## 1 NAME OF THE MEDICINAL PRODUCT

**Trade/Brand Name: COVOVAX™**

SARS-CoV-2 rS Protein (COVID-19) recombinant spike protein Nanoparticle Vaccine

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains 5 micrograms of SARS-CoV-2 spike protein* and is adjuvanted with Matrix-M1.

Adjuvant Matrix-M1 containing per 0.5 mL dose: Fraction-A (42.5 micrograms) and Fraction-C (7.5 micrograms) of *Quillaja saponaria* Molina extract.

* SARS-CoV-2 recombinant spike protein is 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.

Both **COVOVAX™** (manufactured by Serum Institute of India Pvt Ltd) and Nuvaxovid (manufactured by Novavax) are SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccines.

## 3 PHARMACEUTICAL FORM

Dispersion for injection (injection).

**COVOVAX™** is colourless to slightly yellow, clear to mildly opalescent, free to practically free from visible particles.

# 4 CLINICAL PARTICULARS

## 4.1 Therapeutic indications

**COVOVAX™** is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.

The vaccine is approved for restricted use in emergency situation that may prevent COVID-19 disease.

## 4.2 Posology and method of administration

Posology

*Individuals 18 years of age and older*

**COVOVAX™** 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.

It is recommended that individuals who receive a first dose of **COVOVAX™,** complete the vaccination course with **COVOVAX™**.

*Paediatric population*
The safety and efficacy of SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine 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

**COVOVAX™** is intended for Intramuscular (IM) injection only, preferably in the deltoid muscle.

For instructions on administration, see section 6.6.

## 4.3 Contraindications

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

## 4.4 Special warnings and precautions for use

Hypersensitivity and anaphylaxis

Events of anaphylaxis have been reported with COVID-19 vaccines. 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 **COVOVAX™**.

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 at the injection site following an intramuscular administration in these individuals.

Immunocompromised individuals

The efficacy, safety, and immunogenicity of the SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine has been assessed in a limited number of immunocompromised individuals. The efficacy of **COVOVAX™** 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 **COVOVAX™** 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 0.5 mL, that is to say, essentially 'potassium-free'.

## 4.5 Interaction with other medicinal products and other forms of interaction

Co-administration of SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine 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 SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine with other vaccines has not been studied.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

There is limited experience with use of SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine 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 COVOVAX™ 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 **COVOVAX™** 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 **COVOVAX™** 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

**COVOVAX™** 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

**Overall summary of the safety profile from the Overseas studies:**

The safety of Nuvaxovid [Novovax SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine] 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 at least one dose of Nuvaxovid (n = 19,898) or placebo (n = 10,454), 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

Very common (≥ 1/10),
Common (≥ 1/100 to < 1/10),
Uncommon (≥ 1/1,000 to < 1/100),
Rare (≥ 1/10,000 to < 1/1,000),
Very rare (< 1/10,000),
Not known (cannot be estimated from the available data).

**Table 1: Adverse reactions from Nuvaxovid Clinical Trials**

| **MedDRA SOC** | **Frequency** | **Adverse reactions** |
|---|---|---|
| General disorders and administration site conditions | Very common | Injection site pain[a], injection site tenderness[a], fatigue[a], malaise[a, b] |
| | Common | Injection site redness[a, c], injection site swelling[a], pyrexia[a], chills, pain in extremity |
| | Uncommon | Injection site pruritis |
| Nervous system disorders | Very common | Headache |
| Musculoskeletal and connective tissue disorders | Very common | Myalgia[a], arthralgia[a] |
| Gastrointestinal system disorders | Very common | Nausea or vomiting[a] |
| Skin and subcutaneous tissue disorders | Uncommon | Rash, erythema, pruritus, urticaria |
| Blood and lymphatic system disorders | Uncommon | Lymphadenopathy |

[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).

**Overall summary of the safety profile from the Indian study:**

**COVOVAX™** was safe and well tolerated in the phase 2/3 clinical trial in India. In the Phase 2 part (n=200), 200 adults received **COVOVAX™** or Placebo in 3:1 ratio. During 14 day follow up post-second dose, there were no causally related serious adverse events (SAEs) reported. In the Phase 3 part (n=1396), participants received **COVOVAX™** or Novavax SARS-CoV-2 rS Protein Nanoparticle Vaccine (Novavax vaccine) in 3:1 ratio

[1046 in **COVOVAX™** group and 350 in Novavax SARS-CoV-2 rS Protein Nanoparticle Vaccine (Novavax vaccine) group]. All 1396 participants received the first dose while 1375 participants received the second dose. An interim analysis included data collected until Day 36 visit (14 days after second dose) of all 1396 participants.

Demographic characteristics were generally similar among participants across both the groups.

Overall, the incidence of solicited reactions (injection site reactions: pain, tenderness, erythema, swelling and induration; and systemic reactions: fever, headache, fatigue, malaise, arthralgia, myalgia, nausea and vomiting), unsolicited adverse events and serious adverse events (SAEs) was comparable in the study and control groups.

Among 1396 participants who received the first dose, a total of 5 SAEs in 5 (0.4 %) participants were reported; in 3 (0.3%) participants in **COVOVAX™** group and in 2 (0.6%) participants in Novavax vaccine group. The SAEs in the **COVOVAX™** group included pyrexia, limb crushing injury, and joint effusion (1 participant each). The SAEs in the Novavax vaccine group included dengue fever and retinal vein occlusion reported in 1 participant each. All SAEs were assessed as not related to study vaccine. All SAEs resolved without any sequelae except for event of limb crushing injury which was ongoing at the time of data cut off.

**Table 2: Adverse drug reactions from COVOVAX™ study in India (Data until Day 36 visit)**

| **MedDRA SOC** | **Frequency** | **Adverse reactions** |
|---|---|---|
| Gastrointestinal disorders | Common | Nausea |
| | Uncommon | Vomiting |
| General disorders and administration site conditions | Very common | Injection site pain, pyrexia |
| | Common | Injection site tenderness, injection site erythema, injection site swelling, injection site induration, fatigue, pain, malaise |
| | Uncommon | Asthenia, chills, injection site pruritus, injection site rash |
| Musculoskeletal and connective tissue disorders | Common | Myalgia, arthralgia |
| | Uncommon | Pain in extremity, back pain |
| Nervous system disorders | Very common | Headache |
| | Rare | Dizziness, somnolence |
| Skin and subcutaneous tissue disorders | Rare | Pruritus |

## 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

**COVOVAX™** 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-M1 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.

**Efficacy data from the Overseas studies**:

The clinical efficacy, safety, and immunogenicity of Nuvaxovid [Novovax SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine] 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 $\geq$ 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 days 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 47years (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) $\geq 30$ 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 ≥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 3.

**Table 3: 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) |
|---|---|---|---|---|---|---|---|
| | Partici-pants N | COVID-19 cases n (%) [2] | Incidence Rate Per Year Per 1,000 People[2] | Partici-pants 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 deviation 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 $\geq 30$ kg/m$^2$, chronic lung disease, diabetes mellitus type 2, cardiovascular disease, and chronic kidney disease).

Efficacy results reflect enrolment that occurred during the time period when strains classified as Variants of Concern or Variants of Interest were predominantly circulating in the 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-EEF) 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 4: 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.

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).

