

COVID-19 Vaccine (recombinant, adjuvanted), NVX-CoV2373, COVOVAX™, NUVAXOVID™

EUL holder for Covovax™: Serum Institute of India Pvt. Ltd. (SIPL)

EUL holder for Nuvaxovid™: Novavax CZ a.s.



The COVID-19 Vaccine NVX-CoV2373 (Covovax™, Nuvaxovid™) is a protein subunit vaccine against coronavirus disease 2019 (COVID-19). It consists of recombinant SARS-CoV-2 spike proteins' fragments assembled into nanoparticles which cannot cause disease. These nanoparticles help the body's immune system to create antibodies and subsequently respond to an infection with live SARS-CoV-2. This vaccine contains Matrix-M saponin-based adjuvant to generate a more powerful response of the immune system.

A Phase 3 study in the United Kingdom during the SARS-CoV-2 Alpha variant predominance involving individuals aged 18 years and older showed that two vaccine doses have an efficacy of 90% against mild, moderate or severe COVID-19 and 87% against moderate or severe COVID-19 from 7 days after the second dose. The median duration of the follow up was 56 days after the second dose. In a Phase 3 study in Mexico and the USA during circulation of multiple variants, vaccine efficacy against mild, moderate or severe COVID-19 was 90% and 100% against moderate or severe COVID-19, with a median follow up of 64 days after the second dose. In a Phase 2a/b study conducted in South Africa during the predominance of the Beta variant, vaccine efficacy against mild, moderate or severe disease was 49%, with a median follow up of 105 days after the second dose.

The data reviewed by WHO support the conclusion that the known benefits of Covovax™/Nuvaxovid™ outweigh the risks that are known or considered possible, and WHO recommends the use of Covovax™/Nuvaxovid™ in individuals aged ≥18 years.

Date of WHO Emergency Use Listing (EUL) recommendation:

Covovax™: 17 December 2021

Nuvaxovid™: 20 December 2021

Although produced in different manufacturing sites and assigned different product names, these vaccines are considered equivalent.

Date of prequalification (PQ): currently no information

National regulatory authorities (NRAs) can use reliance approaches for in-country authorization of vaccines based on WHO PQ/EUL or emergency use authorizations by stringent regulatory authorities (SRAs) (🇺🇸).

Product characteristics

Presentation	Fully liquid, recombinant, adjuvanted suspension for injection in glass vials
Number of doses in a vial	Covovax™: 1 and 10 (one dose 0.5 mL) Nuvaxovid™: 10 (one dose 0.5 mL)
Vaccine syringe type and needle size	Auto-disable (AD) syringes: 0.5 mL Needles for intramuscular injection 23G × 1" (0.60 × 25 mm)

¹ Contents will be updated as new information becomes available.

Schedule and administration

Recommended for age	18 years of age and above, without an upper age limit
Recommended schedule	<p>2 doses (0.5 mL each) at a recommended interval of 3 to 4 weeks: Dose 1: at the start date Dose 2: 21–28 days after first dose.</p> <p>If the second dose is inadvertently administered earlier than 3 weeks after the first, the dose does not need to be repeated. If the second dose is inadvertently delayed beyond 3 weeks, it should be given at the earliest possible opportunity.</p> <p>According to current recommendation, all vaccinated individuals should receive two doses and the same product should be used.</p> <p>Additional dose of a vaccine may be needed as part of an extended primary series for immunocompromised and other populations where the immune response after standard primary series is deemed likely to be insufficient.</p> <p>The need for and timing of boosters is being assessed. While administration of a booster dose following the primary series has elicited a strong immune response, data on the duration of continued protection are currently still missing.</p>
Route and site of administration	Intramuscular (i.m.) administration The preferred site is the deltoid muscle.
Dosage	0.5 mL (single dose)
Diluent	None needed
Mixing syringe	None needed
Preparation/reconstitution/dilution requirement	<p><u>No dilution is required.</u> During the vaccination session, keep between +2 and +8 °C and protected from light.</p> <p>Vaccine administration:</p> <ol style="list-style-type: none"> 1. Vaccine is ready to use, do not dilute. 2. Gently swirl the vial, do not shake. 3. Visually inspect the contents of the vial to ensure that the liquid is colourless to slightly yellow, clear to mildly opalescent, and that no visible particulate matter or other coloration is present in the vial. If visible particles or discoloration are present, do not use and discard the vial. 4. Record date and time of the first use (first puncture and withdrawal of the first dose) on the vial label when using multi-dose vials. 5. Draw up the vaccine dose (0.5 mL) from the vial at the time of administration, pre-loading of syringes is not recommended. 6. Before withdrawing each following vaccine dose from a multi-dose vial, swirl the vial gently, do not shake. 7. Preferably, use the vaccine from the vial immediately after first puncture or within 6 hours afterwards. Discard if vaccine is not used within this time or at the end of vaccination session, whichever comes first. <p>If any liquid remains in the multi-dose vaccine vial after withdrawing the final dose, discard the vial and do not combine residual vaccine from multiple vials.</p>

Schedule and administration contd.

