observer-blinded, placebo-controlled study (Study 2019nCoV-301). A total of 2,122 participants received two doses of NUVAXOVID (0.5 mL 3 weeks apart) as the primary vaccination series. A total of 1,499 participants received a booster dose of NUVAXOVID approximately 9 months after receiving Dose 2 of the primary series. A subset of 220 participants who received the booster dose of NUVAXOVID were evaluated for solicited adverse reactions within 7 days after the booster dose (Ad Hoc Booster Safety Analysis).

The most frequent solicited adverse reactions were tenderness (71.6%), pain (63.7%), headache (68.4%), fatigue (65.8%), muscle pain (61.6%), malaise (46.8%), and nausea/vomiting (26.3%) with a median duration of 1 to 2 days following vaccination. No new safety concerns from the time of the booster dose administration to 28 days after administration were noted among participants.

Booster Dose Following Primary Vaccination with Other COVID-19 Vaccine

The safety of NUVAXOVID as a heterologous booster in individuals whose primary vaccination series was with other COVID-19 vaccines, has been reported in the COV-BOOST study conducted in the UK (ISRCTN 73765130). This was an independent randomised, controlled, phase 2 trial that evaluated a single heterologous booster vaccination against COVID-19 in adults aged 30 years and older, with no history of laboratory-confirmed SARS-CoV-2 infection, at least 10 weeks after a primary vaccination series. Within the group assigned to receive a full dose of NUVAXOVID (0.5 mL) were 115 participants who previously received 2 doses of VAXZEVRIA (median age 65 years) and 114 who had received 2 doses of COMIRNATY (mean age 63 years). The booster dose of NUVAXOVID was given a median of 76 days after the VAXZEVRIA primary series and 105 days after the COMIRNATY primary series. Additionally, another 220 participants received a half dose of NUVAXOVID (0.25 mL). Review of the adverse reactions over the 28 days following NUVAXOVID booster did not identify any new safety concerns, as compared with adverse reactions reported following 2 doses of NUVAXOVID given as a primary series. The safety data are limited by the small sample size of the study.

Description of Selected Adverse Reactions

Throughout the clinical trials, an increased incidence of hypertension following vaccination with NUVAXOVID (n=46, 1.0%) as compared with placebo (n=22, 0.6%) was observed in older adults during the 3 days following vaccination.

Post-marketing Experience

The following adverse reactions have been spontaneously reported during post-authorisation use of NUVAXOVID. As these reactions were derived from spontaneous reports, the frequencies could not be determined and are thus considered as not known.

Table 2: Adverse Reactions from Post-marketing Experience

System Organ Class	Adverse Drug Reaction
Immune system disorders	Anaphylaxis
Cardiac disorders	Pericarditis, myocarditis
Nervous system disorders	Hypoaesthesia, paraesthesia
Ear and labyrinth disorders	Tinnitus

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

No case of overdose has been reported. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Other viral vaccines, ATC code: J07BX03

Mechanism of Action

NUVAXOVID is composed of purified full-length SARS-CoV-2 recombinant spike (S) protein that is stabilised in its prefusion conformation. The addition of the saponin-based Matrix-M adjuvant facilitates activation of the cells of the innate immune system, which enhances the magnitude of the S protein-specific immune response. The 2 vaccine components elicit B- and T-cell immune responses to the S protein, including neutralising antibodies, which protect against COVID-19.

Clinical Trials

Two early phase clinical trials were conducted as clinical Study 2019nCoV-101; a Phase 1 (first-in-human)/Phase 2, randomized, observer-blinded, placebo-controlled trial evaluating the safety and immunogenicity of 5-µg and 25-µg doses of SARS-CoV-2 rS with or without 50 µg Matrix-M adjuvant. The Phase 1 study in 131 healthy adult participants aged 18 – 59 was conducted in Australia (Part 1), and the Phase 2 study in 1,283 healthy adult participants aged 18 – 84 was conducted in both Australia and the US (Part 2).

Part 1: Two-dose regimens of 5 µg or 25 µg SARS-CoV-2 rS with 50 µg Matrix-M adjuvant, administered 21 to 28 days apart as a bedside mixture, induced robust immune responses (anti-S protein IgG, wild-type neutralising, and hACE2 receptor binding inhibition), peaking 2 weeks after second vaccination (Day 35). Matrix-M adjuvant was antigen sparing, induced high levels of functional antibodies, and showed a Th1-biased immune response. No dose response was seen between the 5-µg and 25-µg doses.

