

COVID-19 Vaccine Janssen (Ad26.COVS2-S [recombinant])

EUL holder: Janssen–Cilag International NV (Belgium)

19 JULY 2022 UPDATE INCLUDES NEW INFORMATION ON:

- authorized and WHO recommended schedules (primary and booster doses, heterologous schedules);
- extended shelf life for thawed unopened vaccine vials;
- contraindications for use and safety;
- guidance on the use of COVID-19 Vaccine Janssen in special populations (i.e. immunocompromised persons, persons living with HIV);
- co-administration with other vaccines;
- vaccine effectiveness and impact against circulating variants of concern.

Sections that have been updated are indicated with **.



The COVID-19 Vaccine Janssen (Ad26.COVS2-S [recombinant]) is a non-replicating adenoviral vector vaccine against coronavirus disease 2019 (COVID-19). The vector virus carries the gene coding for the Spike protein of SARS-CoV-2, which instructs the host cells to produce this protein. The presence of the spike protein on the host cell surface triggers the production of antibodies and the induction of memory immune cells that provide protection against infection and disease. Efficacy shown in clinical trials (ENSEMBLE 1) in participants who received a single dose of COVID-19 Vaccine Janssen was 67% against symptomatic SARS-CoV-2 infection, 77% against severe/critical COVID-19 after 14 days and 85% after 28 days, and 93% against hospitalizations. However, with the emergence of variants of concern, lower vaccine effectiveness (VE) has been observed. The ENSEMBLE 2 trial and subsequent studies from South Africa showed improved vaccine efficacy with two doses of vaccine given 2 months apart, especially against symptomatic infections, including when caused with SARS-CoV-2

variants of concern, for example Omicron variant. The primary analysis of ENSEMBLE 2 results shows that VE against moderate to severe/critical COVID-19 was 75%, and VE against severe/critical COVID19 was 100% when evaluated at least 14 days after the second vaccination. However, as with other COVID-19 vaccines, the vaccine efficacy wanes over several months.

Date of WHO Emergency Use Listing (EUL) recommendation: 12 March 2021

Date of prequalification (PQ): not applicable

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	Preservative-free, multi-dose suspension for injection
Number of doses	One vial (2.5 mL) contains 5 doses of vaccine
Vaccine syringe type and needle size	Auto-disable (AD) syringe: 0.5 mL Needle 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
	WHO SAGE recommends prioritization of different population groups according to the WHO SAGE roadmap (📄) for prioritizing uses of COVID-19 vaccines.
Recommended schedule – primary vaccination series**	Primary vaccination: One dose WHO SAGE recommends an additional, second dose in moderate to severe immunocompromised persons as a part of an extended primary series, to be administered 1 to 3 months after the first dose.
Recommended schedule – booster doses**	Booster dose: at least 2 months after the primary vaccination of one dose WHO SAGE refers to the booster dose as ‘second dose’. Between the two doses WHO SAGE recommends an interval of 2 to 6 months, with preference for 6 months as a longer interval has been shown to result in a better immune response. ²
Heterologous use of vaccines	A booster dose of COVID-19 Vaccine Janssen may also be administered to eligible individuals who have completed their primary vaccination series with an approved mRNA COVID-19 vaccine (‘heterologous schedule’). ³
Route and site of administration	Intramuscular (i.m.) administration The preferred site is deltoid muscle.
Dosage	0.5 mL (single dose)
Diluent	None needed
Mixing syringe	None needed
Preparation**/ reconstitution/ dilution requirement	<u>No dilution is required.</u> Thaw each vial before use: Thaw vaccine in refrigerator at +2 to +8 °C: • Individual vials take about 2 hours to thaw. • A carton of 10 vials takes about 12 hours to thaw. Once thawed, do not re-freeze. Vaccine administration: 1. Once thawed, the vaccine is ready to use, do not dilute. 2. Inspect the vial visually to make sure that the liquid is colourless to slightly yellow, and clear to very opalescent suspension. If any particulate matter and discoloration are present, do not use. Discard the vial. 3. Swirl the vial gently in an upright position for 10 seconds, do not shake. 4. Record date and time of the first use (first puncture and withdrawal of the dose) on the vial label. 5. Draw up the vaccine dose (0.5 mL) when ready to vaccinate, pre-loading of syringes is not recommended. 6. Before withdrawing each following vaccine dose, swirl the vial gently in an upright position for 10 seconds and do not shake. 7. Preferably, use the vaccine immediately after first puncture or within 6 hours afterwards. Discard if vaccine is not used within this time or at the end of the session, whichever comes first.

