

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Nuvaxovid dispersion for injection
COVID-19 Vaccine (recombinant, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial which contains 10 doses of 0.5 mL

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

Adjuvant Matrix-M containing per 0.5 mL dose: Fraction-A (42.5 micrograms) and Fraction-C (7.5 micrograms) of *Quillaja saponaria* Molina extract.

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection (injection).

The dispersion is colourless to slightly yellow, clear to mildly opalescent (pH 7.2)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nuvaxovid is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.

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

4.2 Posology and method of administration

Posology

Individuals 18 years of age and older

Nuvaxovid is administered intramuscularly as a course of 2 doses of 0.5 mL each. It is recommended to administer the second dose 3 weeks after the first dose (see section 5.1).

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.

Paediatric population

The safety and efficacy of Nuvaxovid in children and adolescents aged less than 18 years have not yet been established. No data are available.

Elderly population

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

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.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions on handling and 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

Traceability

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

Hypersensitivity and anaphylaxis

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

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.

Excipients

Sodium

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Potassium

This vaccine contains potassium, less than 1 mmol (39 mg) per dose, that is to say, essentially 'potassium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Co-administration of Nuvaxovid with inactivated influenza vaccines has been evaluated in a limited number of participants in an exploratory clinical trial sub-study, 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 clinical significance of this is unknown.

Concomitant administration of Nuvaxovid with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is limited experience with use of Nuvaxovid in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition, or post-natal development, see section 5.3.

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

Breast-feeding

It is unknown whether Nuvaxovid is excreted in human milk.

No effects on the breast-fed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to Nuvaxovid is negligible.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity, see section 5.3.

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 effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of safety profile

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, 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 one 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 age 18 years and older enrolled in the two 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 in those aged 65 years and above.

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

Licensed inactivated seasonal influenza vaccines were co-administered to participants on the same day as 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.

Tabulated list of adverse reactions

Adverse reactions observed during clinical studies are listed below according to the following frequency categories:

Very common ($\geq 1/10$),

Common ($\geq 1/100$ to $< 1/10$),

Uncommon ($\geq 1/1,000$ to $< 1/100$),

Rare ($\geq 1/10,000$ to $< 1/1,000$),

Very rare ($< 1/10,000$),

Not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Adverse reactions from Nuvaxovid clinical trials

MedDRA System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)
Blood and lymphatic system disorders			Lymphadenopathy
Nervous system disorders	Headache		
Vascular disorders			Hypertension
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 ^a Chills Pain in extremity	Injection site pruritus

a Higher frequencies of these events were observed after the second dose.

b This term also included events reported as influenza-like illness

c This term includes both injection site redness and injection site erythema (common).

Description of selected adverse reactions

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#) and include batch/Lot number if available.

4.9 Overdose

No case of overdose has been reported. In the event of an overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccine, 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 two vaccine components elicit B- and T-cell immune responses to the S protein, including neutralising antibodies, which may contribute to protection against COVID-19.

Clinical efficacy

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, and a Phase 2a/b study, Study 3, conducted in South Africa.

Study 1 (2019nCoV-301)

Study 1 is an ongoing Phase 3, multicentre, randomised, observer-blinded, placebo-controlled study in participants 18 years of age and older in 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 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 HIV infection.

Enrolment of adults completed in February 2021. Participants will be followed for up to 24 months after the second dose for assessments of safety, and efficacy against COVID-19. Following collection of sufficient safety data to support application for emergency use authorisation, initial recipients of placebo were invited to receive two injections of Nuvaxovid 21 days apart and initial recipients of Nuvaxovid to receive two 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 two 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 was 47 years (range: 18 to 95 years); 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/m²); chronic lung disease; diabetes mellitus type 2, cardiovascular disease; chronic kidney disease; or human immunodeficiency virus (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) through a central laboratory. Vaccine efficacy is presented in [Table 2](#).

Table 2: Vaccine efficacy against PCR-confirmed COVID-19 with onset from 7 days after second vaccination ¹ - PP-EFF analysis set; Study 2019nCoV-301

Subgroup	Nuvaxovid			Placebo			% Vaccine Efficacy (95% CI)
	Participants N	COVID-19 cases n (%) ²	Incidence Rate Per Year Per 1,000 People ²	Participants N	COVID-19 cases n (%) ³	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}

¹ VE evaluated in participants without major protocol deviations, who are seronegative (for SARS-CoV-2) at baseline and do not have a laboratory confirmed current SARS-CoV-2 infection with symptom onset up to 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 VE = 100 × (1 – relative risk) (Zou 2004).