Part 2: Two-dose regimens of 5 µg or 25 µg SARS-CoV-2 rS with 50 µg Matrix-M adjuvant, administered 21 days apart as co-formulated drug product (NUVAXOVID), showed similar results (to Part 1), at Day 35.

Both dose levels were well tolerated and induced robust immune responses after the second vaccination (Day 35). Collectively, the data from Part 1 and Part 2 of Clinical Study 2019nCoV-101 supported selection and further development of the 2-dose 5 µg adjuvanted vaccine. The clinical efficacy, safety, and immunogenicity of NUVAXOVID is being evaluated in 2 pivotal, placebo-controlled, Phase 3 studies: Study 1 (2019nCoV-301) conducted in North America and Study 2 (2019nCoV-302) conducted in the United Kingdom, and a Phase 2a/b study (Study 3) conducted in South Africa.

Study 1 (2019nCoV-301) - 2-dose Primary Series

Study 1 is an ongoing Phase 3, multicentre, randomised, observer-blinded, placebo-controlled study conducted in participants 18 years of age and older in United States (US) and Mexico (main study) expanded to include a paediatric cohort including participants 12 to 17 years of age in the US (paediatric expansion).

Efficacy in Adults 18 years of age or older

Upon enrolment in the main study, participants were stratified by age (18 to 64 years and ≥ 65 years) and assigned in a 2:1 ratio to receive NUVAXOVID or placebo. The study excluded participants who were significantly immunocompromised due to immunodeficiency disease; active cancer on chemotherapy; received chronic immunosuppressive therapy or received immunoglobulin or blood derived products within 90 days; were pregnant or breastfeeding; or had a history of laboratory-confirmed diagnosed COVID-19. Participants with clinically stable underlying comorbidity were included as were participants with well-controlled human immunodeficiency virus (HIV) infection.

Enrolment of adults completed in February 2021. Participants will be followed for up to 24 months after the first dose for assessments of safety, and efficacy against COVID-19. Following collection of sufficient safety data to support an application for emergency use authorisation, initial recipients of placebo were invited to receive 2 injections of NUVAXOVID 21 days apart and initial recipients of NUVAXOVID to receive 2 injections of placebo 21 days apart ('blinded crossover'). All participants were offered the opportunity to continue to be followed in the study.

The primary efficacy analysis population (referred to as the Per-Protocol Efficacy [PP-EFF] analysis set) included 25,452 participants who received either NUVAXOVID (n=17,312) or placebo (n=8,140), received 2 doses (Dose 1 on Day 0; Dose 2 at Day 21, median 21 days [IQR 21 – 23], range 14 – 60), did not experience an exclusionary protocol deviation, and did not have evidence of SARS-CoV-2 infection through 7 days after the second dose.

Demographic and baseline characteristics were balanced amongst participants who received NUVAXOVID and those who received placebo. In the PP-EFF analysis set for participants who received NUVAXOVID, the median age range was 47 years (range: 18 to 95 years); 88.2% (n=15,264) were 18 to 64 years old and 12% (n=2,048) were aged 65 and older; 48% were female; 94% were from the United States and 6% were from Mexico; 76% were White, 11% were Black or African American, 6% were American Indian (including Native Americans) or Alaskan Native, and 4% were Asian; 22% were Hispanic or Latino. A total of 16,493 (95.3%) participants had at least 1 pre-existing comorbidity or lifestyle characteristic associated with an increased risk of severe COVID-19 was present in 16,493 (95%) participants. Comorbidities included: obesity (body mass index (BMI) ≥ 30 kg/m^2); chronic lung disease; diabetes mellitus type 2; cardiovascular disease; chronic kidney disease; or HIV. Other high-risk characteristics included age ≥ 65 years (with or without comorbidities) or age < 65 years with comorbidities and/or living or working conditions involving known frequent exposure to SARS-CoV-2 or to densely populated circumstances.

COVID-19 cases were confirmed by polymerase chain reaction (PCR) testing through a central laboratory. Vaccine efficacy is presented in Table 3.

