COVID-19 Vaccine Explainer

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COVID-19 Vaccine ChAdOx1-S [recombinant]

Developed by Oxford University and AstraZeneca

10 MAY 2021 UPDATE INCLUDES:

- information for interchangeability of ChAdOx1-S/nCoV-19 [recombinant] vaccine products
- addition in vaccine effectiveness information in age group 65 and older
- information on thrombosis with thrombocytopenia syndrome (TTS)
- insights with regard to use of COVID-19 vaccines in pregnancy
- recommendations for persons living with HIV and persons who have previously had SARS-CoV-2 infection, and
- addition in labelling and packaging section.

Sections that have been updated are indicated with **.

Manufacturers[2] **:

- **SK Bioscience Co. Ltd. [COVID-19 Vaccine (ChAdOx1-S [recombinant])]**
- **Serum Institute of India Pvt. Ltd. [COVISHIELD™, ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)]**
- **AstraZeneca AB, EU approved nodes [COVID-19 Vaccine (ChAdOx1-S [recombinant])]**

The ChAdOx1-S/nCoV-19 [recombinant] vaccine is a replication-deficient adenoviral vector vaccine against coronavirus disease 2019 (COVID-19). The vaccine expresses the SARS-CoV-2 spike protein gene, which instructs the host cells to produce the protein of the S-antigen unique to SARS-CoV-2, allowing the body to generate an immune response and to retain that information in memory immune cells. Efficacy shown in clinical trials in participants who received the full series of vaccine (2 doses) in clinical trials in United Kingdom, Brazil and South Africa irrespective of interval between the doses, was 61%, based on a median follow-up of 80 days, but tended to be higher when this interval was longer. Additional data from the interim analyses of the trial in the United States show a vaccine efficacy of 76% against symptomatic SARS-CoV-2 infection. All data reviewed support the conclusion that the known and potential benefits of ChAdOx1-S/nCoV-19 [recombinant] vaccine outweigh the known and potential risks.

Date of WHO Emergency Use Listing (EUL) recommendation:**

- COVID-19 Vaccine (ChAdOx1-S [recombinant], SK Bioscience Co. Ltd: 15 February 2021
- COVISHIELD™, ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant), Serum Institute of India Pvt. Ltd: 15 February 2021
- COVID-19 Vaccine (ChAdOx1-S [recombinant]), AstraZeneca AB: 15 April 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).

[1] Contents are updated as new information becomes available.

[2] AstraZeneca is partnering with several manufacturers to ensure supply. All manufacturing partners are subject to Current Good Manufacturing Practice (CGMP) and appropriate Quality Systems. In this document the AstraZeneca vaccine manufactured at various sites are referred to as ChAdOx1-S/nCoV-19 [recombinant], used as a common designation.

Product characteristics

Presentation	Liquid, preservative-free, multi-dose suspension
Number of doses**	SK Bioscience: 10 doses per vial (each dose of 0.5 mL)
	COVISHIELD™: 2 doses per vial (each dose of 0.5 mL) 10 doses per vial (each dose of 0.5 mL)
	AstraZeneca AB, EU approved nodes: 2 doses per vial (each dose of 0.5 mL) 10 doses per vial (each dose of 0.5 mL)
Vaccine syringe type and needle size	Auto-disable (AD) syringe: 0.5 mL Needle for intramuscular injection 23G x 1" (0.60 × 25 mm)

Schedule and administration

Recommended for age	18 years of age and above, including persons 65 years of age and older
Recommended schedule**	2 doses (0.5 mL each) can be administered with an interval of 4–12 weeks. WHO recommends an interval 8–12 weeks: Dose 1: at the start date Dose 2: 8 to 12 weeks after first dose. If the second dose is inadvertently administered earlier than 4 weeks after the first, the dose does not need to be repeated. If the second dose is inadvertently delayed, it should be given at the earliest possible opportunity. Both doses are necessary for protection, and it is recommended that both doses are administered with ChAdOx1-S/nCoV-19 [recombinant] vaccine products. ChAdOx1-S/nCoV-19 [recombinant] vaccine products are considered fully equivalent, even if produced at different manufacturing sites or assigned different product names, and are interchangeable for both doses.
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	**No dilution is required.** **Vaccine administration:** 1. Vaccine is ready to use, do not dilute. 2. Do not shake. 3. Inspect the vial to make sure that the liquid is clear to slightly opaque, and colourless to slightly brown. If visible particles or discoloration are present, discard the vial. 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 at the time of administration, pre-loading of syringes is not recommended. 6. Use all vaccine in the vial within 6 hours after first puncture. After withdrawing the final dose, some liquid may remain in the vial. Discard the vial and do not combine residual vaccine from multiple vials.
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.

