

Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222, SII Covishield, SK Bioscience)

Interim guidance

First issued 10 February 2021

Updated 21 April 2021



Background

This interim guidance has been developed on the basis of the advice issued by the Strategic Advisory Group of Experts (SAGE) on Immunization at its extraordinary meeting on 8 February 2021 (1), and updated on 21 April 2021.

Declarations of interests were collected from all external contributors and assessed for any conflicts of interest. Summaries of the reported interests can be found on the [SAGE meeting website](#) and [SAGE Working Group website](#).

These Interim recommendations refer to a generic group of ChAdOx1-S [recombinant] vaccines against COVID-19 that are produced by different manufacturers (AstraZeneca AZD1222-Vaxzevria; Serum Institute India (SII) Covishield; and SK Bioscience), but which all rely on the AstraZeneca core clinical data for regulatory evaluation, and are listed under the emergency use listing procedure by WHO. Consequently, these vaccines are considered fully equivalent, even if produced at different manufacturing sites or assigned different products names, and the Interim recommendations here apply universally to all ChAdOx1-S vaccines.

The guidance is based on the initial evidence summarized in the *Background document on the AZD1222 vaccine against COVID-19 developed by Oxford University and AstraZeneca* and the *Background paper on COVID-19 disease and vaccines*.

Annexes which include GRADE and evidence-to-recommendations (ETR) tables have also been updated to reflect the updated recommendations:

<https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-recommendation-AZD1222-GRADE-ETR-2021.1> .

All referenced documents are available on the SAGE COVID-19 webpage: <https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials>.

Methods

SAGE applies the principles of evidence-based medicine and has set in place a thorough methodological process for issuing and updating recommendations (2). A detailed description of the methodological processes as they apply to COVID-19 vaccines can be found in the SAGE evidence framework for COVID-19 vaccines (3). This framework contains guidance on considering data emerging from clinical trials and post-introduction effectiveness and safety monitoring.

General goal and strategy for the use of the vaccine against COVID-19

The COVID-19 pandemic has caused significant morbidity and mortality throughout the world, as well as major social, educational and economic disruptions. There is an urgent global need to develop effective and safe vaccines and to make them available at scale and equitably across all countries.

Based on the phase 3 trials in the United Kingdom, Brazil and South Africa, the ChAdOx1-S [recombinant] vaccine against COVID-19 has an efficacy of 63% (95% CI: 51–72%) against symptomatic SARS-CoV-2 infection, as shown by the primary analysis of data irrespective of interdose interval (data cut off 7 December 2020) from trial participants who received 2 standard doses with an interval of about 4 to 12 weeks. Vaccine efficacy tended to be higher when the interval between doses was longer. This, together with the finding of higher antibody levels with increasing interdose interval, supports the conclusion that longer dose intervals within the 4–12 weeks range are associated with greater vaccine efficacy. No vaccinated persons were hospitalized as from 22 days after dose 1, compared with 14 unvaccinated persons who were hospitalized for COVID-19 in the same time frame. At the time of analysis, the median follow-up time after the second dose was 80 days. More detailed data on the efficacy and safety of this vaccine can be found in the 1 March 2021 *Background document on the AZD1222 vaccine against COVID-19 developed by Oxford University and AstraZeneca* (<https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials>). By 8 April 2021, additional data from interim analyses of the phase 3 trial conducted by AstraZeneca in the United States became available to SAGE (data cut off 5 March 2021). This trial enrolled 32 449 participants, with 22% of the trial population aged 65 years or older. The primary analysis included events from 15 days post second dose, with an interdose interval of 28 days. The case definition of symptomatic SARS-CoV-2 infection differed slightly to the Oxford University led trials. The vaccine efficacy against symptomatic SARS-CoV-2 infection was 76% (95% CI: 68–82%). No severe or critically ill cases occurred in the vaccinated group; 8 cases occurred in the placebo group. Vaccine efficacy in trial participants aged 65 years or older was 85% (95% CI: 58–94%). The data reviewed by WHO support the conclusion that the known and potential benefits of the vaccine outweigh the known and potential risks. As sufficient vaccine supply will not be immediately available to immunize all who could benefit from it, countries are recommended to use the WHO Prioritization Roadmap (4) and the WHO Values Framework (5) as guidance for their prioritization of target groups. As long as vaccine supplies are very limited (stage I in the WHO Prioritization Roadmap), in settings with community transmission, the Roadmap recommends that priority be given initially to health workers and older people with and without comorbidities. As more vaccine becomes available, additional priority groups should be vaccinated as outlined in the WHO Prioritization Roadmap (4), taking into account national epidemiological data, vaccine-specific characteristics as outlined in product information approved by regulatory authorities, and other relevant considerations.