Table 3: Vaccine Efficacy Analyses of PCR-confirmed COVID-19 with Onset from 7 Days After Second Vaccination[1] - PP-EFF Analysis Set; Study 1 (2019nCoV-301)

Subgroup	NUVAXOVID			Placebo			% Vaccine Efficacy (95% CI)
	Partici-pants N	COVID-19 cases n (%)	Incidence Rate Per Year Per 1,000 People[2]	Partici-pants N	COVID-19 cases n (%)	Incidence Rate Per Year Per 1,000 People[2]	
Primary efficacy endpoint							
All participants	17,312	14 (0.1)	3.26	8,140	63 (0.8)	34.01	90.40% (82.88, 94.62) [3,4]

[1] VE evaluated in participants without major protocol deviations who were seronegative (for SARS-CoV-2) at baseline and did not have a laboratory confirmed current SARS-CoV-2 infection with symptom onset up to 6 days after the second dose, and who had received the full prescribed regimen of the trial vaccine.

[2] Mean disease incidence rate per year in 1,000 people.

[3] Based on log-linear model of PCR-confirmed COVID-19 infection incidence rate using Poisson regression with treatment group as fixed effects and robust error variance, where VE = 100 × (1 – relative risk).

[4] Met primary efficacy endpoint criterion for success with a lower bound confidence interval (LBCI) > 30%.

Vaccine efficacy of NUVAXOVID to prevent the onset of COVID-19 from 7 days after Dose 2 was 90.4% (95% CI 82.9 – 94.6). No cases of moderate or severe COVID-19 were reported in the 17,312 NUVAXOVID participants compared with 4 cases of severe COVID-19 reported in the 8,140 placebo recipients in the PP-EFF analysis set.

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates for male and female participants and racial groups, and across participants with medical comorbidities associated with high risk of severe COVID-19. There were no meaningful clinical differences in overall vaccine efficacy in participants who were at increased risk of severe

COVID-19 including those with 1 or more comorbidities that increase the risk of severe COVID-19 (eg, BMI ≥ 30 kg/m^2, chronic lung disease, diabetes mellitus type 2, cardiovascular disease, and chronic kidney disease).

Efficacy results reflect enrolment that occurred during the time period when strains classified as Variants of Concern or Variants of Interest were predominantly circulating in the 2 countries (US and Mexico) where the study was conducted. Sequencing data were available for 61 of the 77 endpoint cases (79%). Of these, 48 out of 61 (79%) were identified as Variants of Concern or Variants of Interest. The most common Variants of Concern were Alpha with 31/61 cases (51%), Beta (2/61, 4%) and Gamma (2/61, 4%), while the most common Variants of Interest were Iota with 8/61 cases (13%) and Epsilon 3/61 (5%).

Efficacy in Adolescents 12 to 17 years of age

The assessment of efficacy and immunogenicity of NUVAXOVID in adolescent participants 12 to 17 years of age occurred in the US in the ongoing paediatric expansion portion of the Phase 3 2019nCoV-301 study.

A total of 1,799 participants assigned in a 2:1 ratio to receive 2 doses of NUVAXOVID (n=1,205) or placebo (n=594) by intramuscular injection 21 days apart represented the primary efficacy population.

COVID-19 was defined as first episode of PCR-confirmed mild, moderate, or severe COVID-19 with at least 1 or more of the predefined symptoms within each severity category. There were 20 cases of PCR-confirmed symptomatic mild COVID-19 (NUVAXOVID, n=6; placebo, n=14) resulting in a point estimate of efficacy of 79.5% (95% CI: 46.8%, 92.1%).

At the time of this analysis, the Delta (B.1.617.2 and AY lineages) variant of concern (VOC) was the predominant variant circulating in the US and accounted for all cases where sequence data are available (11/20, 55%).

Immunogenicity in Adolescents 12 to 17 years of age

An analysis of the SARS-CoV-2 neutralising antibody response 14 days after Dose 2 (Day 35) was conducted in adolescent participants seronegative to anti-SARS-CoV-2 nucleoprotein (NP)/PCR-negative at baseline compared with that observed in seronegative/PCR-negative adult participants aged 18 to less than 26 years from the main study, in adults (Per Protocol Immunogenicity (PPIMM) Population, before crossover). Noninferiority (lower bound 95% CI for the geometric mean ratio [GMR] > 0.67 [1.25]) was met as presented in Table 4.