**Immunogenicity data from the Indian study:**

Geometric Mean ELISA Units (GMEUs) of IgG antibodies against spike (S) protein were comparable between the groups at baseline – Day 1. GMEUs increased significantly after each dose of vaccine in both the groups and were comparable. There was > 92% seroconversion in both the groups on Day 36 (14 days after second dose). The immunogenicity data indicates that **COVOVAX™** is comparable in terms of anti-S IgG antibody titers and seroconversion rates to Novavax vaccine (see Tables 6 and 7).

**Table 5: Summary of Anti-S IgG antibodies**

| **Timepoint** | **Statistic** | **COVOVAX™ (N=340) n (%)** | **Novavax vaccine (N=110) n (%)** |
|---|---|---|---|
| Baseline | N | 340 | 110 |
| | GMEU | 2172.3 | 1708.6 |
| | 95% CI | (1799.8, 2621.8) | (1230.7, 2372.2) |
| | | | |
| 21 (+7) days after Dose 1 | N | 340 | 110 |
| | GMEU | 38350.9 | 34603.6 |
| | 95% CI | (33043.7, 44510.4) | (26002.6, 46049.5) |
| | | | |
| 14 (+7) days after Dose 2 | N | 338 | 109 |
| | GMEU | 143506.4 | 152276.9 |
| | 95% CI | (133203.2, 154606.7) | (132441.4, 175083.1) |

**Table 6: Summary of Proportion of Participants with Seroconversion for Anti-S IgG Antibodies**

| **Timepoint** | **Statistic** | **COVOVAX™ (N=340) n (%)** | **Novavax vaccine (N=110) n (%)** |
|---|---|---|---|
| 21 (+7) days after Dose 1 | N Evaluated | 340 | 110 |
| | Seroconversion, n (%) | 281 (82.6) | 92 (83.6) |

| **Timepoint** | **Statistic** | **COVOVAX™ (N=340) n (%)** | **Novavax vaccine (N=110) n (%)** |
|---|---|---|---|
| | 95% CI | (78.2, 86.5) | (75.4, 90.0) |
| | | | |
| 14 (+7) days after Dose 2 | N Evaluated | 338 | 109 |
| | Seroconversion, n (%) | 314 (92.9) | 105 (96.3) |
| | 95% CI | (89.6, 95.4) | (90.9, 99.0) |

## 5.2 Pharmacokinetic properties

Not applicable.

## 5.3 Preclinical safety data

Non-clinical data reveal no special hazards 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 novel Matrix-M1 adjuvant and 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 µg SARS-CoV-2 rS protein (approximately 200-fold excess relative to the human dose of 5 µg on a weight-adjusted basis) with 10 µg Matrix-M1 adjuvant (approximately 40-fold excess relative to the human dose of 50 µg on a weight-adjusted basis). No vaccine-related adverse effects on fertility, pregnancy/lactation, or development of the embryo/fetus and offspring through post-natal Day 21 were observed.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of Excipients

The excipients used in the manufacturing of **COVOVAX™** are listed below:

Adjuvant Matrix-M1
Disodium hydrogen phosphate heptahydrate
Sodium dihydrogen phosphate monohydrate
Sodium chloride
Polysorbate 80
Water for Injections

## 6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products, vaccines or diluted.

## 6.3 Shelf-life

Unopened vial

The expiry date of vaccine is indicated on the label and packaging.

Once opened (first needle puncture) multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2ºC and +25ºC. All opened (punctured) multidose vials of **COVOVAX™** should be discarded at the end of immunization session or six hours after the first needle puncture, whichever comes first.

## 6.4 Special Precautions for Storage

Store in a refrigerator (+2ºC to +8ºC). Do not freeze. Keep vials in outer carton to protect from light.

Opened multidose vial (after the first use)

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

## 6.5 Nature and Contents of Container

**COVOVAX™** is supplied as ready to use liquid in rubber-stoppered single and multidose vial in below listed presentations

- 1-dose - 0.5 mL per vial
- 2-doses - 1.0 mL per vial
- 10-doses - 5.0 mL per vial
- 20-doses - 10 mL per vial

Not all pack sizes may be marketed.

## 6.6 Instructions for Use, Handling and Disposal

**Administration:**

**COVOVAX™** is a Colourless to slightly yellow, clear to mildly opalescent, free to practically free from visible particles. The vaccine should be discarded if particulate matter or differences in the described appearance are observed.

**Do not shake the vial.**

Each vaccine dose of 0.5 mL is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual. It is normal for liquid to remain in the vial after withdrawing the final dose. When low dead volume syringes and/or needles are used, the amount remaining in the vial may be sufficient for an additional dose. Care should be taken to ensure a full 0.5 mL dose is administered. Where a full 0.5 mL dose cannot be extracted, the remaining volume should be discarded. Do not pool excess vaccine from multiple vials.

The vaccine does not contain any preservative. Aseptic technique should be used for withdrawing the dose for administration.

After the first opening, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2ºC and +25ºC. Discard any unused vaccine.

To facilitate the traceability of the vaccine, the name and the batch number of the administered product must be recorded for each recipient.

**Disposal**

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

## 7 MARKETING AUTHORIZATION

**Manufactured by:**
**Serum Institute of India Pvt. Ltd.**
212/2, Hadapsar, Pune 411028, India.

**Serum Institute of India Pvt. Ltd.**
S. No. 105-110, Manjari Bk., Pune 412307, India.

**Marketed by:**
**Serum Institute Life Sciences Pvt. Ltd.**
401, Sarosh Bhavan, 16-B/1, Dr. Ambedkar Road, Pune - 411 001, INDIA

## 8 MARKETING AUTHORISATION NUMBER (S)

Permission in Form CT-23 (Permission No. MF/BIO/21/000138) ➔ for Manjari premises
Permission in Form CT-23 (Permission No. MF/BIO/21/000137) ➔ for Hadapsar premises

## 9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

28th December 2021

Date Updated: February 2022

FACT SHEET FOR VACCINE RECIPIENT
APPROVED FOR EMERGENCY USE AUTHORIZATION (EUA) OF

# SARS-CoV-2 rS Protein (COVID-19) recombinant spike protein Nanoparticle Vaccine

## COVOVAX™

This vaccine has been given emergency use authorization for prevention of COVID-19. It does not have a marketing authorization, however, this approval for the restricted use in emergency situation grants permission for the vaccine to be used for active immunization of individuals aged 18 years and older for the prevention of coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 in individuals 18 years of age and older.

**Reporting of side effects**

As with any new medicine, this vaccine will be closely monitored to allow quick identification of new safety information. You can help by reporting any side effects, you may get after vaccination to the Serum Institute of India Pvt. Ltd. who is the manufacturer of **COVOVAX™** vaccine on 24 x 7 Toll-Free Number: 1800 1200124 or at **pharmacovigilance@seruminstitute.com.**
For more information read this fact sheet carefully.

You are being offered the Serum Institute of India Pvt. Ltd. (SIIPL) **COVOVAX™** Vaccine to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Fact Sheet contains information to help you understand the risks and benefits of the **COVOVAX™** Vaccine, which you may receive because there is currently a pandemic of COVID-19.

The **COVOVAX™** is a vaccine and may prevent you from getting COVID-19 disease.

Read this Fact Sheet for information about the **COVOVAX™** Vaccine. Talk to the healthcare provider / doctor if you have questions. It is your choice to receive the **COVOVAX™** Vaccine.

The **COVOVAX™** vaccination course consists of two separate doses of 0.5 ml each. The second dose should be administered at 3 weeks after the first dose.

For intramuscular (IM) injection only.

The **COVOVAX™** may not protect everyone.

