PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

NUVAXOVID ™

COVID-19 Vaccine (Recombinant protein, Adjuvanted)

Suspension for intramuscular injection

Multidose Vial, 5 mcg / 0.5 mL (per dose)

(contains 10 doses of 0.5 mL)

Active Immunizing Agent

Novavax, Inc.
21 Firstfield Road
Gaithersburg, MD, 20878

Imported by:
Innomar Strategies Inc.
3470 Superior Ct
Oakville, ON, L6L 0C4

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

NUVAXOVID ™ (COVID-19 Vaccine (Recombinant protein, Adjuvanted)) is indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

1.1 Pediatrics

The safety and efficacy of NUVAXOVID in individuals under 18 years of age have not yet been established.

1.2 Geriatrics

Clinical studies of NUVAXOVID include participants 65 years of age and older and their data contribute to the overall assessment of safety and efficacy (See ADVERSE REACTIONS and **Error! Reference source not found.**

2 CONTRAINDICATIONS

NUVAXOVID is contraindicated in individuals who are hypersensitive to the active ingredient or to any ingredients in the formulation, including any non-medicinal ingredient, or component of the container. (For a complete listing, see DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING).

3 SERIOUS WARNING AND PRECAUTIONS

At the time of approval, there are no known serious warnings or precautions associated with this product.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

NUVAXOVID is a suspension for intramuscular injection that should be administered by a trained healthcare worker.

4.2 Recommended Dose and Dosage Adjustment

The vaccination course for NUVAXOVID is a series of two doses of 0.5 mL each. The second dose is to be administered 3 weeks after the first dose.

There are no data available on the interchangeability of NUVAXOVID with other COVID-19 vaccines to complete the vaccination series.

4.3 Reconstitution

NUVAXOVID must not be reconstituted, mixed with other medicinal products, or diluted.

4.4 Administration

Administration

Use aseptic techniques for preparation and administration to ensure the sterility of each dose.

NUVAXOVID is colourless to slightly yellow, clear to mildly opalescent suspension, free of particles.

- Gently swirl the multidose vial before and in between each dose withdrawal. Do not shake.
- Prior to administration, visually inspect the contents of the vial for visible particulate matter and/or discolouration prior to administration. Also, visually inspect the vial for cracks or any abnormalities, such as evidence of tampering. If any of these conditions exists, the vaccine should not be administered.

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.

- Do not inject the vaccine intravascularly, subcutaneously, or intradermally.
- Do not mix the vaccine in the same syringe with any other vaccines or medicinal products.
- Do not pool excess vaccine from multiple vials.

NUVAXOVID does not contain a preservative. Store the opened vial between 2°C to 25°C for up to 6 hours of first needle puncture.

- Record the date and time of discard on the vial label.
- Discard this vaccine if not used within 6 hours after first puncture of the vial.

5 OVERDOSAGE

In the case of a suspected vaccine overdose, monitoring of vital functions and symptomatic treatment are recommended. Contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Suspension One dose (0.5 mL) contains 5 mcg of SARS-CoV-2 recombinant spike protein (original [Wuhan] strain) Multidose vial (5 mL, containing 10 doses of 0.5 mL)	• Disodium hydrogen phosphate heptahydrate • Hydrochloric acid (for adjustment of pH) • Polysorbate 80 • Sodium chloride • Sodium dihydrogen phosphate monohydrate • Sodium hydroxide (for adjustment of pH) • Water for Injection For adjuvant: • Cholesterol • Disodium hydrogen phosphate dihydrate • Phosphatidylcholine • Potassium chloride • Potassium dihydrogen phosphate • Sodium chloride

Composition

SARS-CoV-2 recombinant spike protein (original [Wuhan] strain)	5 mcg
Matrix-M adjuvant (*Quillaja saponaria* saponins fraction-A and fraction-C)	50 mcg

NUVAXOVID does not contain any preservatives or human-derived materials.

NUVAXOVID is supplied as 5 mL of suspension in a clear glass vial (type I glass) with a stopper (bromobutyl rubber) and an aluminium overseal with blue plastic flip-off cap. The vials are packaged in a secondary carton containing a total of ten (10) multidose vials per carton. Each vial contains 10 doses of 0.5 mL.

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and genericname of the vaccine, the product lot number and expiry date.

7 WARNINGS AND PRECAUTIONS

General

Vaccination should be postponed in individuals suffering from an acute severe febrile illness or acute infection.

As with any vaccine, vaccination with NUVAXOVID may not protect all recipients.

Individuals may not be optimally protected until 7 days after their second dose. (See CLINICAL TRIALS).

Acute Allergic Reactions

Events of anaphylaxis have been reported with COVID-19 vaccines. 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; 30 minutes is a preferred interval when there is a specific concern about a possible vaccine reaction. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of NUVAXOVID.

Hematologic

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.