Schedule and administration contd.

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 ChAdOx1-S/nCoV-19 [recombinant] vaccine. • People who have had blood clots associated with low platelet levels (thrombosis with thrombocytopenia syndrome or TTS) after their first dose of ChAdOx1-S/nCoV-19 [recombinant] vaccine should not be given a second dose.
Precautions**	• While no specific risk factors have yet been identified, current data from Europe suggest that the risk of TTS may be higher in younger adults compared to older adults. There is a considerable geographic variation in the reported incidence of TTS. Very few cases have been reported from non-European countries despite extensive use of vaccine. Therefore, benefit-risk assessments and recommendations may differ from country to country (see important reminders below). • Although no severe allergic reactions or anaphylaxis have been recorded after ChAdOx1-S/nCoV-19 [recombinant] vaccine, all persons should be vaccinated by a health care professional in settings where appropriate medical treatment is available. 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 April 2021)	• For persons with **comorbidities** such as obesity, cardiovascular disease, respiratory disease and diabetes that have been studied in clinical trial and that have been identified as increasing the risk of severe COVID-19, vaccination is recommended. • For persons **above 65 years of age**, vaccination is recommended. Data from phase 3 trial in the United States showed an efficacy of 85% against symptomatic COVID-19 in the age group of 65 years and older. Post-introduction effectiveness studies from the United Kingdom show high rates of protection against hospitalizations, severe COVID-19 and death in older persons including those over the age of 80 years. • For persons with comorbidities such as obesity, cardiovascular disease, respiratory disease and diabetes that have been studied in clinical trial and that have been identified as increasing the risk of severe COVID-19, vaccination is recommended. • **Pregnant women** with COVID-19 are at higher risk of developing severe disease compared with non-pregnant women of reproductive age. While available data on vaccination of pregnant women are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy, studies are underway. Based on previous experience with other vaccine use during pregnancy, the effectiveness of the ChAdOx1-S/nCoV-19 [recombinant] vaccine in pregnant women is expected to be comparable to that observed for non-pregnant women in similar age groups. Compared with non-pregnant women, pregnancy is associated with higher rates of thrombosis, thrombocytopenia, and haemorrhage; however, it is currently not known whether pregnancy is associated with a higher risk of TTS following vaccination. In the interim, WHO recommends the use of ChAdOx1-S/nCoV-19 [recombinant] vaccine in pregnant women only if the benefits of vaccination to the pregnant woman outweigh the potential risks. To make this assessment, pregnant women 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)	• Breastfeeding offers substantial health benefits to lactating women and their breastfed children. Vaccine efficacy is expected to be similar in **lactating women** as in other adults. However, there are no data on the effects of the vaccine on **breastfed children**. As the ChAdOx1-S/nCoV-19 [recombinant] vaccine is not a live virus vaccine, it is biologically and clinically unlikely to pose a risk to the breastfeeding child. On the basis of these considerations, WHO recommends the use of ChAdOx1-S/nCoV-19 [recombinant] in lactating women as in other adults. WHO does NOT recommend discontinuing breastfeeding after vaccination. • Available data are currently insufficient to access vaccine efficacy or vaccine-associated risks in **severely immunocompromised persons**, who may have diminished immune response to vaccine. Nevertheless, if part of a recommended group for vaccination, they may be vaccinated, given that the vaccine is non-replicating. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment. • Persons with **autoimmune conditions** who have no contraindications to vaccination may be vaccinated. • Data are currently insufficient to allow assessment of vaccine efficacy or safety of ChAdOx1-S/nCoV-19 [recombinant] vaccine for **persons living with HIV**. It is possible that their immune response to the vaccine may be reduced. Persons living with HIV who are part of a group recommended for vaccination may be vaccinated, given that the vaccine is non-replicating. Where possible, information and 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 should be deferred for at least 90 days to avoid interference of treatment with vaccine-induced immune response.
SARS-CoV-2 variants	WHO currently recommends the use of ChAdOx1-S/nCoV-19 [recombinant] vaccine according to prioritization roadmap, even 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	Store in the original carton 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: until expiry date stated on the label. The expiry date refers to the last day of that month. **Opened vials** (after first needle puncture) should be kept cooled at temperatures between +2 °C and +8 °C during the immunization session.
Freeze sensitivity	**Do not freeze.**
Light sensitivity	Store in the original outer carton 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 within 6 hours after opening.
Wastage rates	Will be dependent on country context.
Buffer stock needed	Will be dependent on country context.