### WHAT YOU NEED TO KNOW BEFORE YOU GET THIS VACCINE

#### WHAT IS COVID-19 ?

COVID-19 disease is caused by a coronavirus called SARS-CoV-2. This type of coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

#### WHAT IS THE SIIPL COVOVAX™ VACCINE ?

The **COVOVAX™** vaccine is approved for restricted use in emergency situation that may prevent COVID-19 caused by a coronavirus called SARS-CoV-2 in individuals 18 years of age and older.

#### WHAT SHOULD YOU MENTION TO YOUR HEALTHCARE PROVIDER / DOCTOR BEFORE YOU GET COVOVAX™ VACCINE ?

**Tell the healthcare provider / doctor about all of your medical conditions, including:**

- If you have ever had a severe allergic reaction (anaphylaxis) after any drug, food, any vaccine or any ingredients of **COVOVAX™** vaccine
- If you have fever
- If you have a problem with bleeding or bruising, or if you are taking a blood thinning medicines (anticoagulant)
- If you have a problem with liver related disorder and/or inflammation of the gall bladder
- If 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 you are pregnant or plan to become pregnant
- If you are breastfeeding
- If you have received another COVID-19 vaccine

If you have any of the above conditions, you should consult your healthcare provider / doctor before deciding to take the vaccine.

**Vaccination in patients with bleeding disorders or receiving a blood thinning medicine (anticoagulants):**
As with other intramuscular injections, **COVOVAX™** should be given with caution to individuals with a problem with bleeding or bruising, or those taking a blood thinning medicine (anticoagulant) because bleeding or bruising may occur following an intramuscular injection in these individuals.
A fine-gauge needle (23-gauge or smaller caliber) should be used for the vaccination in such individuals, followed by firm pressure on the injection site, without rubbing, for at least 2 minutes. If possible, vaccination could be scheduled prior to the use of these medications, so that the patients' risk of bleeding is not increased by their therapeutic action.

**Patients with weak immune system or receiving immunosuppressive medicines:**
Currently limited amount of data are available in individuals with a weakened immune system or who are taking chronic treatment that suppresses or prevents immune responses. People with weakened immune systems due to other illnesses or medications might be at increased risk for severe COVID -19. They may receive **COVOVAX™**. However, people with weakened immune systems should also be aware of the potential for reduced immune responses to **COVOVAX™**, as well as the need to continue following all current guidance to protect themselves against COVID-19 (see below).

#### WHO SHOULD GET THE COVOVAX™ VACCINE ?

**COVOVAX™** Vaccine has been authorized for emergency use in individuals 18 years of age and older caused by SARS-CoV-2.

#### WHO SHOULD NOT GET THE COVOVAX™ VACCINE ?

You should not get the **COVOVAX™** Vaccine if you have ever had a serious allergic reaction (including anaphylaxis) to:

- a previous dose of **COVOVAX™**
- any ingredient of **COVOVAX™** (listed below)

If you are not sure, talk to your doctor, pharmacist or nurse.

Signs of an allergic reaction may include pain at injection site and/or tenderness, fatigue, malaise, swelling at injection site, pyrexia, chills, headache, nausea or vomiting. Contact your doctor or healthcare professional immediately or go to the nearest hospital emergency room right away if you have an allergic reaction. It might get worsen if not treated immediately.

People with a history of severe allergic reactions not related to vaccines or injectable medications such as food, pets, environmental, or latex allergies may get vaccinated. People with a history of allergies to oral medications or a family history of severe allergic reactions may also get vaccinated.

#### WHAT ARE THE INGREDIENTS IN THE COVOVAX™ VACCINE ?

The **COVOVAX™** Vaccine includes the following ingredients:
SARS-CoV-2 rS Protein DS
Adjuvant Matrix-M1
Disodium hydrogen phosphate heptahydrate
Sodium dihydrogen phosphate monohydrate
Sodium chloride
Polysorbate 80
Water for injections

#### HOW IS THE COVOVAX™ GIVEN ?

The **COVOVAX™** Vaccine will be given to you as an intramuscular (IM) injection only, preferably in the deltoid muscle.

The **COVOVAX™** vaccination course consists of two separate doses of 0.5 ml each.
If you receive one dose of the **COVOVAX™** vaccine, then the second dose should be administered at 3 weeks after the first dose.

**If you miss your second dose**
If you forget to go back at the scheduled time, ask your healthcare provider / doctor for advice. It is important that you return for your second dose of **COVOVAX™** vaccine.

#### HAS THE COVOVAX™ VACCINE BEEN USED BEFORE ?

The **COVOVAX™** is used in clinical trials, a large number of participants received two doses in clinical studies.

#### WHAT ARE THE BENEFITS OF THE COVOVAX™ VACCINE ?

In ongoing clinical trials, the **COVOVAX™** Vaccine has been shown to prevent COVID-19 following 2 doses given between 3 weeks apart. The duration of protection against COVID-19 disease is currently unknown.

Protection against COVID-19 starts from approximately 7 days after the second dose of **COVOVAX™**. Individuals may not be fully protected until 7 days after the second dose is administered. However, please note that as with any vaccine, **COVOVAX™** may not protect everyone who is vaccinated from COVID-19.

#### WHAT ARE THE RISKS OF THE COVOVAX™ VACCINE ?

Like all medicines, this vaccine can cause side effects, although not everybody gets them.
Get urgent medical attention from your doctor if you get symptoms of a severe allergic reaction. Such reactions may include a combination of any of the following symptoms:

- feeling faint or light-headed
- pain in a muscle or group of muscles
- physical discomfort
- swelling and extreme pain at injection site

After vaccination, you may have more than one side effect at the same time. If any of your symptoms are persistent, please seek advice from your healthcare provider / doctor.

Side effects that have been reported with the **COVOVAX™** Vaccine include:

Very Common (may affect more than 1 in 10 people)

- Injection site pain
- Injection site tenderness
- Feeling tired (fatigue)
- Malaise
- Headache
- Fever
- Soreness of muscles
- Joint pain
- Nausea or vomiting

Common (may affect up to 1 in 10 people)

- Chills
- Injection site redness
- Injection site swelling
- Injection site induration (hardness)
- Pain in extremity (legs or arms)
- Body ache

Uncommon (may affect up to 1 in 100 people)

- Asthenia (weakness or lack of energy)
- Injection site pruritus (itching)
- Injection site rash
- Rash
- Skin redness
- Itching
- Hives
- Enlarged lymph nodes
- Back pain

Rare

- Dizziness (feeling dizzy)
- Sleepiness

Adverse reactions were usually mild to moderate in severity with a median duration of less than or equal to 2 days for local injection site reactions and less than or equal to 1 day for systemic reactions following vaccination.

When compared with Dose 1, local and systemic adverse reactions were more frequently reported after Dose 2.
In case you need medical advice, kindly consult your healthcare provider / doctor.

These may not be all the possible side effects of the **COVOVAX™** Vaccine. Serious and unexpected side effects may occur. If you notice any side effects not mentioned in this leaflet, please inform your healthcare provider / doctor.

If you experience unusually high or prolonged fever, or other symptoms, alternative causes should be considered and contact your healthcare provider / doctor to seek further medical advice.