Multi-dose vial policy After the first dose has been withdrawn, keep between +2 and +8 °C during the in-use period, and discard any unused vaccine in the vial 6 hours after first puncture or at the end of the immunization session, whichever comes first. Keep opened vaccine vial in the foam pad of the vaccine carrier.

Contraindications

- Known history of anaphylaxis to any component of the vaccine.
- Persons who developed anaphylaxis after the first dose should not receive a second dose of the Covovax™/Nuvaxovid™ vaccine.

Precautions

- All persons should be vaccinated by a health-care professional in settings where appropriate medical treatment is available in case of allergic reactions. An observation period of 15 minutes after vaccination should be ensured.
- For persons with a history of anaphylaxis to any other vaccine or injectable therapy, regardless of route of administration, a risk assessment should be conducted by a health professional. Such individuals should be observed 30 minutes after vaccination in health-care setting where anaphylaxis can be immediately treated.
- Vaccination of people suffering from acute severe febrile illness (body temperature over 38.5 °C) should be postponed until they are afebrile.
- Vaccination of persons with acute COVID-19, including those with disease onset in the period between the two doses, should be postponed until they have recovered from acute illness and criteria for discontinuation of isolation have been met.

Special population groups For persons with **comorbidities**, the phase 3 trials demonstrated that the vaccine has similar efficacy in persons with cardiovascular, respiratory, neurological, kidney, liver and immunocompromising conditions, diabetes, and obesity. Vaccination is recommended for persons with comorbidities that have been identified as at increased risk of severe COVID-19 and death.

Persons aged 60 years or more made up 16% of participants of the phase 2 and 3 efficacy studies in the United Kingdom; the vaccine showed 89% and 95% efficacy against mild, moderate or severe COVID-19 but with a wide confidence interval (CI:20-100). In other studies, the sample size was insufficient to enable the vaccine efficacy estimation. The trial data across studies indicate that the safety profile for this age group is acceptable. Post-introduction effectiveness studies are not yet available. Use of vaccine in persons aged ≥65 years is recommended.

Available data on administration in **pregnant women** are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy. No vaccine-specific studies are currently planned in pregnant women. The safety data specific to Covovax™/Nuvaxovid™ vaccine adjuvant Matrix-M come from the clinical trials which did not include a sufficient number of pregnant women to allow conclusions on adjuvant safety. Post-marketing surveillance data are being collected via pregnancy registries, but the data on use in pregnant women and on neonatal outcomes are not yet available. On the basis of previous experience with other protein-based vaccines, it is expected that the vaccine effectiveness in pregnant women will be similar to that observed in non-pregnant women of similar age. Given that COVID-19 has increased risk of severe outcomes in pregnant women, WHO recommends the use of Covovax™/Nuvaxovid™ in pregnant women if the benefits of vaccination outweigh the potential risks (e.g. if there is elevated community transmission and no other WHO EUL COVID-19 vaccine with a more established safety record in pregnancy is locally available). To help pregnant women make this assessment, they should be provided with information about the risks of COVID-19 in pregnancy (including, for example, that some pregnant women are at increased risk of infection, or have comorbidities that add to their risk of severe disease), the likely benefits of vaccination in the current epidemiological context, and the current limitations of the safety data in pregnant women. WHO does not recommend pregnancy testing prior to vaccination. WHO does not recommend delaying pregnancy or terminating pregnancy because of vaccination.

Schedule and administration contd.

Special population groups (continued)

There are no data on potential benefits or risks of Covovax™/Nuvaxovid™ to **breastfed children**. As this is not a live virus vaccine, it is unlikely to pose a risk to the breastfed child. Vaccine effectiveness is expected to be similar in lactating women as in other adults. WHO does not recommend discontinuing breastfeeding because of vaccination.

Preliminary findings highlight the safety and immunogenicity of 2 doses of Covovax™/Nuvaxovid™ in **persons living with HIV** that is well controlled (i.e. current CD4 count >200 cells/μl and viral suppression). Such persons may be vaccinated with the primary series of two doses, given that the vaccine is non-replicating. It is possible that their immune response to the vaccine may be reduced, which may lower its clinical effectiveness. Where possible, information and counselling should be provided to inform individuals on the potential benefits and risks. Testing for HIV infection prior to vaccine administration is not necessary.