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

Vaccine efficacy of Nuvaxovid to prevent the onset of COVID-19 from seven days after Dose 2 was 90.4% (95% CI 82.9 – 94.6). No cases of 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 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 (e.g. BMI ≥ 30 kg/m², 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 two 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 identified 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%).

Study 2 (2019nCoV-302)

Study 2 is an ongoing Phase 3, multicentre, 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) 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 hospitalisation 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 analysis set (PP-EFF) 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 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, median age was 56.0 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 one comorbid condition.

Table 3: 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% (79.7, 94.9) ²
65 to 84 years of age	1,953	1 (0.10) ²	---	1,957	9 (0.9) ²	---	88.9% (20.2, 99.7) ⁴

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 [Zou 2004].

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.

Licensed seasonal influenza vaccine co-administration sub-study

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 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. A 30% reduction in antibody responses to Nuvaxovid was noted as assessed by an anti-spike IgG assay with seroconversion rates similar to participants who did not receive concomitant influenza vaccine (see section 4.5 and section 4.8).

Study 3 (2019nCoV-501)

Study 3 is an ongoing Phase 2a/b, multicentre, 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.

Enrolment was completed in November 2020.

The primary efficacy analysis set (PP-EFF) included 2,770 participants who received either Nuvaxovid (n = 1,408) or placebo (n = 1,362), received two 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 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, 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 (3.62%) cases for Nuvaxovid versus 96 (7.05%) 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.

Elderly population

Nuvaxovid was assessed in individuals 18 years of age and older. The efficacy of Nuvaxovid was consistent between elderly (≥ 65 years) and younger individuals (18 to 64 years).

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Nuvaxovid in one or more subsets of the paediatric population in prevention of COVID-19, see section 4.2 for information on paediatric use.

Conditional approval

This medicinal product has been authorised under a so-called ‘conditional approval’ scheme. This means that further evidence on this medicinal product is awaited. The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeat-dose toxicity, local tolerance and reproductive and developmental toxicity.

Genotoxicity and Carcinogenicity

In vitro genotoxicity studies were conducted with the Matrix-M adjuvant. The adjuvant was shown to be non-genotoxic. Carcinogenicity studies were not performed. Carcinogenicity is not expected.

Reproductive toxicity

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium hydrogen phosphate heptahydrate
Sodium dihydrogen phosphate monohydrate
Sodium chloride
Polysorbate 80
Sodium hydroxide (for adjustment of pH)
Hydrochloric acid (for adjustment of pH)
Water for injections

Adjuvant (Matrix-M)

Cholesterol
Phosphatidylcholine (including all-rac- α -Tocopherol)
Potassium dihydrogen phosphate
Potassium chloride
Disodium hydrogen phosphate dihydrate
Sodium chloride
Water for injections

For adjuvant: see also section 2.

6.2 Incompatibilities

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

6.3 Shelf life

Unopened vial

9 months at 2°C to 8°C, protected from light.

Unopened Nuvaxovid vaccine has been shown to be stable up to 12 hours at 25°C. Storage at 25°C is not the recommended storage or shipping condition but may guide decisions for use in case of temporary temperature excursions during the 9-month storage at 2°C to 8°C.

Punctured vial

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

From a microbiological point of view, after first opening (first needle puncture), the vaccine should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 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

5 mL of dispersion in a vial (type I glass) with a stopper (bromobutyl rubber) and an aluminium overseal with blue plastic flip-off cap.

Each vial contains 10 doses of 0.5 mL.

Pack size: 10 multidose vials

6.6 Special precautions for disposal and other handling

Handling instructions and administration

This vaccine should be handled by a healthcare professional using aseptic techniques to ensure the sterility of each dose.

Preparation for use:

- The vaccine comes ready to use.
- Unopened vaccine should be stored at 2°C to 8°C and kept within the outer carton to protect from light.
- Immediately prior to use, remove the vaccine vial from the carton in the refrigerator.
- Record the date and time of discard on the vial label. Use within 6 hours after first puncture.

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 dispersion 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 ten (10) doses 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.
 - 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 does not contain a preservative. Store the opened vial between 2°C to 25°C for up to 6 hours after first puncture, see section 6.3.

Discard:

- Discard this vaccine if not used within 6 hours after first puncture of the vial, see section 6.3.