Labelling and packaging*

For AMC92 countries, UNICEF will supply only 10-dose vials.	
Vaccine Vial Monitor (VVM) (if yes, location and type)	Initial pandemic supply will not include a VVM.
Information on vial label**	SK Bioscience: batch number, expiry date, serial number
	COVISHIELD™ 10-dose: batch number, expiry date, serial number
	AstraZeneca AB, EU approved nodes: • 8-dose: batch number, expiry date • 10-dose: batch number, expiry
Information on secondary packaging**	SK Bioscience: 2D datamatrix, batch number, expiry date, serial number
	COVISHIELD™ 10-dose: batch number, expiry date, serial number
	AstraZeneca AB, EU approved nodes: to be finalized
Information on tertiary packaging**	SK Bioscience: 2D datamatrix, batch number, expiry date, serial number
	COVISHIELD™ 10-dose: batch number, expiry date, serial number
	AstraZeneca AB, EU approved nodes: • 8-dose: 2D datamatrix, batch number, expiry date, serial number • 10-dose: 2D datamatrix, batch number, expiry date, serial number
Secondary packaging dimension and volume**	SK Bioscience: Box holding 10 vials/100 doses; 13.2 x 5.7 x 5.0 cm Volume per dose: 3.76 cm^3/dose
	COVISHIELD™: 1. 2-dose: Box holding 50 vials/100 doses; 18.5 × 9.5 × 4 cm Volume per dose: 7.03 cm^3 2. 10-dose: Box holding 50 vials/500 doses; 18.5 × 9.5 × 6 cm Volume per dose: 2.109 cm^3
	AstraZeneca AB, EU approved nodes: 1. Carton of ten 5mL vials/80 doses; 8.1 × 4.1 × 10.6 cm Volume per dose: 4.40 cm^3 2. Carton of ten 10R vials/100 doses; 13.5 × 5.5 × 5.5 cm Volume per dose: 4.08 cm^3 3. Carton of ten 6mL vials/100 doses; 14.5 × 6.8 × 5.1 cm Volume per dose: 5.03 cm^3 4. Carton of ten 5mL vials/100 doses; 13.2 × 5.7 × 5.0 cm Volume per dose: 3.76 cm^3
Tertiary packaging dimension**	SK Bioscience: Carton containing 24 secondary boxes with a total of 240 vials (2400 doses) External dimensions 24.8 × 28.8 × 18.0 cm
	COVISHIELD™: 1. 2-dose: Carton containing 6 secondary boxes with a total of 300 vials (600 doses); external dimensions 31 × 19 × 9.3 cm 2. 10-dose: Carton containing 6 secondary boxes with a total of 300 vials (3000 doses); external dimensions 31 × 19 × 13.3 cm
	AstraZeneca AB, EU approved nodes: 1. 24 secondary packaged cartons containing 10 vials per carton (240 vials/1920 doses); external dimensions: 26.2 × 22.8 × 18.8 cm 2. 16 secondary packaged cartons containing 10 vials per carton (160 vials/1600 doses); external dimensions: 29.0 × 25.0 × 13.1 cm 3. 24 secondary packaged cartons containing 10 vials per carton (240 vials/2400 doses); external dimensions: 31.0 × 21.8 × 22.8 cm 4. 24 secondary packaged cartons containing 10 vials per carton (240 vials /2400 doses); external dimensions: 24.8 × 28.8 × 18.0 cm

*Labelling and packaging may be subject to change, depending on supply source.