No data are available regarding the response to two- or three-dose primary series of Covovax™/Nuvaxovid™ in **moderately and severely immunocompromised persons (ICP)** (i.e. transplant recipients, persons with active cancer, immunodeficiency, on active treatment with immunosuppressives, and persons living with HIV with CD4 cell count of <200 cells/μL). Based on the available evidence for other vaccine types/platforms and vaccine immunology, it is expected that Covovax™/Nuvaxovid™ will induce lower immune response rate in immunocompromised than in persons without immunocompromising conditions. Based on the emerging evidence and significant risk of severe COVID-19 for ICPs if infected, WHO recommends an extended primary series including a third dose, to be given at least 1 month and within 3 months after dose 2 of the primary series, in order to increase protection as quickly as possible in this population group. If more than 3 months have elapsed since dose 2, the third dose should be given at the earliest opportunity or as discussed with the treating physician. Information and, where possible, counselling about the limitations in the data on administration of an additional dose to ICPs should be provided to inform individual benefit–risk assessment.

For persons who have received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment, vaccination should be deferred for at least 90 days to avoid interference of treatment with vaccine-induced immune response as a precautionary measure.

Persons in special settings such as refugee and detention camps, prisons, slums and other settings with high population densities where physical distancing is not implementable, should be prioritized for vaccination, taking into account national epidemiological data, vaccine supply and other relevant considerations.

Stability and storage

Vaccine storage temperature	Store in the original packaging in a refrigerator at +2 to +8 °C. Do not store in a freezer.
Shelf life at different temperatures	Unopened vials in a refrigerator between +2 and +8 °C: 9 months or until expiry date stated on the label.
Freeze sensitivity	Do not freeze.
Light sensitivity	Store in the original outer packaging to protect from light. Avoid exposure to direct sunlight and ultraviolet light.
Conditions before use	Vaccine is ready to use; it may be used if kept cooled at +2 °C to +8 °C. It does not contain preservative.
Wastage rates	Will be dependent on country context.
Buffer stock needed	Will be dependent on country context.

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Labelling and packaging	
Vaccine Vial Monitor (VVM)	Not included
Information on vial label	Name and type of vaccine, method of administration, dosage, storage temperature, manufacturing and expiry date, batch number, contents by weight/volume/unit
Information on secondary packaging	Name of vaccine, pharmaceutical form, method of administration, dosage, composition (active substance and excipients), manufacturing date, batch number, storage conditions, expiry date, authorisation number, name and address of manufacturer
Information on tertiary packaging	Type of vaccine, name of manufacturer, presentation, batch number, date of expiry, quantity and storage conditions
Secondary packaging dimension and volume per dose	<p><u>Covovax™</u> Single-dose vials: Primary carton holding 50 vials (50 doses); 18.5 × 9.5 × 4.5 cm Volume per dose: 15.82 cm³ Secondary carton holds 6 primary cartons with a total of 300 vials (300 doses)</p> <p>10-dose vials: Primary carton holding 50 vials (500 doses); 18.5 × 9.5 × 6 cm Volume per dose: 2.11 cm³ Secondary carton holds 6 primary cartons with a total of 300 vials (3000 doses)</p> <p><u>Nuvaxovid™</u> 10-dose vials: Carton holding 10 vials (100 doses); 3.6 × 9.2 × 6.2 cm Volume per dose: 2.05 cm³</p>
Tertiary packaging dimension	<p><u>Covovax™</u> Single-dose vials: Box containing 4 secondary cartons of 300 vials each (1200 doses) and 24 coolant packs; external dimensions: 71.5 × 60.5 × 63.5 cm</p> <p>10-dose vials: Box containing 4 secondary cartons of 300 vials each (12 000 doses) and 24 coolant packs; external dimensions: 71.5 × 60.5 × 63.5 cm</p> <p><u>Nuvaxovid™</u> 10-dose vials: Case/shipper containing 30 secondary cartons with a total of 300 vials (3000 doses): external dimensions: 20 × 29 × 14 cm</p>

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Safety information*

Possible events (by frequency)

- Observed events were usually mild to moderate in severity and short lived: equal or less than 2 days for local and equal or less than 1 day for systemic events. They were more frequently reported after the second dose than after the first dose.
- Observed events were less frequently reported in older age groups (≥65 years of age).