Driving and Operating Machinery

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

Fertility

It is unknown whether NUVAXOVID has an impact on fertility. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility or reproductive toxicity (see 16 NON-CLINICAL TOXICOLOGY).

Immune

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the vaccine.

Syncope

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent injury from fainting and manage syncopal reactions.

7.1 Special Populations

7.1.1 Pregnant Women

The safety and efficacy of NUVAXOVID in pregnant women have not yet been established.

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

7.1.2 Breast-feeding

It is unknown if NUVAXOVID is excreted in human milk. A risk to the newborns/ infants cannot be excluded. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for immunization against COVID-19.

7.1.3 Pediatrics

The safety and efficacy of NUVAXOVID in children and adolescents less than 18 years of age have not yet been established.

7.1.4 Geriatrics

Clinical studies of NUVAXOVID include participants 65 years of age and older and their data contribute to the overall assessment of safety and efficacy (See ADVERSE REACTIONS and CLINICAL TRIALS sections).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety profile of NUVAXOVID presented below is based on data generated from an interim analysis of pooled data from 3 ongoing clinical trials conducted in South Africa, the United Kingdom, the United States, and Mexico. At the time of the analysis, a total of 48,698 participants ≥ 18 years of age received at least one dose of NUVAXOVID (n=29,297) or placebo (n=19,401). At the time of vaccination, the median age of participants who received NUVAXOVID was 48 years (range 18 to 95 years): 84.1% of participants were between 18 and 64 years of age and 15.9% of participants were ≥ 65 years of age.

Of the pooled reactogenicity data, which includes participants ≥ 18 years of age who received at least one dose of NUVAXOVID (n=21,395) or placebo (n=12,197), the most frequent adverse reactions were injection site tenderness (68%), injection site pain (56%), fatigue (45%), myalgia (44%), headache (41%), malaise (35%), arthralgia (20%), and nausea or vomiting (11%). Adverse reactions were usually mild to moderate in severity with a median duration of ≤ 2 days for local events and ≤ 1 day for systemic events following vaccination.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another vaccine. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse vaccine reactions in real-world use.

The safety analysis of the pooled data was performed once the median follow-up duration of at least 2 months after vaccination was completed. The median duration of follow-up was 70 days post-Dose 2, with 32,993 (66%) participants completing more than 2 months follow-up. Participants are being monitored for adverse reactions through approximately 12 to 24 months after Dose 2.

When compared with Dose 1, local and systemic adverse reactions were more frequently reported after Dose 2.

Solicited Local and Systemic Adverse Reactions

The frequency and severity of solicited local and systemic reactions were collected within 7 days following each dose of NUVAXOVID or placebo in participants who recorded reactogenicity events in a diary in the pooled safety population.

The reported frequency and severity of solicited local reactions are presented by age group in

Table 2 (18 to 64 years of age) and Table 3 (≥ 65 years of age).

Table 2: Frequency and Percentages of Participants with Solicited Local Adverse Reactions, by Maximum Severity, Within 7 Days of Each Dose – (Participants 18 to 64 Years of Age)

Solicited Local Adverse Reactions	NUVAXOVID		Placebo	
	Dose 1 N=18,871 n (%)	Dose 2 N=17,967 n (%)	Dose 1 N= 10,782 n (%)	Dose 2 N=10,173 n (%)
Tenderness (Grade ≥1)	9,571 (50.7)	12,444 (69.3)	1,656 (15.4)	1,460 (14.4)
Grade 3[c]	175 (0.9)	869 (4.8)	19 (0.2)	18 (0.2)
Grade 4[b]	1 (<0.1)	3 (<0.1)	1 (<0.1)	0 (0)
Pain (Grade ≥1)	6647 (35.2)	10361 (57.7)	1238 (11.5)	1294 (12.7)
Grade 3[a]	74 (0.4)	332 (1.9)	7 (0.1)	14 (0.1)
Grade 4[b]	0	5 (<0.1)	0	1 (<0.1)
Erythema (Grade ≥1)	184 (1.0)	1,130 (6.3)	30 (0.3)	30 (0.3)
Grade 3[d]	4 (<0.1)	139 (0.8)	1 (<0.1)	2 (<0.1)
Swelling (Grade ≥1)	163 (0.9)	1038 (5.8)	34 (0.3)	26 (0.3)
Grade 3[e]	6 (<0.1)	82 (0.5)	4 (<0.1)	1 (<0.1)

Source: pooled safety data from studies 2019n-501, -301, -302 (excluding data from influenza vaccine substudy)

[a] Grade 3 pain: Defined as any use of narcotic pain reliever or prevents daily activity.

[b] Grade 4 pain, tenderness: Defined as Emergency Room (ER) visit or hospitalization.

[c] Grade 3 tenderness: Defined as significant discomfort at rest.

[d] Grade 3 erythema/redness: Defined as >10 cm.

[e] Grade 3 induration/swelling: Defined as >10 cm or prevents daily activity.