#### WHAT SHOULD I DO ABOUT SIDE EFFECTS ?

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

**Call the healthcare provider / doctor if you have any side effects that bother you or do not go away.**

In addition, you can report side effects after vaccination to Serum Institute of India Pvt. Ltd. who is the manufacturer of **COVOVAX™** vaccine as below:

- 24x7 Call Center Toll-Free Number **(For Reporting of Adverse Events Only)**: 1800 1200124
- **pharmacovigilance@seruminstitute.com**

#### WHAT IF I DECIDE NOT TO GET THE COVOVAX™ VACCINE ?

It is your choice to receive or not receive the **COVOVAX™** Vaccine. You may prefer to consult your healthcare provider / doctor.

#### CAN I RECEIVE THE COVOVAX™ VACCINE WITH OTHER VACCINES ?

There is no information on the use of the **COVOVAX™** Vaccine with other vaccines.

#### WHAT IF I AM PREGNANT OR BREASTFEEDING?

You may discuss your options with the healthcare provider / doctor.

#### WILL THE COVOVAX™ VACCINE GIVE ME COVID-19 INFECTION ?

No. The **COVOVAX™** is spike protein based COVID-19 Vaccine, does not contain SARS-CoV-2 and cannot give you COVID-19 infection.

#### KEEP YOUR VACCINATION CARD

When you get your dose, please discuss with your healthcare provider / doctor regarding the option of your vaccination record on digital platform, if available.

#### AFTER VACCINATION, DO I NEED TO CONTINUE TAKING PRECAUTIONS TO PREVENT COVID-19 INFECTION ?

People who get vaccinated should continue to follow all current guidance to protect themselves against COVID-19 after they are vaccinated.

That means:

- Wearing a mask
- Staying at least six feet away from others
- Avoiding crowds
- Washing hands with soap and water or using hand sanitizer

#### HOW CAN I LEARN MORE ?

- Ask the healthcare provider / doctor.
- Contact your local or state public health department.

**Prepared:** 31 December 2021

*Manufactured by:*
**SERUM INSTITUTE OF INDIA PVT. LTD.**
S. No. 105 - 110, Manjari Bk., Pune 412 307, INDIA

*Marketed by:*
**SERUM INSTITUTE LIFE SCIENCES PVT. LTD.**
401, Sarosh Bhavan, 16-B/1, Dr. Ambedkar Road,
Pune - 411 001, INDIA



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# आपात स्थिति में प्रयोग (ईयूए) करने के लिए अनुमोदित SARS-CoV-2 rS Protein (कोविड-19) पुनःसंयोजक स्पाइक प्रोटीन नैनोपार्टिकल टीका प्राप्त करने वाले व्यक्ति के लिए तथ्य पत्र (फैक्ट शीट)

## कोवोवैक्स™

यह टीका कोविड-19 की रोकथाम के लिए आपात स्थिति में प्रयोग करने के लिए अनुमोदित है। इस टीके के विपणन करने की अनुमति नहीं है, लेकिन आपातस्थिति में सीमित प्रयोग के लिए अनुमोदित यह टीका 18 वर्ष और उससे अधिक उम्र के लोगों में SARS-COV-2 के कारण होने वाले कोरोना वाइरस रोग 2019 (कोविड-19) की रोकथाम हेतु 18 वर्ष और उससे अधिक उम्र के लोगों के सक्रिय टीकाकरण करने के लिए इस्तेमाल किया जा सकता है।

**प्रतिकूल प्रभावों की रिपोर्टिंग**

जैसा कि हर नयी दवा के साथ होता है, इस टीके के संबंध में सुरक्षा संबंधी नयी जानकारी जिससे त्वरित रूप से पता की जा सके, टीके की बारीकी से निगरानी की जाएगी। सीरम इंस्टिट्यूट ऑफ इंडिया प्राइवेट लिमिटेड द्वारा निर्मित **कोवोवैक्स** ™ से टीकाकरण के बाद किसी भी प्रतिकूल प्रभाव की सूचना हमें 24 x 7 टोल-फ्री नम्बर: 1800 1200124 या **pharmacovigilance@seruminstitute.com** पर देकर आप मदद कर सकते हैं। और जानकारी के लिए इस तथ्य पत्र को ध्यान से पढ़ें।

आपको सीरम इंस्टिट्यूट ऑफ इंडिया प्राइवेट लिमिटेड (एसआईआईपीएल) का **कोवोवैक्स**™ टीके की पेशकश की जा रही है SARS-CoV-2 के कारण होने वाले कोरोना वाइरस रोग 2019 (कोविड-19) की रोकथाम करने के लिए। इस तथ्य पत्र में **कोवोवैक्स**™ टीके के जोखिमों और लाभों को समझने में मदद करने के लिए जानकारी दी गई है। कोविड-19 महामारी के कारण आपको यह टीका दिया जा सकता है।

**कोवोवैक्स**™ एक टीका है जिससे आप कोविड-19 रोग से पीड़ित होने से बच सकते हैं।

**कोवोवैक्स**™ टीके के बारे में जानकारी प्राप्त करने के लिए इस तथ्य पत्र को पढ़ें। अगर आपको कुछ पूछना है तो स्वास्थ्य सेवा प्रदाता / डॉक्टर से बात करें। यह आपकी इच्छा पर निर्भर करता है कि आप **कोवोवैक्स**™ लेंगे या नहीं।

**कोवोवैक्स**™ टीके के कोर्स में 0.5 ml की दो अलग अलग खुराके हैं। प्रथम खुराक प्राप्त करने के 3 सप्ताह पूरे होने पर दूसरी खुराक दी जानी चाहिए।

यह केवल मांसपेशीय इंजेक्शन(आईएम) के रूप में ही दिया जाना चाहिए।

हो सकता है कि **कोवोवैक्स**™ सबको सुरक्षा न प्रदान करें।

### वो बातें जिनकी आपको जानकारी होनी चाहिए इस टीके को प्राप्त करने से पहले

**कोविड-19 क्या है?**

कोविड-19 एक रोग है जो SARS-CoV-2 नामक कोरोना वायरस से होता है। इस प्रकार का कोरोना वायरस पहले कभी नहीं देखा गया था। आपको किसी कोविड-19 से पीड़ित व्यक्ति के संपर्क में आने से यह रोग हो सकता है। मुख्य रूप से यह श्वसन तंत्र का रोग है जो अन्य अंगों को प्रभावित कर सकता है। कोविड-19 से पीड़ित लोगों में विभिन्न प्रकार के लक्षण नज़र आ सकते हैं, मामूली लक्षणों से लेकर गंभीर लक्षणों तक। वाइरस के संपर्क में आने के 2 से 14 दिनों के भीतर यह लक्षण नज़र आ सकते हैं। वो लक्षण जो दिख सकते हैं: बुखार या कंपकंपी; खाँसी; साँस फूलना; थकान; मांसपेशियों या शरीर में दर्द; सरदर्द; हाल ही में स्वाद या गंध न महसूस होना; गले में खराश; बंद नाक या बहती नाक; उलटी अथवा मतली; दस्त।

**एस आई आई पी एल कोवोवैक्स™ टीका क्या है?**

**कोवोवैक्स**™ टीका 18 वर्ष और उससे अधिक उम्र के लोगों में SARS-CoV-2 से होने वाले कोविड-19 रोग की रोकथाम के लिए आपात स्थितियों में सीमित उपयोग के लिए अनुमोदित किया गया है।