Table 4: Adjusted Ratio of Geometric Mean of Microneutralisation Assay Neutralising Antibody Titers for SARS-CoV-2 S Wild-Type Virus at 14 Days After Dose 2 and Presented by Age Group (PPIMM Analysis Set)[1]

Assay	Timepoint	Paediatric Expansion (12 to 17 Years) N=390	Adult Main Study (18 to < 26 Years) N=416	12 to 17 Years versus 18 to < 26 Years
		GMT 95% CI[2]	GMT 95% CI [2]	GMR 95% CI [2]
Microneutralisation (1/dilution)	Day 35 (14 days after Dose 2)	3859.6 (3422.8, 4352.1)	2633.6 (2388.6, 2903.6)	1.46 (1.25, 1.71) [3]

Abbreviations: ANCOVA = analysis of covariance; CI = confidence interval; GMR = ratio of GMT, which is defined as the ratio of 2 GMTs for comparison of 2 age cohorts; GMT = geometric mean titer; LLOQ = lower limit of quantitation; MN = microneutralisation; N = number of participants in assay-specific PP-IMM Analysis Set in each part of study with non-missing response at each visit; PP-IMM = Per-Protocol Immunogenicity; SARS-CoV-2 = severe acute respiratory syndrome coronavirus2.

[1] Table includes participants in the active vaccine group only.

[2] An ANCOVA with age cohort as main effect and baseline MN Assay neutralising antibodies as covariate was performed to estimate the GMR. Individual response values recorded as below the LLOQ were set to half LLOQ.

[3] Represents (n1, n2) populations defined as:

n1 = number of participants in adult main study (18 to < 26 years) with non-missing neutralising antibodies result

n2 = number of participants in paediatric expansion (12 to < 18 years) with non-missing neutralising antibodies result

Study 2 (2019nCoV-302)

Study 2 is an ongoing Phase 3, multicenter, randomised, observer-blinded, placebo-controlled study in participants 18 to 84 years of age in the United Kingdom (UK). Upon enrolment, participants were stratified by age (18 to 64 years; 65 to 84 years) to receive NUVAXOVID or placebo. The study excluded participants who were significantly immunocompromised due to immunodeficiency disease; current diagnosis or treatment for cancer; autoimmune disease/condition; received chronic immunosuppressive therapy or received immunoglobulin or blood derived products within 90 days; bleeding disorder or continuous use of anticoagulants; history of allergic reactions and/or anaphylaxis; were pregnant; or had a history of laboratory-confirmed diagnosed COVID-19. Participants with clinically stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 4 weeks before enrolment were included. Participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV) were not excluded from enrolment.

Enrolment was completed in November 2020. Participants are being followed for up to 12 months after the primary vaccination series for assessments of safety, and efficacy against COVID-19.

The primary efficacy PP-EFF analysis set included 14,039 participants who received either NUVAXOVID (n=7,020) or placebo (n=7,019), received 2 doses (Dose 1 on day 0; Dose 2 at median 21 days [IQR 21 – 23], range 16 – 45), did not experience an exclusionary protocol deviation, and did not have evidence of SARS-CoV-2 infection through 7 days after the second dose.

Demographic and baseline characteristics were balanced amongst participants who received NUVAXOVID and participants who received placebo. In the PP-EFF analysis set for participants who received NUVAXOVID, the median age was 56 years (range: 18 to 84 years); 72% (n=5,067) were 18 to 64 years old and 28% (n=1,953) were aged 65 to 84; 49% were female; 94% were White; 3% were Asian; 1% were multiple races, < 1% were Black or African American; and < 1% were Hispanic or Latino; and 45% had at least 1 comorbid condition.