Table 3: Frequency and Percentages of Participants with Solicited Local Adverse Reactions, by Maximum Severity, Within 7 Days of Each Dose – (Participants ≥65 Years of Age)

Solicited Local Adverse Reactions	NUVAXOVID		Placebo	
	Dose 1 N=2,524 n (%)	Dose 2 N=2,292 n (%)	Dose N=1,415 n (%)	Dose 2 N=1,261 n (%)
Tenderness (Grade ≥1)	833 (33.0)	1258 (54.9)	160 (11.3)	121 (9.6)
Grade 3[b]	11 (0.4)	35 (1.5)	2 (0.1)	1 (0.1)
Pain (Grade ≥1)	486 (19.3)	927 (40.5)	109 (7.7)	120 (9.5)
Grade 3[a]	4 (0.2)	14 (0.6)	1 (0.1)	1 (0.1)
Erythema (Grade ≥1)	20 (0.8)	120 (5.2)	5 (0.4)	4 (0.3)
Grade 3[c]	0 (0)	8 (0.4)	0 (0)	0 (0)
Swelling (Grade ≥1)	18 (0.7)	131 (5.7)	1 (0.1)	7 (0.6)
Grade 3[d]	1 (<0.1)	10 (0.4)	0 (0)	1 (0.1)

Source: pooled safety data from studies 2019n-501, -301, -302 (excluding data from influenza vaccine substudy)
[a] Grade 3 pain: Defined as any use of narcotic pain reliever or prevents daily activity.
[b] Grade 3 tenderness: Defined as significant discomfort at rest.
[c] Grade 3 erythema/redness: Defined as >10 cm.
[d] Grade 3 induration/swelling: Defined as >10 cm or prevents daily activity.

The reported frequency and severity of solicited systemic reactions are presented in Table ***4*** (18 to 64 years of age) and Table 5 (≥65 years of age).

Table 4: Frequency and Percentages of Participants with Solicited Systemic Adverse Reactions, by Maximum Severity, Within 7 Days of Each Dose – (Participants 18 to 64 Years of Age)

Solicited Systemic Adverse Reactions	NUVAXOVID		Placebo	
	Dose 1 N=18,871 n (%)	**Dose 2 N= 17,967 n (%)**	**Dose 1 N=10,782 n (%)**	**Dose 2 N=10,173 n (%)**
Fatigue (Grade ≥1)	4,699 (24.9)	8,407 (46.8)	2,188 (20.3)	1,933 (19.0)
Grade 3[e]	228 (1.2)	1403 (7.8)	111 (1.0)	116 (1.1)
Grade 4[d]	4 (<0.1)	4 (<0.1)	1 (<0.1)	3 (<0.1)
Muscle pain (Grade ≥1)	4,289 (22.7)	8,267 (46.0)	1,362 (12.6)	1,090 (10.7)
Grade 3[e]	99 (0.5)	856 (4.8)	41 (0.4)	43 (0.4)
Grade 4[d]	3 (<0.1)	5 (<0.1)	2 (<0.1)	4 (<0.1)
Headache (Grade ≥1)	4,780 (25.3)	7,775 (43.3)	2,404 (22.3)	1,880 (18.5)
Grade 3[c]	155 (0.8)	548 (3.1)	81 (0.8)	63 (0.6)
Grade 4[d]	5 (<0.1)	5 (<0.1)	1 (<0.1)	2 (<0.1)
Malaise (Grade ≥1)	2,701 (14.3)	6,623 (36.9)	1,148 (10.7)	1,086 (10.7)
Grade 3[e]	138 (0.7)	1073 (6.0)	60 (0.6)	65 (0.6)
Grade 4[d]	8 (<0.1)	9 (0.1)	2 (<0.1)	2 (<0.1)
Joint pain (Grade ≥1)	1,503 (8.0)	3,854 (21.5)	719 (6.7)	658 (6.5)
Grade 3[e]	64 (0.3)	436 (2.4)	30 (0.3)	31 (0.3)
Grade 4[d]	2 (<0.1)	5 (<0.1)	0 (0)	2 (<0.1)
Nausea or vomiting (Grade ≥1)	1,255 (6.7)	2,032 (11.3)	617 (5.7)	528 (5.2)
Grade 3[a]	21 (0.1)	39 (0.2)	14 (0.1)	13 (0.1)
Grade 4[b]	5 (<0.1)	7 (<0.1)	3 (<0.1)	2 (<0.1)
Fever (Grade ≥1)	107 (0.6)	1,023 (5.7)	72 (0.7)	48 (0.5)
Grade 3[f]	16 (0.1)	71 (0.4)	13 (0.1)	9 (0.1)
Grade 4[g]	6 (<0.1)	2 (<0.1)	1 (<0.1)	0 (0.)

Source: pooled safety data from studies 2019n-501, -301, -302 (excluding data from influenza vaccine substudy)

[a] Grade 3 nausea/vomiting: Defined as prevents daily activity or requires outpatient intravenous hydration.