² WHO SAGE recommends that countries may consider using one dose of vaccine only (i.e. no second/booster dose) if facing vaccine supply constraints or vaccine delivery challenges. This may be a preferred option for vaccinating geographically and socially hard-to-reach populations where delivering a second dose is programmatically challenging. Even in these populations, WHO SAGE recommends that all efforts should be taken to provide two doses when the opportunity arises (i.e. primary and booster), in particular to the highest and high priority-use groups.

³ For individuals who have received a single dose of COVID-19 Vaccine Janssen, WHO SAGE considers that any COVID-19 vaccine that is authorized in country based on WHO EUL can also be used to complete the primary series or as a booster dose. However, the preferred sequence is for the COVID-19 Vaccine Janssen to be followed by either mRNA or protein subunit vaccine.

Schedule and administration contd.

Preparation**/ reconstitution/ dilution requirement	A maximum of 5 doses can be withdrawn from one vial. Do not combine residual vaccine from multiple vials. Discard any remaining vaccine in the vial after 5 doses have been withdrawn.
Multi-dose vial policy	After the first dose has been withdrawn, keep between +2 °C and +8 °C during the in-use period, and discard any unused vaccine in the vial after 6 hours, 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. • A history of confirmed thrombosis with thrombocytopenia syndrome (TTS) following vaccination with any COVID-19 vaccine. • A history of previous capillary leak syndrome (CLS).
Precautions**	• All persons should be vaccinated under health care supervision, with the appropriate medical treatment available in case of allergic reactions. As a precautionary measure, an observation period of at least 15 minutes should be ensured post vaccination. • Vaccination of people suffering from acute severe febrile illness (body temperature higher than 38.5 °C) should be postponed until they are afebrile. • Vaccination of persons with acute COVID-19 should be postponed until they have recovered from acute illness and criteria for discontinuation of isolation have been met. • Minor infections such as cold or those with low-grade fever should not delay vaccination.
Special population groups** (based on available data as of December 2021)	• For persons with comorbidities such as hypertension, chronic lung disease, significant cardiac disease, obesity, diabetes, and human immunodeficiency virus (HIV) infection that have been studied in phase 3 clinical trial and that have been identified as increasing the risk of severe COVID-19, vaccination is recommended. • Vaccination is recommended for older persons as the risk of severe COVID-19 and death increases steeply with age. • Available data on administration in pregnant women are insufficient to assess vaccine-associated risks in pregnancy though studies in pregnant women are planned in the coming months. However, it should be noted that COVID-19 Vaccine Janssen is a non-replicating vaccine. This vaccine and vaccines against other diseases using the same platform have shown no safety issues in pregnant women. Until more data are available, WHO recommends the use of COVID-19 Vaccine Janssen in pregnancy only if the benefit of vaccination to the pregnant woman outweighs the potential risks. To help pregnant women make this assessment, they should be provided with information about the risks of COVID-19 in pregnancy, the likely benefits of vaccination in the local epidemiological context, and the current limitations of the safety data in pregnant women. WHO does not recommend pregnancy testing prior to vaccination or delaying or terminating pregnancy because of vaccination. • COVID-19 Vaccine Janssen efficacy in breastfeeding women is expected to be similar as in other adults. Data are not available on the potential benefits or risks of the COVID-19 Vaccine Janssen to breastfed children. As this is not a live virus vaccine, it is biologically and clinically unlikely to pose a risk to the breastfeeding child. WHO recommends the use of COVID-19 Vaccine Janssen in lactating women as in other adults. WHO does not recommend discontinuing breastfeeding because of vaccination.

Schedule and administration contd.