Safety information*

Possible events (by frequency)**	• Majority of adverse events observed were mild to moderate and usually resolved within a few days. • Observed events were generally milder and less frequently reported in older adults (≥65 years) than in younger adults (18–64 years) • Generally, when compared with the first dose, events reported after the second dose were milder and less frequent. **Very common (≥1/10):** Tenderness, pain, warmth, itching or bruising at the injection site, fatigue, chills, headache, nausea, vomiting, myalgia, arthralgia **Common (≥1/100 to <1/10):** Swelling or redness at the injection site, fever (≥38 °C) **Uncommon (≥1/1 000 to <1/100):** Lymphadenopathy, decreased appetite, dizziness, abdominal pain, hyperhidrosis (abnormal sweating), pruritus, rash **Very rare (< 1/10 000):** Neuroinflammatory disorder (transverse myelitis) has been reported but a causal relationship with ChAdOx1-S/nCoV-19 [recombinant] has not been established. Outside of clinical trials, a very rare syndrome of blood clotting combined with low platelet counts (i.e. thrombosis with thrombocytopenia syndrome or TTS) has been reported around 4 to 20 days following vaccination. A causal relationship between the vaccine and the TTS is considered plausible although the biological mechanism is still being investigated.
Co-administration of vaccines/medicines	There should be a minimum interval of 14 days between administration of this and any other vaccine against other diseases, until data on co-administration become available.

*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 with acute PCR-confirmed COVID-19 should not be vaccinated until after they have recovered from acute illness and the criteria for discontinuation of isolation have been met. The optimum minimal interval between a natural infection and vaccination is not yet known.

With regard to thrombosis with thrombocytopenia syndrome (TTS), in countries with ongoing SARS-CoV-2 transmission, the benefit of vaccination in protecting against COVID-19 far outweighs the risks. Benefit-risk assessments may differ among countries, 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 risk of severe COVID-19 outcomes, including COVID-19 related thromboembolic events, increases with age.

Vaccination should be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Testing is not recommended for the purpose of decision-making about vaccination. Based on current data and given 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, in settings with circulating variants of concern with evidence of immune escape, earlier vaccination 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.

Encourage a vaccine recipient to complete the vaccination series to optimize protection and schedule the time for the second dose. All ChAdOx1-S/nCoV-19 [recombinant] vaccines covered by the explainer are considered equivalent and interchangeable for both doses. When scheduling vaccination for occupational groups (e.g. health workers) consideration should be given to the reactogenicity profile of ChAdOx1-S/nCoV-19 [recombinant] vaccine observed in clinical trials, occasionally leading to time off work in the 24–48 hours following vaccination.

Any unused ChAdOx1-S/nCoV-19 [recombinant] vaccine or waste material should be disposed of in accordance with local requirements. If contents of the vial leaks out, spills should be disinfected with an appropriate antiviral disinfectant.

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. Preliminary findings of slightly reduced ChAdOx1-S/nCoV-19 [recombinant] vaccine effectiveness against B1.1.1.7 variant and marked reduction of ChAdOx1-S/nCoV-19 [recombinant] vaccine effectiveness in mild to moderate disease against B.1.351 variant need to be demonstrated in ongoing clinical trials and post-implementation evaluations. This highlights the urgent need for a coordinated approach for surveillance and evaluation of variants and their potential impact on vaccine effectiveness.

Resources and more information at**:

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/951851/uk-clean-spc-covid-19-vaccine-astrazeneca-reg174.pdf

https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-endorsement_en.pdf

https://www.seruminstitute.com/product_covishield.php

https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1

https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria-previously-covid-19-vaccine-astrazeneca

https://extranet.who.int/pqweb/vaccines/covid-19-vaccine-chadox1-s-recombinant-0

https://extranet.who.int/pqweb/sites/default/files/documents/pl-azd1222-en.pdf

https://extranet.who.int/pqweb/sites/default/files/documents/smpc-azd1222-en.pdf