Intended use

Persons aged 18 years and above.

Administration

The recommended schedule is two doses (0.5 ml) given intramuscularly into the deltoid muscle. According to the manufacturer's product label, the vaccine can be administered with an interval of 4 to 12 weeks (6). In light of the observation that two-dose efficacy and immunogenicity increase with a longer interdose interval, WHO recommends an interval of 8 to 12 weeks between the two doses. If the second dose is inadvertently administered less than 4 weeks after the first, the dose does not need to be repeated. If administration of the second dose is inadvertently delayed beyond 12 weeks, it should be given at the earliest possible opportunity. It is recommended that all vaccinated individuals receive two doses.

Booster doses

There is currently no evidence indicating a need for further doses once an individual has received two doses. The need for, and timing of, additional doses will be evaluated as further data accumulate.

Interchangeability with other COVID-19 vaccines

All ChAdOx1-S [recombinant] products covered by this recommendation (AstraZeneca AZD1222, SII Covishield, and SK Bioscience) are considered equivalent and interchangeable for both doses.

Currently, it is recommended that both doses should be administered with ChAdOx1-S products. Studies are underway to assess whether COVID-19 vaccines using a different platform can be used interchangeably in the dosing schedule. Recommendations may be updated as further information becomes available.

Co-administration with other vaccines

There should be a minimum interval of 14 days between administration of ChAdOx1-S [recombinant] vaccine and any other vaccine against other conditions. This recommendation may be amended as data on co-administration with other vaccines become available.

Contraindications

A history of anaphylaxis to any component of the vaccine is a contraindication to vaccination. People who have an anaphylactic reaction following the first dose of this vaccine should not receive a second dose of the same vaccine.

Precautions

No severe allergic reactions or anaphylaxis caused by ChAdOx1-S [recombinant] vaccine have been recorded in the context of clinical trials. However, as for all vaccines, ChAdOx1-S [recombinant] vaccine should be given under health care supervision, with the appropriate medical treatment available in case of allergic reactions. As for any other vaccine, an observation period of 15 minutes after vaccination should be ensured.

A very rare syndrome of blood clotting combined with low platelet counts, described as thrombosis with thrombocytopenia syndrome (TTS),¹ has been reported around 4 to 20 days following vaccination with the ChAdOx1-S [recombinant] vaccine. A causal relationship between the vaccine and TTS is considered plausible although the biological mechanism for this syndrome is still being investigated. Most of these cases were reported from the United Kingdom and the European Union (EU). There is considerable geographic variation with regards to the reported incidence, with very few cases reported from non-European countries, despite extensive use of the vaccine in these countries. An estimation of the risk outside Europe needs further data collection and analysis. Data from the United Kingdom (31 March 2021) suggest the risk of TTS is approximately 4 cases per 1 million (1 case per 250 000) vaccinated adults, while the rate is estimated to be approximately 1 case per 100 000 in the EU. Current data from Europe suggest that the risk may be higher in younger adults compared with older adults; no specific risk factors have yet been identified.

In countries with ongoing SARS-CoV-2 transmission, the benefit of vaccination in protecting against COVID-19 far outweighs the risks. However, benefit–risk assessments 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 risk of severe COVID-19 disease outcomes including COVID-19 related thromboembolic events increases with age.

It is currently unknown whether there is a risk of TTS following the second dose. As data from additional studies become available, enabling better understanding of the pathophysiology of TTS and its relationship to the vaccine, recommendations on vaccination will be updated, if appropriate. People who have had blood clots associated with low platelet levels (TTS) after their first dose of should not be given their second dose.

Vaccination of specific populations

Populations for which supportive data are available from immunogenicity and clinical trials

Persons aged 65 years and over

While the relatively small number of older participants and their late recruitment in the phase 3 trials in the United Kingdom, Brazil and South Africa were insufficient for accurate efficacy assessment, data recently released from the phase 3 trial of the vaccine in the United States, which included a larger number of participants aged 65 years or older, showed an efficacy of 85% (95% CI: 58–94%) in this age group. The trial data also indicate that the vaccine is safe for this age group. Furthermore, post-introduction vaccine effectiveness studies from the United Kingdom have shown high rates of protection against hospitalizations, severe COVID-19 and death in older persons, including those over the age of 80 years. WHO recommends the vaccine for use in persons aged 65 years and older.