Table 5: Vaccine Efficacy Analysis of PCR-confirmed COVID-19 with Onset at Least 7 Days After the Second Vaccination - (PP-EFF population): Study 2 (2019nCoV-302)

Subgroup	NUVAXOVID			Placebo			% Vaccine Efficacy (95% CI)
	Partici-pants N	COVID-19 cases n (%)	Incidence Rate Per Year Per 1,000 People[1]	Partici-pants N	COVID-19 cases n (%)	Incidence Rate Per Year Per 1,000 People[1]	
Primary efficacy endpoint							
All participants	7,020	10 (0.1)	6.53	7,019	96 (1.4)	63.43	89.7 (80.2, 94.6) [2,3]
Subgroup analyses of the primary efficacy endpoint							
18 to 64 years of age	5,067	9 (0.2)	12.30	5,062	87 (1.7)	120.22	89.8 [2] (79.7, 94.9)
65 to 84 years of age	1,953	1 (0.10) [3]	—	1,957	9 (0.9) [2]	—	88.9% [4] (20.2, 99.7)

[1] Mean disease incidence rate per year in 1000 people.

[2] Based on Log-linear model of occurrence using modified Poisson regression with logarithmic link function, treatment group and strata (age-group and pooled region) as fixed effects and robust error variance.

[3] Met primary efficacy endpoint criterion for success with a lower bound confidence interval (LBCI) > 30% efficacy has been confirmed at the interim analysis.

[4] Based on the Clopper-Pearson model (due to few events), 95% CIs calculated using the Clopper-Pearson exact binomial method adjusted for the total surveillance time.

These results reflect enrolment that occurred during the time period when the B.1.17 (Alpha) variant was circulating in the UK. Identification of the Alpha variant was based on S gene target failure by PCR. Data were available for 95 of the 106 endpoint cases (90%). Of these, 66 out of 95 (69%) were identified as the Alpha variant with the other cases classified as non-Alpha.

No cases of severe COVID-19 were reported in the 7,020 NUVAXOVID participants compared with 4 cases of severe COVID-19 reported in the 7,019 placebo recipients in the PP-EFF analysis set.

Vaccine efficacy of NUVAXOVID to prevent the onset of COVID-19 from 7 days after Dose 2 was 89.7% (PP-EFF analysis set) for any strain or variant of SARS-CoV-2 and 86.3% (post-hoc analysis of the PP-EFF analysis set) for the B.1.1.7 (Alpha) variant of SARS-CoV-2, which comprised 66 out of 95 (69%) of the endpoint cases that were sequenced.

Licensed Seasonal Influenza Vaccine Co-administration Sub-study of Study 2 (2019nCoV-302)

Overall, 431 participants were co-vaccinated with inactivated seasonal influenza vaccines; 217 sub-study participants received NUVAXOVID and 214 received placebo. Demographic and baseline characteristics were balanced amongst participants who received NUVAXOVID and participants who received placebo. In the per-protocol immunogenicity (PP-IMM) analysis set for participants who received NUVAXOVID (n=191), median age was 40.0 years (range: 22 to 70 years); 93% (n=178) were 18 to 64 years old and 7% (n=13) were aged 65 to 84, 43% were female; 75% were White; 23% were multiracial or from ethnic minorities; and 27% had at least one comorbid condition. Co-administration resulted in no change to influenza vaccine immune responses as measured by hemagglutination inhibition (HAI) assay, while a 30% modest reduction in antibody responses to NUVAXOVID was noted as assessed by an anti-spike IgG assay with seroconversion rates similar to unvaccinated participants.

Study 3 (2019nCoV-501) - 2-dose Primary Series

Study 3 is an ongoing Phase 2a/b, multicenter, randomised, observer-blinded, placebo-controlled study in HIV-negative participants 18 to 84 years of age and people living with HIV (PLWH) 18 to 64 years of age in South Africa. PLWH were medically stable (free of opportunistic infections), receiving highly active and stable antiretroviral therapy, and having an HIV-1 viral load of < 1000 copies/mL.

The PP-EFF included 2,770 participants who received either NUVAXOVID (n=1,408) or placebo (n=1,362), received 2 doses (Dose 1 on Day 0; Dose 2 on Day 21), did not experience an exclusionary protocol deviation, and did not have evidence of SARS-CoV-2 infections through 7 days after the second dose.

Demographic and baseline characteristics were balanced amongst participants who received NUVAXOVID and participants who received placebo. in the RR-EFF analysis set for participants who received NUVAXOVID, median age was 28 years (range 18 to 84 years); 40% were female; 91% were Black/African American; 2% were White; 3% were multiple races; 1% were Asian; and 2% were Hispanic or Latino; and 5.5% were HIV-positive.