Disposal:

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

7. MARKETING AUTHORISATION HOLDER

Novavax CZ a.s.
Bohumil 138
Jevany, 28163
Czechia

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1618/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20th December 2021

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

ANNEX II

- A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**
- E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION**

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Serum Institute of India Pvt. Ltd.
212/2, Off SoliPoonawalla Road, Hadapsar, Pune - 411028, Maharashtra, India

Serum Institute of India Pvt. Ltd.
S. No. 105-110, Manjari BK, Tal -Haveli, Pune-412307, Maharashtra, India

Name and address of the manufacturer responsible for batch release

Novavax CZ a.s.
Bohumil 138, Jevany, 28163, Czechia

In view of the declared Public Health Emergency of International Concern and in order to ensure early supply this medicinal product is subject to a time-limited exemption allowing reliance on batch control testing conducted in the registered site(s) that are located in a third country. This exemption ceases to be valid on 31 March 2022. Implementation of EU based batch control arrangements, including the necessary variations to the terms of the marketing authorisation, has to be completed by 31 March 2022 at the latest.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

Official batch release

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Periodic safety update reports (PSURs)

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Risk management plan (RMP)

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14-a of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	Due date
In order to ensure consistent product quality during shelf life, the MAH should provide additional information on stability of the finished product.	31 January 2023
In order to ensure consistent quality over the product life cycle, the MAH should adequately bridge the reference standards and review the finished product potency limits when additional data become available.	31 July 2022

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON LABEL

1. NAME OF THE MEDICINAL PRODUCT

Nuvaxovid dispersion for injection
COVID-19 Vaccine (recombinant, adjuvanted)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose contains 5 micrograms of SARS-CoV-2 recombinant spike protein adjuvanted with Matrix- M

3. LIST OF EXCIPIENTS

Adjuvant Matrix-M: Fraction-A and Fraction-C of *Quillaja saponaria* Molina extract

Excipients: disodium hydrogen phosphate heptahydrate, sodium dihydrogen phosphate monohydrate, disodium hydrogen phosphate dihydrate, sodium chloride, polysorbate 80, cholesterol, phosphatidylcholine (including all-rac- α -Tocopherol) potassium dihydrogen phosphate, potassium chloride, and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials
Each vial contains 10 doses of 0.5 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use

Read the package leaflet before use.



For more information, scan or visit
www.NovavaxCovidVaccine.com

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

After first puncture, store at 2°C to 25°C, use within 6 hours.

Store in the original carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novavax CZ a.s.

Bohumil 138, Jevany, 28163, Czechia

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1618/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Nuvaxovid dispersion for injection
COVID-19 Vaccine (recombinant, adjuvanted)

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses of 0.5 mL

6. OTHER

Store in a refrigerator.
After first puncture, store at 2°C to 25°C, use within 6 hours.

Date:
Time:

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Nuvaxovid dispersion for injection COVID-19 Vaccine (recombinant, adjuvanted)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Nuvaxovid is and what it is used for
2. What you need to know before you receive Nuvaxovid
3. How Nuvaxovid is given
4. Possible side effects
5. How to store Nuvaxovid
6. Contents of the pack and other information

1. What Nuvaxovid is and what it is used for

Nuvaxovid is a vaccine used to prevent COVID-19 caused by the SARS-CoV-2 virus.

Nuvaxovid is given to adults 18 years of age and older.

The vaccine 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. None of the ingredients in this vaccine can cause COVID-19.

2. What you need to know before you receive Nuvaxovid

Nuvaxovid should not be given

- if you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist, or nurse before you are given Nuvaxovid if:

- you have ever had a severe or life-threatening allergic reaction after receiving any other vaccine injection or after you were given Nuvaxovid in the past,
- you have ever fainted following any needle injection,
- you have a high fever (over 38°C) or severe infection. However, you can have your vaccination if you have a mild fever or upper airway infection like a cold,
- you have bleeding problems, you bruise easily or you use a medicine to prevent blood clots,
- 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).

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist, or nurse before you are given Nuvaxovid.

As with any vaccine, the 2-dose vaccination course of Nuvaxovid may not fully protect all those who receive it and it is not known how long you will be protected.

Children and adolescents

Nuvaxovid is not recommended for children aged below 18 years. Currently, there is no information available on the use of Nuvaxovid in children younger than 18 years of age.

Other medicines and Nuvaxovid

Tell your doctor, pharmacist, or nurse if you are taking, have recently taken, or might take any other medicines or vaccines.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, ask your doctor, pharmacist, or nurse for advice before you receive this vaccine.

Driving and using machines

Some of the side effects of Nuvaxovid listed in section 4 (Possible side effects) may temporarily reduce your ability to drive and use machines (for example, feeling faint or lightheaded or feeling very tired).

Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Nuvaxovid contains sodium and potassium

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

This vaccine contains less than 1 mmol potassium (39 milligrams) per dose, that is to say, essentially 'potassium-free'.

3. How Nuvaxovid is given

Nuvaxovid will be given to you as two separate 0.5 mL injections.

Your doctor, pharmacist, or nurse will inject the vaccine into a muscle, usually in your upper arm.