Persons with comorbidities

Certain comorbidities have been identified as increasing the risk of severe COVID-19 disease and death. The clinical trials demonstrated that the vaccine has similar safety and efficacy profiles in persons with various underlying medical conditions, including those that place them at increased risk for severe COVID-19. The comorbidities studied in the clinical trials included obesity, cardiovascular disease, respiratory disease and diabetes. Vaccination is recommended for persons with comorbidities that have been identified as increasing the risk of severe COVID-19.

¹ [https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-\(gacvs\)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-with-astrazeneca-covid-19-vaccine-\(vaxzevria-and-covishield\)](https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-(gacvs)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-with-astrazeneca-covid-19-vaccine-(vaxzevria-and-covishield)).

Populations for which limited or no data exist from the clinical trials

Children and adolescents below the age of 18 years

There are currently no efficacy or safety data for children or adolescents below the age of 18 years. Until such data are available, vaccination of individuals below 18 years of age is not routinely recommended.

Pregnant women

Pregnant women with COVID-19 are at higher risk of developing severe disease compared with non-pregnant women of reproductive age. COVID-19 in pregnancy has also been associated with an increased risk of preterm birth and of neonates requiring neonatal intensive care. Pregnant women who are aged 35 years or older, or have high body mass index, or an existing comorbidity such as diabetes or hypertension, are at particular risk of serious outcomes from COVID-19.²

Preliminary reproductive toxicity studies in mice have not shown harmful effects of the vaccine in pregnancy. ChAdOx1-S [recombinant] vaccine is a replication-defective vaccine. While available data on vaccination of pregnant women are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy, studies in pregnant women are planned in the coming months, including a pregnancy sub-study and a pregnancy registry. Based on previous experience with other vaccine use during pregnancy, the effectiveness of the ChAdOx1-S [recombinant] vaccine in pregnant women is expected to be comparable to that observed for non-pregnant women in similar age groups. Of note, 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. As data become available, recommendations on vaccination will be updated accordingly.

In the interim, WHO recommends the use of ChAdOx1-S [recombinant] vaccine in pregnant women only if the benefits of vaccination to the pregnant woman outweigh the potential risks. 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.

Lactating women

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 [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, a lactating woman who is part of a group recommended for vaccination according to the WHO Prioritization Roadmap, e.g. health workers, should be offered vaccination on an equivalent basis. WHO does not recommend discontinuing breastfeeding after vaccination.

Persons living with HIV

Persons living with human immunodeficiency virus (PLWH) may be at higher risk of severe COVID-19. Safety and immunogenicity data of two doses of ChAdOx1 [recombinant] vaccine were comparable between PLWH with well-controlled HIV and HIV-negative individuals in a study from South Africa. Data on administration of the vaccine are currently insufficient to allow assessment of vaccine efficacy or safety for persons living with HIV. It is possible that the immune response to the vaccine may be reduced, which may lower its clinical effectiveness. In the interim, given that the vaccine is nonreplicating, persons living with HIV who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling should be provided to inform individual benefit–risk assessment. It is not necessary to test for HIV infection prior to vaccine administration.

Immunocompromised persons

Immunocompromised persons are at higher risk of severe COVID-19. Available data are currently insufficient to assess vaccine efficacy or vaccine-associated risks in severely immunocompromised persons, including those receiving immunosuppressant therapy. It is possible that the immune response to the vaccine may be reduced, which may lower its clinical effectiveness. In the interim, given that the vaccine is nonreplicating, immunocompromised persons who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment.

² <https://www.bmj.com/content/370/bmj.m3320>

Persons with autoimmune conditions

No data are currently available on the safety and efficacy of in persons with autoimmune conditions. Persons with autoimmune conditions who are part of a group recommended for vaccination may be vaccinated.