A total of 147 symptomatic mild, moderate or severe COVID-19 cases among all adult participants, seronegative (to SARS-CoV-2) at baseline, were accrued for the complete analysis (PP-EFF analysis set) of the primary efficacy endpoint, with 51 (4%) cases for NUVAXOVID versus 96 (7%) cases for placebo. The resultant vaccine efficacy of NUVAXOVID was 48.6% (95% CI: 28.4 – 63.1).

These results reflect enrolment that occurred during the time period when the B.1.351 (Beta) variant was circulating in South Africa.

Immunogenicity of NUVAXOVID as a Homologous or Heterologous Booster Dose

Immunogenicity in adults 18 years of age and older – after booster dose

Study 2019nCoV-101, Part 2

The safety and immunogenicity of a booster dose of NUVAXOVID was evaluated in an ongoing Phase 2 randomised, observer-blinded, placebo-controlled clinical study administered as a single booster dose (Study 2019nCoV-101, Part 2) in healthy adult participants aged 18 to 84 years of age who were seronegative to SARS-CoV-2 at baseline. A total of 254 participants received 2 doses of NUVAXOVID (0.5 mL, 5 micrograms 3 weeks apart) as the primary vaccination series. A subset of 105 participants received a booster dose of NUVAXOVID approximately 6 months after receiving Dose 2 of the primary series.

A single booster dose of NUVAXOVID induced an approximate 34-fold increase in the immune response against the Wuhan (ancestral) strain 28 days after receipt of the dose (Day 217) with serum IgG geometric mean titer (GMT) of 204,367 EU compared with a GMT of 6,064 EU pre-booster (Day 189) and an approximate 4.7-fold increase from peak GMT (43,905 EU), 14 days following Dose 2 of the primary series. An approximate 96-fold increase in neutralising antibodies was shown from a GMT of 63 pre-booster (Day 189) to a GMT of 6,023 post-booster (Day 217) and an approximate 4.1-fold increase from a peak GMT (14 days post-Dose 2) of 1,470.

For the variants of concern, 2 assays were used to assess immune responses. An assay comparing anti-rS IgG activity (n=29) across the same strains demonstrated a 5.4-fold (Ancestral), 9.7-fold (Alpha), 6.5-fold (Beta), 11.1-fold (Delta), 9·3-fold (Omicron BA.1) and 11.0-fold (Omicron BA.2) increase from 2 weeks after the primary series (Day 35) to 28 days post-booster (Day 217). A second assay comparing wild-type neutralisation titers (MN_{99}) (n=32) showed a 15.4-fold (Ancestral), 14.0-fold (Delta), and 3.5-fold (Omicron BA.1) increase from 2 weeks after the primary series (Day 35) to 28 days post-booster (Day 217).

Study 2019nCoV-501

In Study 3, an ongoing Phase 2a/b randomised, observer-blinded, placebo-controlled study, the safety and immunogenicity of booster dose was evaluated in healthy HIV-negative adult participants 18 to 84 years of age and medically stable PLWH 18 to 64 years of age who were seronegative to SARS-CoV-2 at baseline. A total of 1,789 participants (PP-IMM Analysis Set) received a booster dose of NUVAXOVID approximately 6 months after completion of the primary series of NUVAXOVID (Day 201).

An approximate 31-fold increase was shown in serum IgG GMT assessed at Day 236 (111,066 EU) from the pre-boost GMT at Day 201 (3,632 EU). An approximate 3.6-fold increase was demonstrated from peak GMT (30,756 EU) at Day 35 following completion of the primary series.

An approximate 52-fold increase in neutralising antibodies was shown from a GMT of 69 pre-booster (Day 201) to a GMT of 3,600 post-booster (Day 236) and an approximate 5.2-fold increase from a peak GMT (14 days post-Dose 2) of 694.

Study 2019nCoV-301 Booster Data

In the open-label booster phase of Study 2019nCoV-301, participants 18 years of age and older received a single booster dose of NUVAXOVID at least 6 months after completion of the primary series. A subset of 226 participants were included in the per-protocol immunogenicity (PP-IMM) analysis set as they did not have serologic or virologic evidence of SARS-CoV-2 infection up to 28 days post booster dose.