[b] Grade 4 nausea/vomiting: Defined as ER visit or hospitalization for hypotensive shock.

[c] Grade 3 headache: Defined as significant; any use of narcotic pain reliever or prevents daily activity.

[d] Grade 4 headache, fatigue/malaise, myalgia, arthralgia: Defined as ER visit or hospitalization.

[e] Grade 3 fatigue/malaise, myalgia, arthralgia: Defined as significant; prevents daily activity.

[f] Grade 3 fever: Defined as 39.0 to 40°C (102.1 to 104°F).

[g] Grade 4 fever: Defined as >40°C (>104°F).

Table 5: Frequency and Percentages of Participants with Solicited Systemic Adverse Reactions, by Maximum Severity, Within 7 Days of Each Dose – (Participants ≥65 Years of Age)

Solicited Systemic Adverse Reactions	NUVAXOVID		Placebo	
	Dose 1 N=2,524 n (%)	**Dose 2 N=2,292 n (%)**	**Dose 1 N=1,415 n (%)**	**Dose 2 N=1,261 n (%)**
Fatigue (Grade ≥1)	412 (16.3)	656 (28.6)	196 (13.9.)	175 (13.9)
Grade 3[d]	21 (0.8)	60 (2.6)	4 (0.3)	12 (1.0)
Muscle pain (Grade ≥1)	311 (12.3)	604 (26.4)	142 (10.0)	118 (9.4)
Grade 3[d]	3 (0.1)	32 (1.4)	4 (0.3)	3 (0.2)
Headache (Grade ≥1)	385 (15.3)	541 (23.6)	215 (15.2)	161 (12.8)
Grade 3[b]	13 (0.5)	17 (0.7)	4 (0.3)	2 (0.2)
Grade 4[c]	1 (<0.1)	1 (<0.1)	0 (0)	0 (0)
Malaise (Grade ≥1)	248 (9.8)	481 (21.0)	108 (7.6)	105 (8.3)
Grade 3[d]	12 (0.5)	38 (1.7)	3 (0.2)	5 (0.4)
Grade 4[c]	0 (0)	0 (0)	0 (0)	0 (0)
Joint pain (Grade ≥1)	155 (6.1)	287 (12.5)	89 (6.3)	71 (5.6)
Grade 3[d]	5 (0.2)	16 (0.7)	5 (0.4)	3 (0.2)
Grade 4[c]	0 (0)	1 (<0.1)	0 (0)	0 (0)
Fever (Grade ≥1)	13 (0.5)	44 (1.9)	9 (0.6)	11 (0.9)
Grade 3[e]	1 (<0.1)	3 (0.1)	0 (0)	2 (0.2)
Grade 4[f]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Nausea or vomiting (Grade ≥1)	93 (3.7)	117 (5.1)	37 (2.6)	41 (3.3)
Grade 3[a]	0 (0)	2 (0.1)	0 (0)	0 (0)

Source: pooled safety data from studies 2019n-501, -301, -302 (excluding data from influenza vaccine substudy)
[a] Grade 3 nausea/vomiting: Defined as prevents daily activity or requires outpatient intravenous hydration.
[b] Grade 3 headache: Defined as significant; any use of narcotic pain reliever or prevents daily activity.
[c] Grade 4 headache, malaise, arthralgia: Defined as ER visit or hospitalization.
[d] Grade 3 fatigue/malaise, myalgia, arthralgia: Defined as significant; prevents daily activity.
[e] Grade 3 fever: Defined as 39.0 to 40°C (102.1 to 104°F).
[f] Grade 4 fever: Defined as >40°C (>104°F).

Unsolicited Adverse Events

Across the pooled studies, participants were monitored for unsolicited adverse events after receipt of Dose 1 through 28 days after Dose 2 (49 days). The overall frequency of unsolicited adverse events for participants who received at least one dose of NUVAXOVID (n=29,297) or placebo (n=19,401) was 157 events/100 person-years (e/100 PY) (18 to 64 years of age) and 153 e/100 PY (≥ 65 years of age) for those who received the vaccine and 133 e/100 PY (18 to 64 years of age) and 124 e/100 PY (≥ 65 years of age) for participants who received placebo.

Serious Adverse Events and Other Adverse Events of Interest

Participants were monitored for unsolicited serious adverse events and adverse events of interest, including but not limited to neurologic, inflammatory, vascular, and autoimmune disorders, from receipt of first vaccination through the respective data cutoff dates for each individual study within the pooled data analysis set. Serious adverse events and adverse events of special interest will continue to be recorded until the end of the studies, approximately 12 to 24 months after Dose 2 across the pooled clinical trials.