It is recommended that you receive the second dose of Nuvaxovid 3 weeks after your first dose to receive the full course of this vaccine.

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.

If you miss an appointment for your second injection of Nuvaxovid ask your doctor or nurse for advice. If you miss a scheduled injection, you may not be fully protected against COVID-19.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them. Most side effects go away within a few days of appearing. If symptoms persist, contact your doctor, pharmacist or nurse.

As with other vaccines, you may feel pain or discomfort at the injection site, or you may see some redness and swelling at this site. However, these reactions usually clear up within a few days.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:

- 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

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common (may affect more than 1 in 10 people):

- 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

Common (may affect up to 1 in 10 people):

- 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)

Uncommon (may affect up to 1 in 100 people):

- enlarged lymph nodes
- high blood pressure
- itchy skin, rash or hives
- redness of the skin
- itchy skin where the injection is given

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via **the national reporting system** listed in [Appendix V](#) and include batch/Lot number if available. By reporting side effects, you can help provide more information on the safety of this vaccine.

5. How to store Nuvaxovid

Keep this medicine out of the sight and reach of children.

Your doctor, pharmacist, or nurse is responsible for storing this vaccine and disposing of any unused product correctly.

Information about storage, expiry, use and handling are described in the section intended for healthcare professionals at the end of the package leaflet.

6. Contents of the pack and other information

What Nuvaxovid contains

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

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

- Matrix-M is included in this vaccine as an adjuvant. Adjuvants are substances included in certain vaccines to accelerate, improve, and/or prolong the protective effects of the vaccine. Matrix-M adjuvant contains Fraction-A (42.5 micrograms) and Fraction-C (7.5 micrograms) of *Quillaja saponaria* Molina extract per 0.5 mL dose.
- The other ingredients (excipients) included in Nuvaxovid are:
 - Disodium hydrogen phosphate heptahydrate
 - Sodium dihydrogen phosphate monohydrate
 - Disodium hydrogen phosphate dihydrate
 - Sodium chloride
 - Polysorbate 80
 - Cholesterol
 - Phosphatidylcholine (including all-rac- α -Tocopherol)
 - Potassium dihydrogen phosphate
 - Potassium chloride
 - Sodium hydroxide (for the adjustment of pH)
 - Hydrochloric acid (for the adjustment of pH)
 - Water for Injections

What Nuvaxovid looks like and contents of the pack

- The dispersion is colourless to slightly yellow, clear to mildly opalescent (pH 7.2).
- 5 mL of dispersion in a vial with a rubber stopper and a blue flip-off top.
- Each vial contains 10 doses of 0.5 mL
- Pack size: 10 multidose vials.

Marketing Authorisation Holder

Novavax CZ a.s.
Bohumil 138
Jevany, 28163
Czechia

Manufacturer

Novavax CZ a.s.
Bohumil 138
Jevany, 28163
Czechia

This leaflet was last revised in {DD month YYYY}.

This vaccine has been given ‘conditional approval’. This means that there is more evidence to come about this vaccine.

The European Medicines Agency will review new information on this vaccine at least every year and this leaflet will be updated as necessary.

Scan the code with a mobile device to get the package leaflet in different languages.



Or visit the URL: <https://www.NovavaxCovidVaccine.com>

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Administer Nuvaxovid intramuscularly, preferably into the deltoid muscle of the upper arm, as two doses, 3 weeks apart.

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.

Handling instructions and administration

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.

This vaccine should be handled by a healthcare professional using aseptic techniques to ensure the sterility of each dose.

Preparation for use:

- The vaccine comes ready to use.
- Unopened vaccine should be stored in a refrigerator (2°C – 8°C) and kept within the outer carton to protect from light.
- Immediately prior to use, remove the vaccine vial from the carton in the refrigerator.
- Record the date and time of discard on the vial label. Use within 6 hours after first puncture.

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 dispersion.

- Visually inspect the contents of the vial for visible particulate matter and/or discoloration 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 ten (10) doses 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.
 - 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 does not contain a preservative. Store the opened vial between 2°C to 25°C for up to 6 hours after first puncture.

Discard:

- Discard this vaccine if not used within 6 hours after first puncture of the vial, see section 6.3.

Disposal:

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

ANNEX IV

**CONCLUSIONS ON THE GRANTING OF THE CONDITIONAL MARKETING
AUTHORISATION PRESENTED BY THE EUROPEAN MEDICINES AGENCY**

Conclusions presented by the European Medicines Agency on:

- **Conditional marketing authorisation**

The CHMP having considered the application is of the opinion that the risk-benefit balance is favourable to recommend the granting of the conditional marketing authorisation as further explained in the European Public Assessment Report.