Prespecified immunogenicity non-inferiority analyses included an assessment of MN_{50} geometric mean titer (GMT) ratio and difference in seroconversion rates. Seroconversion for a participant was defined as achieving a 4-fold rise in MN_{50} from baseline (before the booster dose and before the first dose of the primary series).

The analysis of the GMT ratio of MN_{50} following the booster dose compared to the primary series met the non-inferiority criteria for a booster response (lower limit of the 95% CI > 0.67) and point estimate > 0.83.

The analysis of the difference in seroconversion rates following the booster dose compared to the primary series met the non-inferiority criteria for a booster response (lower limit of the 95% CI > -10%).

In addition, a single booster dose of NUVAXOVID elicited a robust immune response (serum IgG antibody) against the Omicron BA.1 variant at 28 days after booster vaccination that were higher than that reported at 14 days after primary series vaccination in the same participants.

Immunogenicity in Participants 12 to 17 Years of Age – After Booster Dose

The safety and immunogenicity of a booster dose of NUVAXOVID was evaluated in a Phase 3, multinational, multicentre, randomized, observer-blinded, placebo-controlled Paediatric Expansion study involving 220 adolescents 12 to 17 years of age conducted in the US. Of these, 110 participants received a booster dose after first receiving placebo during the initial (pre-crossover) vaccination period followed by active vaccination during the blinded crossover period [Cohort 1] and 110 received a booster dose after first receiving active vaccination during the initial (pre-crossover) vaccination period followed by placebo during the blinded crossover period [Cohort 2]) from 58 sites in the US. All adolescent participants aged 12 to 17 years of age were seronegative to SARS-CoV-2 at baseline.

The study assessed the immune response (neutralizing antibody against SARS-CoV-2 wild-type virus, serum immunoglobulin G [IgG] antibody to SARS-CoV-2 S protein immediately prior to and at 28 days after administration of a booster dose of NUVAXOVID and evaluated the overall

safety profile of NUVAXOVID through 28 days after the booster dose in 220 randomly selected adolescent participants aged 12 to 17 years of age.

A total of 2,122 participants received two doses of NUVAXOVID (0.5 mL, 5 micrograms 3 weeks apart) as the primary vaccination series. A total of 1,499 participants received a booster dose of NUVAXOVID approximately 9 months after receiving Dose 2 of the primary series, and of those 220 were selected for immunogenicity analysis.

A single booster dose of NUVAXOVID induced an approximate 34.2-fold increase in the immune response against the Wuhan (ancestral) strain 28 days after receipt of the dose with a serum IgG geometric mean ELISA unit (GMEU) of 388,263.3 EU/mL compared to a GMEU of 11,339.4 EU/mL pre-booster and an approximate 2.5-fold increase from peak GMEU (156,286.4 EU/mL), 14 days following Dose 2 of the primary series.

An approximate 27.7-fold increase in neutralizing antibodies was shown from a GMT of 426.7 pre-booster to a GMT of 11824.4 post-booster and an approximate 2.7-fold increase from a peak GMT (14 days post-Dose 2) of 4434.0.

A single booster dose of NUVAXOVID administered to adolescent participants 12 through 17 years of age elicited robust immune responses (neutralizing antibody (MN50), serum IgG antibody, and hACE2 receptor binding inhibition) against the SARS-CoV-2 wild-type virus (ancestral Wuhan strain) at 28 days after the booster dose of NUVAXOVID and were higher than those reported at 14 days after the second dose of NUVAXOVID of the primary vaccination series. Based on neutralizing antibody responses, non-inferiority was achieved for GMFRs and for the differences in SCRs using the baseline of the first dose of NUVAXOVID in the pre-crossover period (Cohort 2). Higher immune responses for pseudovirus-based neutralizing antibody against the Omicron BA.4/5 variant and serum IgG antibody against the Omicron BA.1 variant were also seen after the single booster dose of NUVAXOVID.