**कोवोवैक्स™ टीका लेने से पहले आपको अपने स्वास्थ्य प्रदाता / डॉक्टर को क्या बताना चाहिए?**

**स्वास्थ्य प्रदाता / डॉक्टर को अपनी स्वास्थ्य संबंधी समस्याओं के बारे में सब कुछ बताएं, जिसमें शामिल होना चाहिए:**

- अगर आपको किसी दवा, खाद्य पदार्थ, किसी टीके या **कोवोवैक्स**™ टीके के किसी भी सामग्री के कारण गंभीर अलर्जी (तीव्रग्राहिता) हुई है।
- अगर आपको बुखार है
- अगर आपको रक्तस्राव या नील पड़ने की समस्या हो, या फिर आप खून पतला करने की दवा (ऐंटिकॉग्युलेंट) लेते हैं
- यदि आपको लीवर संबंधी कोई विकार हो और /या गॉल ब्लैडर में सूजन हो
- यदि आपका प्रतिरक्षा तंत्र ठीक से काम नहीं करता (रोगक्षम-अपर्याप्तता) या फिर आप ऐसी दवाएं लेते हैं जो प्रतिरक्षा तंत्र को कमज़ोर करती है (जैसे की उच्च खुराक के कॉर्टिकोस्टेरॉइड्स, इम्यूनोसप्रेसेंट या कैंसर के लिए दवाएं)
- अगर आप गर्भवती हैं या गर्भ धारण करने के बारे में सोच रही हैं
- अगर आप स्तनपान कराती हैं
- अगर आपको कोविड-19 के खिलाफ कोई अन्य टीका दिया जा चुका है

यदि उपरोक्त स्थितियों में से कोई भी आप पर लागू होती है, तो इस टीके को लेने से पहले आप अपने स्वास्थ्य प्रदाता /डॉक्टर से इसके बारे में परामर्श करें।

**ऐसे रोगियों का टीकाकरण जिन्हें रक्त के बहने से संबंधित विकार है या जो रक्त पतला करने की दवा ले रहे हैं (ऐंटिकॉग्युलेंट):**

अन्य मांसपेशिय इंजेक्शन की तरह, जिन लोगों को रक्त बहने या नील पड़ने की परेशानी होती है या रक्त पतला करने की कोई दवा ले रहे हों (ऐंटिकॉग्युलेंट), उन लोगों को **कोवोवैक्स**™ टीका लगाते समय एहतियात बरता जाना चाहिए क्योंकि ऐसे लोगों में मांसपेशिय इंजेक्शन लगाने के कारण रक्त बह सकता है या नील पड़ सकता है।

ऐसे लोगों का टीकाकरण करने के लिए बहुत ही महीन सूई (23-गेज या उससे कम कैलिबर की) का प्रयोग किया जाना चाहिए, और टीका लगाने के बाद इन्जेक्शन लगे स्थान को बिना घिसे कम से कम 2 मिनट तक दबा कर रखा जाना चाहिए। अगर संभव हो तो टीकाकरण इस प्रकार की दवाएं लेने से पहले किया जाना चाहिए, जिससे रोगी में दवा के प्रभाव से रक्त के बहने का जोखिम बढ़ न जाए।

**कमजोर प्रतिरक्षा तंत्र वाले रोगी या इम्युनोसप्रेसिव दवाएं लेने वाले रोगी:**

जिन लोगों की प्रतिरक्षा क्षमता कम है या जो प्रतिरक्षा क्षमता कम करने वाली उपचार पद्धतियाँ करा रहे हैं, फिलहाल उन के बारे में जानकारी सीमित है। जिन लोगों की अन्य बीमारियों के कारण या दवाओं के कारण प्रतिरक्षा क्षमता कम है, उन्हें गंभीर कोविड-19 होने का ज्यादा खतरा है। उन्हें **कोवोवैक्स**™ लगाया जा सकता है। लेकिन कम प्रतिरक्षा क्षमता वाले लोगों को यह भी पता रहना चाहिए कि **कोवोवैक्स**™ से टीकाकरण करने पर शायद कोविड-19 से प्रतिरक्षा औरों की तुलना में कम हो सकती है और अपने आप को रोग से सुरक्षित रखने के लिए उन्हें कोविड-19 संबंधी सभी वर्तमान दिशा-निर्देशों का पालन करते रहना चाहिए।(नीचे देखें)

**किन लोगों को कोवोवैक्स™ टीका लेना चाहिए?**

**कोवोवैक्स**™ टीका 18 वर्ष और उससे अधिक उम्र के लोगों के लिए SARS-CoV-2 के कारण होने वाले रोग से सुरक्षित रखने के लिए आपात स्थितियों में सीमित उपयोग के लिए अनुमोदित किया गया है।

**किन लोगों को कोवोवैक्स™ टीका <u>नहीं</u> दिया जाना चाहिए?**

आपको **कोवोवैक्स**™ टीका नहीं लेना चाहिए अगर आपको पहले कभी निम्नलिखित के कारण गंभीर अलर्जी (तीव्रग्राहिता सहित) हुई हो:

- **कोवोवैक्स**™ की पिछली खुराक
- इस टीके में शामिल किसी भी सामग्री (नीचे सूचीबद्ध किया गया है)

यदि आप निश्चित नहीं हैं तो अपने डॉक्टर, दवावाले या नर्स से बात करें।

अलर्जी के प्रभावों में शामिल हैं - इंजेक्शन लगाने के स्थान पर दर्द, और/ या छूने से दर्द, थकान, बेचैनी, इंजेक्शन लगाने के स्थान पर सूजन, पाइरेक्सिया, कंपकंपी, सरदर्द, मतली या उलटी। अगर आप को अलर्जी होती है तो तुरंत अपने डॉक्टर या स्वास्थ्य देखभाल कर्ता से संपर्क करें अथवा नज़दीक के अस्पताल के आपात कक्ष में जाएं। अगर इसका तुरंत उपचार नहीं किया गया, तो यह बिगड़ सकता है।

जिन लोगों को पहले से खाने, पालतु पशुओं, पर्यावरणीय या लेटेक्स से अलर्जी हो लेकिन इस टीके या इन्जेक्ट की जाने वाली दवा से अलर्जी न हों, उन्हें यह टीका दिया जा सकता है। जिन लोगों को खाने/पिलाने वाली दवाओं से अलर्जी हो या उनके परिवार में गंभीर अलर्जी होने का पता हो, वे भी टीकाकरण करा सकते हैं।

**कोवोवैक्स™ टीके में क्या सामग्री शामिल हैं?**

**कोवोवैक्स**™ टीके में निम्नलिखित सामग्री है:

SARS-CoV-2 rS प्रोटीन DS
सहायक मैट्रिक्स -M1
डाइसोडियम हाइड्रोजेन फॉस्फेट हेप्टाहाइड्रेट
सोडियम डाईहाइड्रोजेन फॉस्फेट मोनोहाइड्रेट
सोडियम क्लोराइड
पॉलिसॉर्बेट 80
इंजेक्शन के लिए पानी

**कोवोवैक्स™ टीका कैसे दिया जाता है?**

**कोवोवैक्स**™ टीका केवल मांसपेशीय इंजेक्शन(आईएम) के रूप में ही दिया जाना चाहिए, आदर्श रूप से डेल्टॉइड मांसपेशी में।

**कोवोवैक्स**™ टीके के कोर्स में 0.5 ml की दो अलग अलग खुराके हैं।
अगर आपको **कोवोवैक्स**™ की पहली खुराक दी जा चुकी है, तो प्रथम खुराक प्राप्त करने के 3 सप्ताह पूरे होने पर दूसरी खुराक दी जानी चाहिए।