Special population groups**

(based on available data as of December 2021)

- Based on the emerging evidence and higher risk of severe COVID-19 for **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 (PLWH) with CD4 count of <200 cells/ μ L) if infected and regardless of age, WHO SAGE recommends a second dose for ICPs aged 18 years and older, to be administered 1 to 3 months after the first dose in order to increase protection as quickly as possible. The most appropriate timing may vary depending on the local epidemiology and the extent and timing of immune suppressive therapy, and should be discussed with the treating physician.
- **HIV-positive persons** who are well controlled on highly active antiretroviral therapy and are part of a group recommended for vaccination can be vaccinated, given that the vaccine is non-replicating. Persons with well-controlled HIV were included in the trials and there were no reported differences in safety signals. One study (Sisonke) in South Africa showed high vaccine efficacy in PLWH. Information and, where possible counselling should be provided to inform individual benefit-risk assessment. Testing for HIV infection prior to vaccine administration is not necessary.
- For persons who have received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment, vaccination does not need to be delayed.
- 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.

SARS-CoV-2 variants

WHO currently recommends the use of COVID-19 Vaccine Janssen according to the SAGE prioritization roadmap, if the variants are present in a country. Countries should conduct a benefit-risk assessment according to the local epidemiological situation including the extent of circulating virus variants.

Stability and storage

Vaccine storage temperature

If the vaccine is received frozen, store in the original carton in a freezer at -25 to -15 °C. Do not store on dry ice or below -40 °C.

If the vaccine is received thawed at +2 to +8 °C, store refrigerated at +2 to +8 °C in the original carton. Do not refreeze.

Shelf life at different temperatures**

Frozen unopened vaccine vial in freezer at -25 and -15 °C: 24 months, or until expiry date (it can be printed on the vial and outer carton or accessible via QR code, depending on the supply source).

Thawed unopened vaccine vial in refrigerator at +2 to +8 °C: once removed from the freezer, for a single period of up to 11 months*.

- The expiry date must be updated when the vaccine is removed from the freezer and before it is stored in the refrigerator.
- If a 11 month period is within the original expiry date printed on the outer carton, cross out the original expiry date on the outer carton to mark as not valid. Write down the new expiry date which would be 11 months from the date you removed the vaccine from the freezer.
- If a 11 month period is longer than the original expiry date printed on the outer carton, respect the original expiry date.

* For the lots produced in US sites, WHO recommends the storage at +2 to +8 °C for thawed, unopened vaccines for 9 months.

Thawed opened vial (after first puncture) at +2 to +8 °C: up to 6 hours after the first dose has been withdrawn.

COVID-19 Vaccine Janssen

Stability and storage contd.

Freeze sensitivity	Never refreeze thawed vials. Do not store in insulated passive container with dry ice or ultra-low temperature phase-change material (PCM), or in freezer below -40 °C.
Light sensitivity	Store in the original outer carton to protect from light. Avoid exposure to direct sunlight and ultraviolet light.
Conditions before use	After thawing, visual inspection, and gentle swirling of the vial, vaccine is ready for use.
Wastage rates	Will depend on country context.
Buffer stock needed	Will depend on country context.

Labelling and packaging*

Vaccine Vial Monitor (VVM) (if yes, location and type)	Initial pandemic supply will not include a VVM.
Information on vial label	Lot number, expiry date*, blank box/space to fill in the updated expiry date, after the first puncture of the vial at +2 to +8 °C
Information on secondary packaging	Lot number, expiry date*
Information on tertiary packaging	To be finalized
Secondary packaging dimension and volume	Carton box holding 10 vials/50 doses; 9.3 × 3.8 × 5.4 cm Volume per dose: 3.82 cm ³ /dose
Tertiary packaging dimension	Carton containing 48 secondary packaged carton boxes with a total of 480 vials (2400 doses) [†] External dimensions 39.3 × 24.8 × 13.1 cm [†] Tertiary packaging and pallet configuration may vary according to the mode of transport.

* Labelling and packaging may be subject to change, depending on supply source, e.g. vaccines received as donation from the US Government.