Serious adverse events (SAEs) across both treatment groups were uncommon (defined as ≥1/1,000 to <1/100), with a higher incidence rate in participants who receive placebo (4.09 events per 100 person-years) than in participants who received NUVAXOVID (3.82 events per 100 person-years). A slightly higher incidence rate occurred among participants ≥ 65 years of age. Incidence rates for SAEs in the younger age cohort (18 to 64 years) were 3.31 events per 100 person-years in NUVAXOVID participants and 3.59 events per 100 person-years in placebo participants. Incidence rates for SAEs in the older age cohort (≥ 65 years) was 6.69 events per 100 person-years in NUVAXOVID recipients and 6.65 events per 100 person-years in placebo recipients.

In the younger age cohort (18 to 64 years), there were no SAEs with an incidence rate greater than 0.10 events per 100 person-years in the NUVAXOVID group while 3 events, COVID-19 pneumonia (0.25), COVID-19 (0.23), and appendicitis (0.15) had incidence rates greater than 0.10 events per 100 person-years in the placebo group. In the older age cohort, SAEs that occurred at an incidence rate greater than 0.20 events per 100 person years in participants who received NUVAXOVID were COVID-19 (0.37) and prostate cancer (0.28) compared with pneumonia (0.51), COVID-19 (0.26), COVID 19 pneumonia (0.26), and atrial fibrillation (0.26) in the placebo group.

There were no other notable patterns of imbalance between treatment groups for specific categories of serious adverse events or adverse events of interest.

SAEs of cholecystitis, including acute cholecystitis, occurred with a higher incidence rate per 100 person-years in NUVAXOVID (0.11) than in placebo recipients (0.00), although the percentage of participants experiencing the event was infrequent (0.03%). All participants had a history of or a concurrent finding of cholelithiasis (gallstones) and most participants had additional risk factors including obesity and ≥ 40 years of age. Time to onset ranged from 6 to 64 days from the last dose of vaccine, with more than half of the events occurring more than 1 month following the last dose. All events resolved following cholecystectomy.

Myocarditis was identified in two teenage men shortly after receiving a second dose of vaccine resulting in a mild clinical course with complete resolution and no sequelae. Currently available information is insufficient to determine a causal relationship with the vaccine.

No deaths related to the vaccine were reported in the main and supportive clinical studies.

Non-Serious Adverse Events

The overall frequency of non-serious unsolicited adverse events was higher in the NUVAXOVID group than in placebo with events of fatigue, injection site pain, pyrexia, and myalgia occurring beyond the 7-

day post-injection period largely accounting for the differences between the treatment groups. In addition, an imbalance of chills and pain in the extremity were reported. Chills occurred in 0.56% (n=165) of participants (N=29,297) who received NUVAXOVID and 0.10% (n=20) of participants (N=19,401) who received placebo. Pain in the extremity occurred in 1.46% (n=428) of participants who received NUVAXOVID and 0.37% (n=72) of participants who received placebo.

There were no other notable imbalances between treatment groups for unsolicited non-serious adverse events that would suggest a causal relationship to NUVAXOVID.

8.3 Post-Market Adverse Reactions

Not applicable

9 DRUG INTERACTIONS

No interaction studies have been performed. Co-administration of NUVAXOVID with inactivated influenza vaccines has been evaluated in a limited number of adults (217 that received NUVAXOVID and 214 that received placebo) in an exploratory sub-study of 2019nCoV-302 (See CLINICAL TRIALS sections). The binding antibody response to SARS-CoV-2 was 30% lower when NUVAXVOID was given concomitantly with inactivated influenza vaccine. The clinical significance of this is unknown.

Concomitant administration of NUVAXOVID with non-influenza vaccines has not been studied.

Do not mix NUVAXOVID with other vaccines/products in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

NUVAXOVID is composed of purified full-length SARS-CoV-2 recombinant spike (S) protein nanoparticle 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 two vaccine components elicit B- and T-cell immune responses to the S protein,including neutralizing antibodies, which may contribute to protection against COVID-19.

11 STORAGE, STABILITY AND DISPOSAL

Storage Prior to Use

The unopened NUVAXOVID multidose vials are stored refrigerated between 2° to 8°C (36° to 46°F) for a maximum of 9 months. Store in the original carton to protect from light.

Storage of Punctured vials

Chemical and physical in-use stability has been demonstrated from the time of first needle puncture to administration for 6 hours at 2°C to 25°C.

NUVAXOVID does not contain a preservative. Store the opened vial between 2°C to 25°C for up to 6 hours after first puncture. (See Administration for further discard details and instructions).

12 SPECIAL HANDLING INSTRUCTIONS

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.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: SARS-CoV-2 recombinant spike (rS) protein with Matrix-M adjuvant

Product Characteristics:

SARS-CoV-2 recombinant spike protein is produced in the *Spodoptera frugiperda* insect cell line infected with a baculovirus that encodes full-length, SARS-CoV-2 spike gene-producing trimeric spike proteins from the original (Wuhan) strain. Matrix-M adjuvant contains *Quillaja saponaria* saponin fraction-A and *Quillaja saponaria* saponin fraction-C.