Persons who have previously had SARS-CoV-2 infection

Vaccination should be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Data from clinical trials did not reveal any safety signals. Viral or serological testing for prior infection is not recommended for the purpose of decision-making about vaccination. Within 6 months after an initial natural infection, available data show that symptomatic reinfection is uncommon. Given limited vaccine supply, persons with PCR-confirmed SARS-CoV-2 infection in the preceding 6 months may therefore choose to delay vaccination until near the end of this period. However, emerging data indicate that symptomatic reinfection after natural infection may occur in settings where variants of concerns with evidence of immune escape are circulating. In these settings, earlier immunization after infection may be advisable. When more data on duration of immunity after natural infection become available, the length of this time period may be revised.

Persons with current acute COVID-19

Persons 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 optimal minimum interval between a natural infection and vaccination is not yet known.

Persons who previously received passive antibody therapy for COVID-19

Currently there are no data on the safety or efficacy of vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Hence, as a precautionary measure, WHO recommends that vaccination should be deferred for at least 90 days to avoid interference of the antibody treatment with vaccine-induced immune responses.

Special settings

Persons in 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 as outlined in the WHO Prioritization Roadmap (4), taking into account national epidemiological data, vaccine supply and other relevant considerations.

As noted in the WHO Prioritization Roadmap, national programmes should give special consideration to groups that are disproportionately affected by COVID-19 or that face health inequities as a result of social or structural inequities. Such groups should be identified, barriers to vaccination should be addressed, and programmes should be developed to allow equitable access to vaccines.

In the current period of very limited vaccine supply, preferential vaccination of international travellers would counter the principle of equity. WHO currently recommends that travellers should only be offered COVID-19 vaccination when they are also part of a high-risk group, in epidemiological settings identified in the WHO Prioritization Roadmap, or part of a professional group such as seafarers and aircrew (<https://www.who.int/news/item/25-03-2021-joint-statement-on-prioritization-of-covid-19-vaccination-for-seafarers-and-aircrew>).

Other considerations

SARS-CoV-2 variants

SARS-CoV-2 viruses undergo evolution. Some new virus variants may be associated with higher transmissibility, disease severity, risk of reinfection, or a change in antigenic composition resulting in lower vaccine effectiveness.

Preliminary analyses have shown a slightly reduced vaccine effectiveness of ChAdOx1-S [recombinant] vaccine against B.1.1.7 in the V002 trial in the United Kingdom which is associated with only a limited reduction in neutralizing antibody. Preliminary analyses from the phase 1/2a trial (COV005) in South Africa indicate marked reduction in vaccine effectiveness against mild and moderate disease due to B.1.351 based on a small sample size and substantial loss of neutralizing antibody activity. This study was designed to assess efficacy against disease of any severity, but the small sample size did not allow a specific assessment of vaccine efficacy against severe COVID-19. Indirect evidence is compatible with protection against severe COVID-19; however, this remains to be demonstrated in ongoing clinical trials and post-implementation evaluations.

In view of this, WHO currently recommends the use of ChAdOx1-S [recombinant] vaccine according to the Prioritization Roadmap (4) even if 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.

These preliminary findings highlight the 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

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. However, it is important to note that currently available antibody tests for SARS-CoV-2 assess levels of IgM and/or IgG to the spike or the nucleocapsid protein. The vaccine contains the spike protein; thus, a positive test for spike protein IgM or IgG could indicate either prior infection or prior vaccination. To evaluate for evidence of prior infection in an individual who has received the vaccine, a test that specifically evaluates IgM or IgG to the nucleocapsid protein should be used. A positive nucleocapsid protein-based assay indicates prior infection, while a negative nucleocapsid protein-based assay is expected after vaccination (unless a natural infection has occurred). Antibody testing at an individual level is currently not recommended to assess immunity to COVID-19 following ChAdOx1-S [recombinant] vaccination.

Role of vaccines among other preventive measures

As there is not yet sufficient evidence of an effect of the vaccine on transmission, nonpharmaceutical interventions must continue, including use of face masks, physical distancing, handwashing and other measures as appropriate in particular settings, depending on the COVID-19 epidemiology and potential risks of emerging variants. Government advice on nonpharmaceutical interventions should continue to be followed by vaccinated individuals, as well as those who have not yet been vaccinated. This advice will be updated as information on the impact of vaccination on virus transmission and indirect protection in the community is assessed.