Very common (≥1/10):

Pain and tenderness at the injection site, fatigue, malaise, headache, nausea or vomiting, myalgia, arthralgia

Common (≥1/100 to <1/10):

Redness and swelling at the injection site, pain in extremity, pyrexia, chills

Uncommon (≥1/1000 to <1/100):

Itch at the injection site, rash, erythema, pruritus, urticaria, hypertension, urticaria

Not known (cannot be estimated from available data):

Anaphylaxis, hypersensitivity

Co-administration of vaccines/medicines

Co-administration of Covovax™/Nuvaxovid™ and seasonal inactivated influenza vaccines showed the safety and immunogenicity of the seasonal influenza vaccine and the safety and efficacy of the Covovax™/Nuvaxovid™ vaccine. WHO recommends co-administration of an inactivated influenza vaccine and any dose of Covovax™/Nuvaxovid™. When administering both vaccines during the same visit, use different arm for each vaccine injection.

Until data on co-administration become available, there should be a minimum interval of 14 days between administration of this and vaccines against other diseases except inactivated influenza vaccine.

*From clinical trials

Important reminders

Vaccination session and vaccine administration

Before, during, and after vaccination, all people should continue to follow current guidance for protection from COVID-19 in their area (e.g. wearing a mask, keeping physical distance, hand hygiene, appropriate ventilation). Close contacts of immunocompromised people, particularly caregivers, should be vaccinated if eligible given that protection may remain inadequate in some ICPs even after administration of an additional vaccine dose, while additional public health and social measures at the household level may be warranted, depending on local epidemic circumstances.

Vaccination should be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serological testing is not recommended for the purpose of decision-making about vaccination. Based on current data, symptomatic reinfection is uncommon within 6 months after an initial natural infection, and in the context of limited vaccine supply, persons with PCR-confirmed SARS-CoV-2 infection in the preceding 6 months may choose to delay vaccination until near the end of this period. However, emerging data indicate that symptomatic reinfection may occur in settings where variants with evidence of immune escape are circulating, and in these settings, earlier vaccination after infection may be advisable (e.g. 3 months after natural infection). The length of this time period may be revised when more data on duration of immunity after natural infection become available. The optimal minimum interval between a natural infection and vaccination is not yet known.

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The presence of a minor infection such as a cold or low-grade fever should not delay vaccination.

Encourage a vaccine recipient to complete the vaccination series to optimize protection and schedule the time for the second dose. The same vaccine product should be used for both doses. When scheduling vaccination for occupational groups (e.g. health workers) consideration should be given to the reactogenicity profile observed in clinical trials, occasionally leading to time off work in the 24-48 hours following vaccination.

Government advice on public health and social measures should continue to be followed by both vaccinated and unvaccinated individuals. Country strategies related to COVID-19 control should be designed to minimize disruption to children's participation in education and other aspects of social life.

SARS-CoV-2 variants

As SARS-CoV-2 viruses undergo evolution, new variants may be associated with higher transmissibility, disease severity, risk of reinfection, or a change in antigenic composition. Data from the phase 2 study in Australia and the USA show reduced antibody responses relative to the Wuhan D641G strain by 4-fold for Alpha, 4.8-fold for Beta and 3-fold for Delta variants. No data currently exist for the Omicron variant. These data should be interpreted with caution since the relationship between reduction in antibody responses and vaccine performance against clinical disease has not yet been established. WHO currently recommends the use of Covovax™/Nuvaxovid™ vaccine even if the variants of concern are present in the country. There is an urgent need for a coordinated approach for surveillance and evaluation of variants and their potential impact on vaccine effectiveness. Countries using the vaccine in the presence of variants are encouraged to monitor vaccine effectiveness and study eventual breakthrough infections due to variants.

SARS-CoV-2 tests

Covovax™/Nuvaxovid™ contains a recombinant SARS-CoV-2 spike protein, and a positive result in a test for spike protein IgM or IgG could indicate either prior infection or prior vaccination. However, prior receipt of Covovax™/Nuvaxovid™ will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests for diagnosis of acute/current SARS-CoV-2 infection. Antibody testing is not currently recommended to assess immunity to COVID-19 following vaccination with Covovax™/Nuvaxovid™.

Resources and more information at:

<https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-recommendation-novavax-nvx-cov2373>

<https://extranet.who.int/pqweb/vaccines/who-recommendation-siipl-covid-19-vaccine-rs-proteinnanoparticle>

<https://extranet.who.int/pqweb/vaccines/who-recommendation-novavax-inc-covid-19-vaccine-sars-cov-2-rs-recombinant-adjuvanted>