NUVAXOVID (COVID-19 Vaccine [Recombinant protein, Adjuvanted]) is a sterile, preservative-free, aqueous buffered suspension of the SARS-CoV-2 recombinant spike (rS) protein from the original (Wuhan) strain that is co-formulated with Matrix-M adjuvant and a formulation buffer. (See Table 1 for the full list of non-medicinal ingredients).

NUVAXOVID is a colourless to slightly yellow, clear to mildly opalescent suspension for intramuscular injection (pH 7.2). The vaccine is provided in a multidose vial containing 10 doses per vial. Each dose contains 5 mcg of SARS-CoV-2 recombinant spike protein with 50 mcg of Matrix-M adjuvant.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

NUVAXOVID used in clinical trials contains the recombinant SARS-CoV-2 spike (S)-protein, derived from the original (Wuhan) strain of SARS-CoV-2.

The clinical efficacy, safety, and immunogenicity of NUVAXOVID is being evaluated in two pivotal, placebo-controlled, Phase 3 studies: Study 1 (2019nCoV-301) conducted in North America and Study 2 (2019nCoV-302) conducted in the United Kingdom.

Study 1 (2019nCoV-301)

Study 1 is an ongoing Phase 3, multi-centre, randomised, observer-blinded, placebo-controlled study in participants 18 years of age and older in the United States and Mexico. Upon enrolment, 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 had a history of laboratory-confirmed diagnosed COVID-19. Participants with clinically stable underlying co-morbidity were included as were participants with well-controlled HIV infection. Enrolment of adults completed in February 2021; safety and efficacy events were evaluated until each participant's first blinded crossover vaccination or as of the data cut-off date of 31 May 2021. Participants will be followed for up to 24 months after the second dose for assessments of safety, and efficacy against COVID-19.

Demographic and baseline characteristics were balanced amongst participants who received Nuvaxovid and those who received placebo. Of the 29,949 participants randomized, 15.1% of participants in the vaccine group and 23.3% of participants in the placebo group requested unblinding to receive an authorized COVID-19 vaccine. In the Per-Protocol Efficacy (PP-EFF) analysis set for participants who received NUVAXOVID (n=17,312), which included all participants who received the full prescribed regimen of trial vaccine, had no exclusionary protocol deviations, and did not have evidence of SARSCoV2 infection through 6 days after the second dose, the median age was 47 years (range: 18 to 95years); 88% (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. At least one 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 human immunodeficiency virus (HIV). Other high-risk characteristics included age ≥65years (with or without comorbidities) or age <65years with comorbidities and/or living or working conditions involving known frequent exposure to SARS-CoV-2 or to densely populated circumstances.

Study 2 (2019nCoV-302)

Study 2 is an ongoing Phase 3, multi-centre, randomised, observer-blinded, placebo-controlled study in participants 18 to 84 years of age in the United Kingdom. Upon enrolment, participants were stratified by age (18 to 64 years; 65 to 84 years) and assigned in a 1:1 ratio 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, as were participants with known stable infection with HIV, hepatitis C virus (HCV), or hepatitis B virus (HBV).

Enrolment was completed in November 2020; data cut-off dates for efficacy and safety were 29 January 2021 and 23 February 2021, respectively. Participants are being followed for up to 12 months after the last vaccination for assessments of safety and efficacy against COVID-19.

Demographic and baseline characteristics were balanced amongst participants who received NUVAXOVID and participants who received placebo. Of the 15,187 participants randomized, 33.8% of participants in the vaccine group and 35.4% of participants in the placebo group requested to receive an authorized COVID-19 vaccine. In the Per-Protocol Efficacy (PP-EFF) analysis set for participants who received NUVAXOVID (n=7,020), which included all participants who received the full prescribed regimen of trial vaccine, had no exclusionary protocol deviations, and did not have evidence of SARS-CoV-2 infection through 6 days after the second dose, the median age (range) 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; 95% were White; 3% were Asian; 1.0% were multiple races, 0.4% were Black or African American; 1%were Hispanic or Latino; and 45% had at least one

comorbid condition.

14.2 Study Results

Study 1 (2019nCoV-301)

As of the cut-off date of 31 May 2021, 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 two doses (Dose 1 on day 0; Dose 2 between days 21 to 28), did not experience an exclusionary protocol deviation, and did not have evidence of SARS-CoV-2 infection through 6 days after the second dose.

COVID-19 cases were confirmed by polymerase chain reaction (PCR) through a central laboratory. Vaccine efficacy overall and a subgroup analysis by age and by mild, moderate, or severe COVID-19 are presented in Table 6.