Immunogenicity of a booster dose following primary vaccination with other COVID-19 vaccines

The effectiveness of NUVAXOVID as a heterologous booster in individuals whose primary vaccination series was with other COVID-19 vaccines, has been reported in the COV-BOOST study conducted in the UK (ISRCTN 73765130). This was an independent randomised, controlled, phase 2 trial that evaluated a heterologous booster vaccination against COVID-19 in adults aged 30 years and older, at least 10 weeks after a primary vaccination series, with no history of laboratory confirmed SARS-CoV-2 infection. Within the group assigned to receive NUVAXOVID were 115 individuals who previously received VAXZEVRIA and 114 who had received COMIRNATY. NUVAXOVID induced significantly higher anti-spike IgG at 28 days post booster compared with the control (a quadrivalent meningococcal vaccine). It is noted that the incremental increase in antibody concentrations was lower following a third (booster) dose with NUVAXOVID than following mRNA vaccines. The geometric mean (GM) fold rise after a single booster dose of NUVAXOVID exceeded the pre-specified GM-fold rise of 1.75 (compared with control) that was considered to be an immunologically important difference.

Elderly Population

NUVAXOVID was assessed in participants 18 years of age and older. The efficacy of NUVAXOVID was consistent between elderly (≥ 65 years) and younger individuals (18 to 64 years) for the primary series.

Participants 65 years of age and older were evaluated for efficacy in the two pivotal Phase 3 clinical trials. In the placebo-controlled Phase 3 study conducted in the United States and Mexico (Study 1 [2019nCoV-301]), 11.8% (n=2,048) of enrolled participants that received the primary series were aged 65 years and older.

In the placebo-controlled Phase 3 study conducted in the United Kingdom (Study 2 [2019nCoV-302]), 27.8% (n=1,953) of enrolled participants that received the primary series were aged 65 years and older.

This medicine has been given a provisional consent under Section 23 of the Medicines Act, 1981. This means that further evidence on this medicine is awaited or that there are specific conditions of use. Refer to the consent notice published in the New Zealand Gazette for the specific conditions.

5.2 Pharmacokinetic Properties

Not applicable

5.3 Preclinical Safety Data

Genotoxicity

In vitro genotoxicity studies including bacterial reverse mutation, chromosomal aberrations in Chinese Hamster Ovary (CHO) cells and mammalian micronuclei in CHO cells were conducted with the Matrix-M adjuvant. The adjuvant was shown to be non-genotoxic.

Carcinogenicity

Carcinogenicity studies were not performed. The components of the vaccine are not expected to have carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

- Dibasic sodium phosphate heptahydrate
- Monobasic sodium phosphate monohydrate
- Sodium chloride
- Polysorbate 80

- Sodium hydroxide (for adjustment of pH)
- Hydrochloric acid (for adjustment of pH)
- Water for Injections
- Adjuvant (Matrix M)
    - Quillaja saponaria saponins fraction A
    - Quillaja saponaria saponins fraction C
    - Cholesterol
    - Phosphatidyl choline
    - Monobasic potassium phosphate
    - Potassium chloride

6.2 Incompatibilities

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

6.3 Shelf Life

Twelve months. The expiry date can be found on the packaging.

Unopened Vial

The unopened vaccine is stored refrigerated at 2°C to 8°C, protected from light.

Punctured Vial

Chemical and physical in-use stability has been demonstrated from the time of first needle puncture to administration for 12 hours at 2°C to 25°C.

From a microbiological point of view, after first opening (first needle puncture), the vaccine should be used immediately.

6.4 Special Precautions for Storage

Store in a refrigerator (2°C to 8°C). Do not freeze.

Keep the vials in the outer carton in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and Contents of Container

Multidose Vial

5-dose vial

Each clear glass vial (type I glass) with a stopper (bromobutyl or chlorobutyl rubber) and an aluminium overseal with blue plastic flip-cap contains 2.5 mL of suspension for injection.

Each clear glass vial contains 5 doses of 0.5 mL

Pack size: 2 multidose vials or 10 multidose vials

10-dose vial

Each clear glass vial (type I glass) with a stopper (bromobutyl or chlorobutyl rubber) and an aluminium overseal with blue plastic flip-cap contains 5 mL of suspension for injection.

Each clear glass vial contains 10 doses of 0.5 mL.

Pack size: 10 multidose vials

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.

7 MEDICINE SCHEDULE

Prescription medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

4 February 2022

10 DATE OF REVISION OF THE TEXT

19 April 2024

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2 Dose and method of administration	Update of wording relating to booster use in adolescents.
Section 4.8 – Undesirable effects **Section 5.1 – Pharmacodynamic properties**	New Safety and Efficacy information relating to booster dosing.