**अगर आप दूसरी खुराक लेना भूल जाते हैं**

अगर आप नियत समय पर दूसरी खुराक लेना भूल जाते हैं, तो अपने स्वास्थ्य प्रदाता/डॉक्टर से सलाह लें। जरूरी है कि आप **कोवोवैक्स**™ टीके की दूसरी खुराक लेने वापस आएं।

**क्या कोवोवैक्स™ टीके का पहले इस्तेमाल हुआ है?**

**कोवोवैक्स**™ का प्रयोग नैदानिक परीक्षणों में किया गया है, काफी बड़ी संख्या में प्रतिभागियों को **कोवावैक्स**™ की दो खुराकें दी गई थीं।

**कोवोवैक्स™ टीके के क्या लाभ हैं?**

जारी नैदानिक परीक्षणों में देखा गया है कि **कोवोवैक्स**™ टीके से कोविड-19 रोग की रोकथाम होती है जब 3 सप्ताह के अंतराल पर 2 खुराके दी जाती हैं। कोविड-19 से सुरक्षा की अवधि के बारे में फिलहाल जानकारी नहीं है।

**कोवोवैक्स**™ की दूसरी खुराक दिए जाने के लगभग 7 दिन बाद से कोविड-19 से सुरक्षा प्रदान होती है। दूसरी खुराक दिए जाने के पश्चात 7 दिन तक व्यक्ति पूर्ण रूप से सुरक्षित नहीं होता है। लेकिन ध्यान दें कि किसी भी अन्य टीके की तरह, **कोवोवैक्स**™ से सभी लोगों की सुरक्षा सुनिश्चित नहीं की जा सकती है, जिन्हें कोविड -19 के खिलाफ टीका लगाया गया है।

**कोवोवैक्स™ टीके से संबंधित क्या जोखिम हैं?**

सभी दवाओं की तरह, इस टीके के भी प्रतिकूल प्रभाव हो सकते हैं, हालांकि सभी में यह प्रतिकूल प्रभाव नज़र नहीं आते।

यदि आप में गंभीर अलर्जिक प्रभाव के लक्षण नज़र आते हैं, तो तुरंत अपने डॉक्टर से चिकित्सीय सलाह लें। निम्नलिखित में से एक या उससे अधिक प्रभाव नज़र आ सकते हैं:

- बेहोशी सी महसूस होना या चक्कर आना
- किसी एक मांसपेशी या कई मांसपेशियों में दर्द
- शारीरिक पीड़ा
- इंजेक्शन लगाए जाने के स्थान पर सूजन और बहुत ज्यादा दर्द

टीकाकरण के बाद एक ही समय पर आपमें एक से ज्यादा प्रतिकूल प्रभाव दिख सकते हैं। अगर आपमें इन में से कोई भी लक्षण बने रहते हैं, तो अपने स्वास्थ्य सेवा प्रदाता / डॉक्टर से सलाह लें।

**कोवोवैक्स**™ टीके से जुड़े प्रतिकूल प्रभाव जो रिपोर्ट किए गए हैं, उनमें शामिल हैं:

बहुत आम है (जो 10 में से 1 से अधिक व्यक्ति को प्रभावित करते हैं)

- इंजेक्शन लगने के स्थान में दर्द
- इंजेक्शन लगने के स्थान को दबाने पर दर्द
- थकान महसूस होना (कमज़ोरी)
- बेचैनी
- सरदर्द
- बुखार
- मांसपेशियों में पीड़ा
- जोड़ों में दर्द
- मतली या उलटी

आम है (जो 10 में से 1 व्यक्ति तक को प्रभावित करते हैं)

- कंपकंपी
- इंजेक्शन लगने के स्थान पर लालिमा
- इंजेक्शन लगने के स्थान में सूजन
- इंजेक्शन लगने के स्थान पर इंड्यूरेशन (कड़ापन)
- एक्सट्रीमिटीज़ में दर्द (टांगों और भुजाओं में)
- बदन दर्द

आम नहीं है (जो 100 में से 1 व्यक्ति को प्रभावित करते हैं)

- दुर्बलता (कमज़ोरी या एनर्जी में कमी)
- इंजेक्शन लगने के स्थान में बेहद खुजली
- इंजेक्शन लगने के स्थान में दाने
- दाने
- त्वचा में लालिमा
- खुजली
- पित्ती
- बढ़े लसीका पर्व (लिम्फ नोड्स)
- पीठ में दर्द,

गिना-चुना है

- सिर में चक्कर आना
- उनींदापन

टीकाकरण के बाद होने वाले प्रतिकूल प्रभावों की गंभीरता आमतौर पर हल्के से मध्यम थी और इंजेक्शन लगने के स्थान पर प्रभाव औसतन 2 दिन या उससे कम समय में ठीक हो गई और दैहिक समस्याएं औसतन 1 दिन या उससे कम में ठीक हो गई।

खुराक 1 की तुलना में खुराक 2 के बाद स्थानीय एवं सर्वांगीय प्रतिकूल प्रभाव ज्यादा रिपोर्ट किए गए।
यदि आपको चिकित्सीय सलाहकी जरूरत हो, त कृपया अपने स्वास्थ्य देखभाल कर्ता / डॉक्टर से सलाह लें।

उपरोक्त प्रतिकूल प्रभाव **कोवोवैक्स**™ से संबंधित संभव प्रतिकूल प्रभाव की पूर्ण सूची शायद नहीं है। गंभीर और अप्रत्याशित प्रतिकूल प्रभाव हो सकते हैं। अगर आपको ऐसे कोई भी प्रतिकूल प्रभाव नज़र आते हैं जो इस पत्रक में शामिल नहीं हैं, तो कृपया अपने स्वास्थ्य सेवा प्रदाता / डॉक्टर को सूचित करें।

यदि कोई रोगी असामान्य रूप से तेज बुखार या लंबे समय तक बुखार, या अन्य लक्षणों की रिपोर्ट करता है, तो अन्य कारणों पर विचार किया जाना चाहिए और अपने स्वास्थ्य सेवा प्रदाता / डॉक्टर से चिकित्सीय सलाह ली जानी चाहिए।

**प्रतिकूल प्रभावों के बारे में मुझे क्या करना चाहिए?**

अगर आपको गंभीर अलर्जी होती है, तो नज़दीकी अस्पताल को कॉल करें या वहाँ जाएं।

**स्वास्थ्य प्रदाता / डॉक्टर से बात करें अगर कोई भी प्रतिकूल प्रभाव आपको परेशान करता है या उसकी तीव्रता कम नहीं हो रही है।**

इसके अतिरिक्त आप टीके के बाद होने वाले प्रतिकूल प्रभावों की जानकारी **कोवोवैक्स**™ टीके के निर्माता सीरम इंस्टिट्यूट ऑफ इंडिया प्राइवेट लिमिटेड को निम्नलिखित तरीके से दे सकते हैं:

- 24x7 कॉल सेंटर का टोल फ्री नम्बर **(केवल प्रतिकूल प्रभावों की रिपोर्टिंग के लिए)**: 1800 1200124
- **pharmacovigilance@seruminstitute.com**

**क्या होगा अगर मैं कोवोवैक्स™ टीका नहीं लेने का निर्णय करता हूँ?**

यह आपकी इच्छा पर निर्भर करता है कि आप **कोवोवैक्स**™ टीका लेंगे या नहीं। आप अपने स्वास्थ्य प्रदाता /डॉक्टर से इसके बारे में परामर्श ले सकते हैं।