Safety information*

Possible events** (by frequency)	- Most adverse events occurred 1 to 2 days following vaccination, were mild to moderate in severity and usually resolved within 1 to 2 days. - Observed events were generally milder and less frequently reported in older adults (≥60 years) than in younger adults. Very common (≥1/10): Headache, nausea, myalgia, pain at the injection site, fatigue Common (≥1/100 to <1/10): Swelling or redness at the injection site, chills, arthralgia, cough, fever (≥38 °C) Uncommon (≥1/1000 to <1/100): Rash, muscle weakness, arm or leg pain, feeling weak and generally unwell, sneezing, sore throat, back pain, tremor, hyperhidrosis (abnormal sweating), paraesthesia, diarrhoea, dizziness Rare (≥1/10 000 to <1/1000): Allergic reaction, hives, lymphadenopathy, hypoaesthesia, tinnitus, vomiting, venous thromboembolism (VTE)
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Safety information* contd.**Possible events****
(by frequency)**Very rare (<1/10 000):**

Thrombosis with thrombocytopenia, Guillain-Barré syndrome (GBS)

Not known (cannot be estimated from available data):

Severe allergic reaction (anaphylaxis), capillary leak syndrome (CLS), immune thrombocytopenia, transverse myelitis

In countries with ongoing SARS-CoV-2 transmission, the benefit of vaccination in protecting against COVID-19 far outweighs the risks of TTS, GBS, and CLS. However, benefit-risk assessment may differ from country to country, and countries should consider their epidemiological situation, individual and population-level risks, availability of other vaccines, and alternate options for risk mitigation. The benefit-risk ratio is greatest in older age groups as the risks of severe COVID-19 disease outcomes including COVID-19 related thromboembolic events increases with age.

Co-administration of vaccines/medicines**

WHO SAGE considers that for adults, based on several co-administration studies of COVID-19 vaccines and inferred from co-administration studies of other adult vaccines, COVID-19 vaccines may be given concomitantly, or any time before or after, other adult vaccines including live attenuated, inactivated, adjuvanted, or non-adjuvanted vaccines. When administering both vaccines during the same visit, use different arm for each vaccine injection.

*From clinical studies.

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).

A person presenting with COVID-19 symptoms should not be vaccinated. Vaccination may be offered to people who have recovered from symptomatic or asymptomatic COVID-19. Testing is not recommended for the purpose of decision-making about vaccination. Based on current data, 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, as available data show that within this period, symptomatic reinfection is uncommon. However, emerging data indicate that symptomatic reinfection may occur in settings where variants with evidence of markedly reduced neutralization activity are circulating. In these settings, vaccination earlier than 6 months after infection may be advisable.

Before vaccination, advise vaccine recipient about possible post-vaccination symptoms and observe post-vaccination for at least **15 minutes**.

To alleviate post-vaccination symptoms, antipyretic or analgesic products (e.g. paracetamol-containing products) may be used, if required.

When scheduling vaccination for occupational groups (e.g. health workers) consideration should be given to the reactogenicity profile of this vaccine observed in clinical trials, occasionally leading to time off work in the 24-48 hours following vaccination.

Any unused COVID-19 Vaccine Janssen or waste material should be disposed of in accordance with local requirements. If content of the vial leaks out, spills should be disinfected with an appropriate antiviral disinfectant.

COVID-19 Vaccine Janssen**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, resulting in lower vaccine effectiveness. WHO currently recommends the use of COVID-19 Vaccine Janssen according to the WHO SAGE Prioritization Roadmap (5) even if the variants are present in the country. Countries should conduct a benefit-risk assessment according to the local epidemiological situation including the extent of circulating virus variants.

There is an urgent need for a coordinated approach for surveillance and evaluation of variants and their potential impact on vaccine effectiveness. WHO will continue to monitor the situation; as new data become available, recommendations will be updated accordingly.

SARS-CoV-2 tests**

Currently available antibody tests for SARS-CoV-2 assess levels of IgM and/or IgG to the spike or the nucleocapsid protein and as the vaccine contains the spike protein, a positive test for spike protein IgM or IgG could indicate either prior infection or prior vaccination. To evaluate evidence of prior infection in an individual who has received COVID-19 Vaccine Janssen, a test that specifically evaluates IgM or IgG to the nucleocapsid protein should be used. Antibody testing is not currently recommended to assess immunity to COVID-19 following COVID-19 Vaccine Janssen.

Prior receipt of the vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests for diagnosis of acute/current SARS-CoV-2 infection.

Resources and more information at:**

<https://extranet.who.int/pqweb/vaccines/who-recommendation-janssen-cilag-international-nv-belgium-covid-19-vaccine-ad26cov2-s>

<https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-recommendation-Ad26-COV2.S-2021.1>