Community engagement, effective communication, and legitimacy

Community engagement and effective communication (including risk communication) are essential to the success of COVID-19 vaccination programmes. Prioritization decisions should be made through transparent processes that are based on shared values, the best available scientific evidence, and appropriate representation and input by affected parties. Furthermore, communication about the mechanism of action of vector-based vaccines, and efficacy and safety data derived from clinical trials and post-marketing studies, as well as background mortality, maternal and neonatal outcomes and rates of adverse events of special interest (AESIs) in groups prioritized for vaccination, needs to be strengthened. Strategies should include: (i) culturally acceptable and linguistically accessible communications regarding COVID-19 vaccination made freely available; (ii) active community engagement and involvement of community opinion leaders and trusted voices to improve awareness and understanding of such communications; and (iii) inclusion of diverse and affected stakeholder opinions in decision-making. Such efforts are especially important in subpopulations who may be unfamiliar with or distrustful of health care systems and immunization.

Open, transparent, and evidence-based communication about the potential benefits and risks to recipients and the community is essential to maintain trust. A useful resource for vaccine safety communication is the communication module of the GACVS COVID-19 vaccine safety surveillance manual (<https://www.who.int/publications/i/item/10665338400>).

Vaccination logistics

The vaccine is presented as a 10-dose vial with stopper (elastomeric with aluminium overseal), delivered in packs containing 10 multidose vials. Unopened multidose vials should be stored in a refrigerator (2 °C to 8 °C) and should not be frozen. Once a vial has been opened (first needle puncture), it should be handled according to the WHO policy on opened multidose vaccines and be discarded at the end of the immunization session or within six hours of opening, whichever comes first. Within this period, the product may be kept and used at temperatures up to 30 °C (6, 7). The open vaccine vials should also be kept at cooled temperatures between 2 °C to 8 °C during the in-use period (6, 7).

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

When scheduling vaccination for occupational groups, e.g. health workers, consideration should be given to the reactogenicity profile of ChAdOx1-S [recombinant] vaccine observed in clinical trials, which may occasionally lead to time off work in the 24–48 hours following vaccination.

In considering the programme implications of implementing these recommendations, particular attention should be given to equity, including the feasibility, acceptability, and effectiveness of the programme in resource-constrained settings.

Recommendations on addressing current knowledge gaps through further research

WHO recommends the following post-authorization monitoring activities and research.

- Safety surveillance and monitoring:
 - serious adverse events such as cerebral venous sinus thrombosis, thrombotic events with thrombocytopenia, anaphylaxis and other serious allergic reactions, Bell’s palsy, and transverse myelitis;
 - cases of multisystem inflammatory syndrome following vaccination, cases of COVID-19 following vaccination that result in hospitalization or death;
 - background rates of AESIs (including thromboembolic events, cerebral venous sinus thrombosis, and TTS), maternal and neonatal outcomes, and mortality in groups prioritized for vaccination;
 - incidence by WHO region, age and sex, and pathomechanism of TTS.
- Vaccine effectiveness:
 - vaccine effectiveness in older persons;
 - vaccine effectiveness in relation to time interval between the first and second dose;
 - vaccine effectiveness in relation to new virus variants;
 - vaccine effectiveness over time and whether protection can be prolonged by booster doses;
 - second dose and booster studies with heterologous vaccines;
 - studies to investigate whether this vaccine reduces SARS-CoV-2 transmission and viral shedding;
 - assessment and reporting of breakthrough infections and virus sequence information;
 - head-to-head studies with other vaccines on extent and duration of immunity using standardized neutralization, T-cell and mucosal immunity assays;
 - vaccine effectiveness against post-COVID-19 conditions.
- Subpopulations:
 - prospective studies on the safety of ChAdOx1-S [recombinant] vaccine in pregnant and lactating women;
 - immunogenicity and safety studies in persons below the age of 18 years;
 - safety data on vaccination in immunocompromised persons, including persons living with HIV and persons with autoimmune disease.
- Vaccination logistics
 - immunogenicity and safety studies of co-administration with other vaccines, including influenza and pneumococcal vaccines, to adults and older persons;
 - safety, immunogenicity, and impact of a delayed second dose, as currently implemented by certain countries;
 - interchangeability and “mix and match” studies within and across COVID-19 vaccine platforms;
 - stability of vaccine under alternative cold-chain distribution and storage conditions.
- Virus variants
 - global surveillance of virus evolution and the impact of virus variants on vaccine effectiveness to support update of vaccines;
 - modelling to determine the trade-offs for the use of vaccines with reduced effectiveness against emergent variants;
 - booster studies with updated vaccine formulations.