Table 6: 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)
	Participants N	COVID-19 cases n (%)	Incidence Rate Per Year Per 1,000 People[2]	Participants 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	90.4% (82.9, 94.6) [3,4]
Mild	---	14 (0.1)	---	---	49 (0.6)	---	---
Moderate	---	0	---	---	10 (0.1)	---	---
Severe	---	0	---	---	4 (<0.1)	---	---
Subgroup analyses of the primary efficacy endpoint[5]							
18 to 64 years	15,264	12 (0.1)	4.60	7,194	61 (0.8)	54.11	91.5% (84.2, 95.4)[3]
≥ 65 years of age	2,048	2 (0.1)	5.69	946	2 (0.2)	13.37	57. 5% (-486.9, 96.9) [5]

1 Vaccine efficacy evaluated in participants without major protocol deviations who were seronegative and PCR-negative to SARS-CoV-2 at baseline and do not have a laboratory confirmed current SARS-CoV-2 infection with symptom onset through 6 days after the second dose, and who have received the full prescribed regimen of 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 and age strata as fixed effects and robust error variance, where vaccine efficacy = 100 × (1 – relative risk).

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

5 For participants ≥65 years of age, the event rates were too low (two or fewer events) to allow meaningful

interpretation.

Vaccine efficacy of NUVAXOVID to prevent the onset of COVID-19 from 7 days after Dose 2 was 90.40% (PP-EFF analysis set).

Study 2 (2019nCoV-302)

As of the cut-off date of 29 January 2021, the primary efficacy PP-EFF analysis set included 14,039 participants who received either NUVAXOVID (n= 7,020) or placebo (n= 7,019), received two doses (Dose 1 on day 0; Dose 2 between 21 and 28 days), did not experience an exclusionary protocol deviation, and did not have evidence of SARS-CoV-2 infection through 6 days after the second dose.

Vaccine efficacy overall and a subgroup analysis by age and by severity of COVID-19 are presented in Table 7.

Table 7: Vaccine efficacy analysis of PCR-confirmed COVID-19 with onset at least 7 days after the second vaccination[1] - PP-EFF analysis set: Study 2 (2019nCoV-302)

Subgroup	NUVAXOVID			Placebo			% Vaccine Efficacy (95% CI)
	Participants N	COVID-19 cases n (%)	Incidence Rate Per Year Per 1,000 People[2]	Participants N	COVID-19 cases n (%)	Incidence Rate Per Year Per 1,000 People[2]	
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)[3,4]
Mild	---	1 (<0.1)	---	---	28 (0.4)	---	---
Moderate	---	9 (0.1)	---	---	63 (0.9)	---	---
Severe	---	0	---	---	5 (<0.1)	---	---
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%[3] (79.7, 94.9)
65 to 84 years of age	1,953	1 (0.10)	---	1,957	9 (0.9)	---	88.9%[5] (20.2, 99.7)

1 Vaccine efficacy evaluated in participants without major protocol deviations who were seronegative and PCR-negative to SARS-CoV-2 at baseline and do not have a laboratory confirmed current SARS-CoV-2 infection with symptom onset through 6 days after the second dose, and who have received the full prescribed regimen of trial vaccine.

2 Mean disease incidence rate per year in 1000 people.

3 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.

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

5 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.

Vaccine efficacy of NUVAXOVID to prevent the onset of COVID-19 from 7 days after Dose 2 was 89.7% (PP-EFF analysis set).

15 MICROBIOLOGY

No microbiological information is required for this vaccine product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: In a repeat-dose toxicity study conducted in New Zealand White rabbits, 50 µg SARS-CoV-2 rS with or without 50 µg Matrix-M adjuvant was administered intramuscularly up to 4 times (days 1, 8, 15 and 36) and demonstrated SARS-CoV-2 rS with Matrix-M adjuvant was well-tolerated with no adverse findings. Effects on clinical pathology parameters (fibrinogen, CRP, and/or globulin), which resolved during the recovery interval, and histopathology (subacute inflammation at injection sites and adjacent tissue), which were decreased at the recovery interval, were consistent with immune stimulation following administration of a vaccine.

Carcinogenicity: NUVAXOVID has not been evaluated for carcinogenicity in animals, as carcinogenicity studies were not considered relevant to this vaccine.

Genotoxicity: In vitro genotoxicity studies were conducted with the Matrix-M adjuvant. The adjuvant was shown to be non-mutagenic in both the bacterial reverse mutation assay and mammalian cell micronucleus assay.

Reproductive and Developmental Toxicology: A developmental and reproductive toxicity study was performed in female rats administered four intramuscular doses (two prior to mating; two during gestation) of 5 micrograms SARS-CoV-2 rS protein (approximately 200-fold excess relative to the human dose of 5 micrograms on a weight- adjusted basis) with 10 micrograms Matrix-M adjuvant (approximately 40-fold excess relative to the human dose of 50 micrograms on a weight-adjusted basis). No vaccine-related adverse effects on fertility, pregnancy/lactation, or development of the embryo/foetus and offspring through post-natal Day 21 were observed.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

NUVAXOVID

COVID-19 Vaccine, Adjuvanted

Read this carefully before you start taking **NUVAXOVID**. This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medicalcondition and treatment and ask if there is any new information about **NUVAXOVID**.

What is NUVAXOVID used for?