**क्या मैं अन्य टीकों के साथ कोवोवैक्स™ टीका ले सकता हूँ?**

**कोवोवैक्स**™ टीके का अन्य टीकों के साथ लिए जाने के बारे में अभी तक कोई जानकारी मौजूद नहीं है।

**अगर मैं गर्भवती हूँ या स्तनपान कराती हूँ तो क्या?**

आपके सामने मौजूद विकल्पों के बारे में अपने स्वास्थ्य प्रदाता/डॉक्टर से चर्चा करें।

**क्या कोवोवैक्स™ टीके से मुझे कोविड-19 संक्रमण हो सकता है?**

नहीं। **कोवोवैक्स**™ स्पाइक प्रोटीन आधारित कोविड-19 टीके है जिसमें SARS-CoV-2 मौजूद नहीं है और इससे कोविड-19 संक्रमण नहीं हो सकता।

**अपना टीकाकरण कार्ड अपने पास रखें**

अगर डिजिटल प्लैटफॉर्म पर टीकाकरण रिकॉर्ड का विकल्प उपलब्ध हो तो जब आपको खुराक दे दी जाए, तो अपने स्वास्थ्य प्रदाता/डॉक्टर से इसके बारे में चर्चा करें।

**टीकाकरण के बाद, कोविड-19 के संक्रमण से सुरक्षित रहने के लिए क्या मुझे एहतियात बरतना जारी रखना पड़ेगा?**

टीकाकरण कराने के बाद भी खुद को कोविड-19 से सुरक्षित रखने के लिए सभी वर्तमान दिशा-निर्देशों का पालन करना जारी रखना पड़ेगा।
इसका मतलब है:

- मास्क पहनना
- दूसरों से कम से कम छः फीट की दूरी बनाए रखना
- भीड़ से दूर रहना
- साबुन और पानी से हाथ धोना या हैंड सैनेटाइज़र का प्रयोग करना।

**मुझे इसके बारे में और जानकारी कहाँ से मिल सकती है?**

- अपने स्वास्थ्य प्रदाता/डॉक्टर से पूछें।
- अपने स्थानीय या राज्य के जन स्वास्थ्य विभाग से संपर्क करें।

**तैयार करने की तारीख**: 31 दिसम्बर 2021

**निर्माता:**
**SERUM INSTITUTE OF INDIA PVT. LTD.**
S. No. 105 - 110, Manjari Bk., Pune 412 307, INDIA

™ पंजीकरण के तहत ट्रेडमार्क

**विपणन:**
**SERUM INSTITUTE LIFE SCIENCES PVT. LTD.**
401, Sarosh Bhavan, 16-B/1, Dr. Ambedkar Road,
Pune - 411 001, INDIA

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

# SARS-CoV-2 rS Protein (COVID-19) recombinant spike protein Nanoparticle Vaccine

COVOVAX™

## 1 NAME OF THE MEDICINAL PRODUCT

**Trade/Brand Name: COVOVAX™**
SARS-CoV-2 rS Protein (COVID-19) recombinant spike protein Nanoparticle Vaccine

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains 5 micrograms of SARS-CoV-2 spike protein* and is adjuvanted with Matrix-M1.
Adjuvant Matrix-M1 containing per 0.5 ml dose: Fraction-A (42.5 micrograms) and Fraction-C (7.5 micrograms) of *Quillaja saponaria* Molina extract.
* SARS-CoV-2 recombinant spike protein is 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.
Both **COVOVAX™** (manufactured by Serum Institute of India Pvt Ltd) and Nuvaxovid (manufactured by Novavax) are SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccines.

## 3 PHARMACEUTICAL FORM

Dispersion for injection (injection).
**COVOVAX™** is colourless to slightly yellow, clear to mildly opalescent, free to practically free from visible particles.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**COVOVAX™** is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.
The vaccine is approved for restricted use in emergency situation that may prevent COVID-19 disease.

### 4.2 Posology and method of administration

Posology
*Individuals 18 years of age and older*
**COVOVAX™** 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.
It is recommended that individuals who receive a first dose of **COVOVAX™**, complete the vaccination course with **COVOVAX™**.
*Paediatric population*
The safety and efficacy of SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine 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
**COVOVAX™** is intended for Intramuscular (IM) injection only, preferably in the deltoid muscle.
For instructions on administration, see section 6.6.

### 4.3 Contraindications

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

### 4.4 Special warnings and precautions for use

Hypersensitivity and anaphylaxis
Events of anaphylaxis have been reported with COVID-19 vaccines. 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 **COVOVAX.™**
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 at the injection site following an intramuscular administration in these individuals.
Immunocompromised individuals
The efficacy, safety and immunogenicity of the SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine has been assessed in a limited number of immunocompromised individuals. The efficacy of **COVOVAX™** 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 **COVOVAX™** 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 0.5 ml, that is to say, essentially 'potassium-free'.

### 4.5 Interaction with other medicinal products and other forms of interaction

Co-administration of SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine 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 SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine with other vaccines has not been studied.

### 4.6 Fertility, pregnancy and lactation

Pregnancy
There is limited experience with use of SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine 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 **COVOVAX™** 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 **COVOVAX™** 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 **COVOVAX™** 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

**COVOVAX™** 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

**Overall summary of the safety profile from the Overseas studies:**
The safety of Nuvaxovid [Novovax SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine] 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 at least one dose of Nuvaxovid (n = 19,898) or placebo (n = 10,454), 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
Very common (≥ 1/10),
Common (≥ 1/100 to < 1/10),
Uncommon (≥ 1/1,000 to < 1/100),
Rare (≥ 1/10,000 to < 1/1,000),
Very rare (< 1/10,000),
Not known (cannot be estimated from the available data).

**Table 1: Adverse reactions from Nuvaxovid Clinical Trials**

| MedDRA SOC | Frequency | Adverse reactions |
|---|---|---|
| General disorders and administration site conditions | Very common | Injection site pain[a], injection site tenderness[a], fatigue[a], malaise[a] |
| | Common | Injection site redness[a,c], injection site swelling[a], pyrexia[a], chills, pain in extremity |
| | Uncommon | Injection site pruritis |
| Nervous system disorders | Very common | Headache |
| Musculoskeletal and connective tissue disorders | Very common | Myalgia[a], arthralgia[a] |
| Gastrointestinal system disorders | Very common | Nausea or vomiting[a] |
| Skin and subcutaneous tissue disorders | Uncommon | Rash, erythema, pruritus, urticaria |
| Blood and lymphatic system disorders | Uncommon | Lymphadenopathy |

[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).

**Overall summary of the safety profile from the Indian study**
**COVOVAX™** was safe and well tolerated in the phase 2/3 clinical trial in India. In the Phase 2 part (n=200), 200 adults received **COVOVAX™** or Placebo in 3:1 ratio. During 14 day follow up post-second dose, there were no causally related serious adverse events (SAEs) reported. In the Phase 3 part (n=1396), participants received **COVOVAX™** or Novavax SARS-CoV-2 rS Protein Nanoparticle Vaccine (Novavax vaccine) in 3:1 ratio [1046 in **COVOVAX™** group and 350 in Novavax SARS-CoV-2 rS Protein Nanoparticle Vaccine (Novavax vaccine) group]. All 1396 participants received the first dose while 1375 participants received the second dose. An interim analysis included data collected until Day 36 visit (14 days after second dose) of all 1396 participants.
Demographic characteristics were generally similar among participants across both the groups.
Overall, the incidence of solicited reactions (injection site reactions: pain, tenderness, erythema, swelling and induration; and systemic reactions: fever, headache, fatigue, malaise, arthralgia, myalgia, nausea and vomiting), unsolicited adverse events and serious adverse events (SAEs) was comparable in the study and control groups.
Among 1396 participants who received the first dose, a total of 5 SAEs in 5 (0.4 %) participants were reported; in 3 (0.3%) participants in **COVOVAX™** group and in 2 (0.6%) participants in Novavax vaccine group. The SAEs in the **COVOVAX™** group included pyrexia, limb crushing injury, and joint effusion (1 participant each). The SAEs in the Novavax vaccine group included dengue fever and retinal vein occlusion reported in 1 participant each. All SAEs were assessed as not related to study vaccine. All SAEs resolved without any sequelae except for event of limb crushing injury which was ongoing at the time of data cut off.