References

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2. SAGE guidance for the development of evidence-based vaccination-related recommendations. Geneva: World Health Organization; 2017 (https://www.who.int/immunization/sage/Guidelines_development_recommendations.pdf, accessed 19 April 2021).
3. Evidence to recommendations for COVID-19 vaccines: evidence framework. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-SAGE-Framework-Evidence-2020-1/>, accessed 20 April 2021).
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5. WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/who-WHO-values-framework-for-the-allocation-and-prioritization-of-covid-19-vaccination>, accessed 20 April 2021).
6. COVID-19 vaccine AstraZeneca. European Medicines Agency (https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-endorsement_en.pdf, accessed 20 April 2021).
7. WHO Policy Statement: Multi-dose Vial Policy (MDVP) (https://www.who.int/immunization/documents/general/WHO_IVB_14.07/en/ accessed 20 April 2021).

Table of updates

Section	Rationale for update
Background, booster and interchangeability	Since the issuance of the 10 February 2021 Interim recommendations, WHO has determined the equivalence of the vaccine products based on ChAdOx1-S. Hence these products are considered as equivalent and interchangeable.
Precautions	Since March 2021, a very rare syndrome of blood clotting combined with low platelet counts, described as thrombosis with thrombocytopenia syndrome (TTS), ³ has been reported following vaccination with the ChAdOx1-S [recombinant] vaccine.
Persons aged 65 and above	Since the issuance of the 10 February 2021 Interim recommendations, post-introduction data have emerged which provide more robust data with regards to the vaccine efficacy/effectiveness in persons aged 65 and above. The following sentence was added: “Post-introduction, vaccine effectiveness studies from the United Kingdom showed high rates of protection against hospitalizations, severe COVID-19 and death in older persons.” Furthermore, interim analyses of the United States phase 3 trial of the AstraZeneca COVID-19 AZD 1222 showed statistically significant high clinical efficacy against COVID-19 in persons aged 65 years and above.
Persons who have previously had SARS-CoV-2 infection	This document was updated to harmonize with the most recent Interim recommendations for other COVID-19 vaccines where SAGE had decided to update the wording to reflect the concerns of reduced protection after natural infections in areas where variants of concern are circulating.
Pregnant and lactating women	To reflect updates in data and insights with regards to the use of COVID-19 vaccines in pregnancy and lactating women.
Persons living with HIV	To reflect recent data: <i>ChAdOx1 nCoV-19 (AZD1222) vaccine in people living with and without HIV</i> . Madhi S, et al. 2021 Epub ahead of print: DOI: 10.21203/rs.3.rs-322470/v1

³ [https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-\(gacvs\)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-with-astrazeneca-covid-19-vaccine-\(vaxzevria-and-covishield\)](https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-(gacvs)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-with-astrazeneca-covid-19-vaccine-(vaxzevria-and-covishield)).

Special settings	<p>This document was updated to harmonize with language used in the most recent Interim recommendations for other COVID-19 vaccines:</p> <p>In the current period of very limited vaccine supply, preferential vaccination of international travellers would counter the principle of equity. WHO currently recommends that travellers should only be offered vaccination against COVID-19 if they are also part of a high-risk group or in epidemiological settings identified in the WHO Prioritization Roadmap. The joint statement on prioritization of seafarers and aircrew was added.</p>
Vaccination logistics	<p>This section was updated to reflect WHO’s open vial policy.</p>
Recommendations on addressing current knowledge gaps through further research	<ol style="list-style-type: none"> (1) Thromboembolic events and TTS were added under safety monitoring. (2) Given that various stringent regulatory authorities have indicated that immunobridging including safety data would suffice for extending the age indication to adolescents and children, the recommendation was rephrased to “immunogenicity and safety studies” to replace the previous recommendation for randomized controlled trials. (3) To harmonize the list for research recommendations with more recent Interim recommendations for other COVID-19 vaccines,

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External: Current members of the Strategic Advisory Group of Experts ([SAGE](#)) on Immunization and the [SAGE Working Group on COVID-19 Vaccines](#).

WHO: Annelies Wilder-Smith, Joachim Hombach, Melanie Marti, Susan Wang, Katherine O’Brien.

WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this interim guidance document will expire 2 years after the date of publication.

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