NUVAXOVID is a vaccine used to prevent the coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus. It can be given to adults aged 18 years and older.

How does NUVAXOVID work?

NUVAXOVID causes the immune system (the body's natural defences) to produce antibodies and specialised white blood cells that work against the virus, to give protection against COVID-19. Noneof the ingredients in this vaccine can cause COVID-19.

The vaccine is given by injection with a needle in the upper arm and will require two doses given 3 weeks apart.

As with any vaccine, NUVAXOVID may not fully protect all those who receive it. Even after you have had both doses of the vaccine, continue to follow the recommendations of local publichealth officials to prevent spread of COVID-19.

Individuals may not be optimally protected until after receiving the second dose of the vaccine.You cannot get COVID-19 from this vaccine.

What are the ingredients in NUVAXOVID?

Medicinal ingredients: 5 micrograms of purified SARS-CoV-2 recombinant spike protein as the active substance.

Non-medicinal ingredients:

- Disodium hydrogen phosphate heptahydrate
- Sodium dihydrogen phosphate monohydrate
- Sodium chloride
- Polysorbate 80
- Sodium hydroxide
- Hydrochloric acid
- Water for Injection

The Matrix-M adjuvant contains cholesterol, phosphatidylcholine, potassium dihydrogen phosphate disodium hydrogen phosphate dihydrate, sodium chloride and potassium chloride.

NUVAXOVID comes in the following dosage forms:

Colourless to slightly yellow, clear to mildly opalescent suspension provided in a clear multidose glass vial with a rubber stopper and a blue flip-off top. Each multidose vial contains 10 doses each of 0.5 mL.

Do not use NUVAXOVID if:

- you are allergic to the active substance or any of the other ingredients of this vaccine
- you have had an allergic reaction to a previous dose of NUVAXOVID
- you currently have symptoms that could be due to COVID-19. Talk with your healthcare professional about your symptoms and getting a COVID-19 test. Your healthcare professional willadvise you when you are able to receive the vaccine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take NUVAXOVID. Talk about any health conditions or problems you may have, including if you:

- Have any allergies or previous problems following administration of NUVAXOVID, such as an allergic reaction or breathing problems
- Have ever fainted following any needle injection
- Have a bleeding problem, bruise easily or use a blood thinning medication
- Have a high fever or severe infection
- Have any serious illness
- Your immune system does not work properly (immunodeficiency) or you are taking medicines that weaken the immune system (such as high-dose corticosteroids, immunosuppressants, or cancer medicines)
- Are pregnant, think you may be pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

There is no information on the use of NUVAXOVID with other vaccines. Tell your healthcare professional if you have recently received any other vaccine.

How is NUVAXOVID given:

- Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm
- During and after each injection of the vaccine, your doctor, pharmacist, or nurse will watch over you for around 15 minutes to monitor for signs of an allergic reaction.

Usual dose:

NUVAXOVID will be given to you as two 0.5 mL injections. Each injection will be given on a separate visit 3 weeks apart. It is very important that you return for the second injection, or the vaccine may not work as well.

Overdose:

In the event of suspected overdose with NUVAXOVID, contact your regional poison control centre.

Missed Dose:

If you forget to go back to your healthcare professional at the scheduled time for your next dose, askyour healthcare professional for advice.

What are possible side effects from using NUVAXOVID?

Like all vaccines, NUVAXOVID can cause side effects.

The following are common or very common side effects of NUVAXOVID. Most of theseside effects are mild and do not last long. Tell your doctor if you have side effects that bother you:

- headache
- feeling sick (nausea) or getting sick (vomiting)
- muscle ache
- joint pain
- tenderness or pain where the injection is given
- feeling very tired (fatigue)
- generally feeling unwell (malaise)
- redness where the injection is given
- swelling where the injection is given
- fever (> 38°C)
- chills
- pain or discomfort in the arm, hand, leg and/or foot (pain in the extremity)

These are not all the possible side effects you may have when taking NUVAXOVID. If you experience any side effects not listed here, tell your healthcare professional.

Should you develop any serious symptoms or symptoms that could be an allergic reaction, seek medical attention immediately. Symptoms of an allergic reaction include:

- feeling faint or light-headed
- changes in your heartbeat
- shortness of breath
- wheezing
- swelling of your lips, face, or throat
- hives or rash
- nausea or vomiting
- stomach pain

If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough

to interfere with your daily activities, tell your healthcare professional.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Novavax, Inc. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, pleasecomplete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html) and send it to your local Health Unit.

Storage:
Do not use this vaccine after the expiry date, which is stated on the label after EXP. The expiry date refers to the last day of that month.

Your doctor or pharmacist is responsible storing, supplying and administering this vaccine, as well as disposing of any unused product correctly.

Keep out of reach and sight of children.

If you want more information about NUVAXOVID:

- Talk to your healthcare professional

Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website /www.NovavaxCovidVaccine.com,or by calling 1-855-239-9172.

This leaflet was prepared by Novavax, Inc.

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