**Table 2: Adverse drug reactions from COVOVAX™ study in India (Data until Day 36 visit)**

| MedDRA SOC | Frequency | Adverse reactions |
|---|---|---|
| Gastrointestinal disorders | Common | Nausea |
| | Uncommon | Vomiting |
| General disorders and administration site conditions | Very common | Injection site pain, pyrexia |
| | Common | Injection site tenderness, injection site erythema, injection site swelling, injection site induration, fatigue, pain, malaise |
| | Uncommon | Asthenia, chills, injection site pruritus, injection site rash |
| Musculoskeletal and connective tissue disorders | Common | Myalgia, arthralgia |
| | Uncommon | Pain in extremity, back pain |
| Nervous system disorders | Very common | Headache |
| | Rare | Dizziness, somnolence |
| Skin and subcutaneous tissue disorders | Rare | Pruritus |

### 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: Other viral vaccines, ATC code: J07BX03
Mechanism of action
**COVOVAX™** 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-M1 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 protect against COVID-19.
Efficacy data from the Overseas studies:
The clinical efficacy, safety, and immunogenicity of Nuvaxovid [Novovax SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine] 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 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 days 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 47years (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/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 ≥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 3.

**Table 3: 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 deviation 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/m$^2$, chronic lung disease, diabetes mellitus type 2, cardiovascular disease, and chronic kidney disease).
Efficacy results reflect enrolment that occurred during the time period when strains classified as Variants of Concern or Variants of Interest were predominantly circulating in the 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-EEF) 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 4: 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) |
|---|---|---|---|---|---|---|---|
| | Participants N | COVID-19 cases n (%) | Incidence Rate Per Year Per 1,000 People[1] | Participants 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.
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).

**Immunogenicity data from the Indian study:**
Geometric Mean ELISA Units (GMEUs) of IgG antibodies against spike (S) protein were comparable between the groups at baseline - Day 1. GMEUs increased significantly after each dose of vaccine in both the groups and were comparable. There was > 92% seroconversion in both the groups on Day 36 (14 days after second dose). The immunogenicity data indicates that **COVOVAX™** is comparable in terms of anti-S IgG antibody titers and seroconversion rates to Novavax vaccine (see Tables 5 and 6).

**Table 5 Summary of Anti-S IgG antibodies**

| Timepoint | Statistic | COVOVAX™ (N=340) n (%) | Novavax vaccine (N=110) n (%) |
|---|---|---|---|
| Baseline | N | 340 | 110 |
| | GMEU | 2172.3 | 1708.6 |
| | 95% CI | (1799.8, 2621.8) | (1230.7, 2372.2) |
| 21 (+7) days after Dose 1 | N | 340 | 110 |
| | GMEU | 38350.9 | 34603.6 |
| | 95% CI | (33043.7, 44510.4) | (26002.6, 46049.5) |
| 14 (+7) days after Dose 2 | N | 338 | 109 |
| | GMEU | 143506.4 | 152276.9 |
| | 95% CI | (133203.2, 154606.7) | (132441.4, 175083.1) |

**Table 6 Summary of Proportion of Participants with Seroconversion for Anti-S IgG Antibodies**

| Timepoint | Statistic | COVOVAX™ (N=340) n (%) | Novavax vaccine (N=110) n (%) |
|---|---|---|---|
| 21 (+7) days after Dose 1 | N Evaluated | 340 | 110 |
| | Seroconversion, n (%) | 281 (82.6) | 92 (83.6) |
| | 95% CI | (78.2, 86.5) | (75.4, 90.0) |
| 14 (+7) days after Dose 2 | N Evaluated | 338 | 109 |
| | Seroconversion, n (%) | 314 (92.9) | 105 (96.3) |
| | 95% CI | (89.6, 95.4) | (90.9, 99.0) |

### 5.2 Pharmacokinetic properties

Not applicable.

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazards 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 novel Matrix-M1 adjuvant and 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 µg SARS-CoV-2 rS protein (approximately 200-fold excess relative to the human dose of 5 µg on a weight-adjusted basis) with 10 µg Matrix-M1 adjuvant (approximately 40-fold excess relative to the human dose of 50 µg on a weight-adjusted basis). No vaccine-related adverse effects on fertility, pregnancy/lactation, or development of the embryo/fetus and offspring through post-natal Day 21 were observed.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of Excipients

The excipients used in the manufacturing of **COVOVAX™** are listed below:
Adjuvant Matrix-M1
Disodium hydrogen phosphate heptahydrate
Sodium dihydrogen phosphate monohydrate
Sodium chloride
Polysorbate 80
Water for Injections

### 6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products, vaccines or diluted.

### 6.3 Shelf-life

The expiry date of vaccine is indicated on the label and packaging.
Once opened (first needle puncture) multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2°C and +25°C. All opened (punctured) multidose vials of **COVOVAX™** should be discarded at the end of immunization session or six hours after the first needle puncture, whichever comes first.

### 6.4 Special Precautions for Storage

Store in a refrigerator (+2°C to +8°C). Do not freeze. Keep vials in outer carton to protect from light.
Discard if vaccine has been frozen.
Opened multidose vial (after the first use)
For storage conditions after the first opening of the medicinal product, see section 6.3.

### 6.5 Nature and Contents of Container

**COVOVAX™** is supplied as ready to use liquid in rubber-stoppered single and multidose vial in below listed presentations
1 dose - 0.5 ml per vial
2 dose - 1 ml per vial
10 doses - 5 ml per vial
20 doses - 10 ml per vial
Not all pack sizes may be marketed.

### 6.6 Instructions for Use, Handling and Disposal

**Administration:**
**COVOVAX™** is a Colourless to slightly yellow, clear to mildly opalescent, free to practically free from visible particles. The vaccine should be discarded if particulate matter or differences in the described appearance are observed.
**Do not shake the vial.**
Each vaccine dose of 0.5 ml is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual. It is normal for liquid to remain in the vial after withdrawing the final dose. When low dead volume syringes and/or needles are used, the amount remaining in the vial may be sufficient for an additional dose. Care should be taken to ensure a full 0.5 ml dose is administered. Where a full 0.5 ml dose cannot be extracted, the remaining volume should be discarded. Do not pool excess vaccine from multiple vials.
The vaccine does not contain any preservative. Aseptic technique should be used for withdrawing the dose for administration.
After the first opening, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2°C and +25°C. Discard any unused vaccine.
To facilitate the traceability of the vaccine, the name and the batch number of the administered product must be recorded for each recipient.
**Disposal**
Any unused vaccine or waste material should be disposed off in accordance with local requirements.

**Date Updated**
February 2022

*Manufactured by:*
**SERUM INSTITUTE OF INDIA PVT. LTD.**
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™ Trademark under registration

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