

## Background

The Astra Zeneca COVID-19 vaccine (also named generically ChAdOx1 vaccine) was approved by WHO under Emergency Use Listing (EUL) on 15 February 2021. This includes two vaccine products referred to as AZ/AZD1222 (produced by AstraZeneca-SKBio in the Republic of Korea) and SII/Covishield produced by the Serum Institute of India (SII). These two vaccine products are provided under the COVAX Facility.

## How safe is the AstraZeneca vaccine?

Data from the clinical trials on the AstraZeneca (AZ) vaccine among 24,244 participants showed that the majority of adverse reactions reported after administration were mild to moderate in severity and usually resolved within a few days of vaccination. Adverse reactions reported after the second dose were milder and less frequent than after the first dose. Reactogenicity was generally milder and less frequent in older adults ( $\geq 65$  years old) than in younger adults (18–64 years).

The most frequently reported adverse reactions were injection site tenderness (63.7%), injection site pain (54.2%), headache (52.6%), fatigue (53.1%), myalgia (44.0%), malaise (44.2%), pyrexia (including feverishness (33.6%) and fever  $>38$  °C (7.9%), chills (31.9%), arthralgia (26.4%) and nausea (21.9%). Five serious adverse events were reported, of which two were in the vaccine group (pyrexia and transverse myelitis) and three were in the control group (autoimmune haemolytic anaemia, increased C-reactive protein and myelitis).

To date, more than 20 million doses of the AZ vaccine have been administered in Europe and more than 27 million SII/Covishield doses have been administered in India. Based on available data, severe adverse events appear to be extremely rare, estimated to occur in two per million people.

In March 2021, following reports of rare blood coagulation disorders in a few individuals who had received the AZ vaccine in Europe, the WHO's Global Advisory Committee on Vaccine Safety (GACVS) and European Medicines Agency (EMA) reviewed all available information and data on thromboembolic events (blood clots) and thrombocytopenia (low platelets) after vaccination. This included clinical trial data and reports based on safety data from Europe, the United Kingdom, India, and Vigibase, the WHO global database of individual case safety reports.

Based on a careful scientific review of the available information, the WHO's GACVS and EMA concluded that the available data did not suggest any overall increase in clotting conditions, and the benefits of the AZ vaccine continue to outweigh any risks with strong potential to prevent infections and reduce deaths. On the basis of these findings, WHO and EMA have recommended that vaccinations with the AZ vaccine should continue. The WHO's GACVS will continue to review the safety data from all COVID-19 vaccines and update any advice as necessary and supports the EMA's plans to further investigate and monitor for any adverse events.

## How does the efficacy of the AstraZeneca vaccine compare with the efficacy of other COVID-19 vaccines?

The initial efficacy estimates with two standard doses of the AZ vaccine in seronegative individuals was 63% (95% CI 52, 72). This is comparable to a similar Adenovirus vector vaccine produced by Johnson & Johnson (Janssen) (66.9%, 95% CI 59, 73) that recently received emergency use authorization from the

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<sup>1</sup> Information included is based on data available at time of publication and may change as new data becomes available.

# Frequently Asked Questions: Astra-Zeneca COVID-19 Vaccine

U.S. Food and Drug Administration (FDA) and approved by WHO under EUL.

Data subsequently reviewed by the WHO SAGE shows that the efficacy of the AZ vaccine is enhanced when the interval between the first and second dose of vaccine is increased. The vaccine efficacy when the two doses were given at an interval of 12 weeks was 81.3% (95% CI 60, 91). Hence SAGE recommends that the two doses of this vaccine be given at an interval of 8 to 12 weeks.

The preliminary findings of a clinical trial among 32,449 participants across trial sites in the United States, Peru and Chile showed that the AZ vaccine had 76% efficacy in preventing symptomatic COVID-19 and had 100% efficacy in preventing severe disease and hospitalisation.

As with other COVID-19 vaccines, the efficacy of the AZ vaccine increases with increasing disease severity. In the clinical trial, no cases of severe disease requiring hospitalization were observed 14 or more days after the second dose, compared to five cases in the control group. These results are similar to those observed for the other vaccines.

## Is the AZ vaccine efficacious when administered to adults $\geq 65$ years of age?

The risk of severe disease and death due to COVID-19 increases steeply with age. Older adults are identified as a priority group in the WHO SAGE Prioritization Roadmap. Because a relatively small number of participants aged 65 years or over were recruited into the AZ clinical trials, there were few cases of COVID-19 in either the vaccine or the control group in this age category, and thus the confidence interval around the efficacy estimate is very wide. The trial data indicate that the vaccine is safe for this age group. Immune responses induced by the COVID-19 vaccines in older persons are well documented and similar to those in other age groups, suggesting that the vaccine is likely to be efficacious in older persons. Taking the totality of available evidence into account, WHO recommends the vaccine for use in persons aged 65 years and older.

Data on the effectiveness of the AZ vaccine following widespread roll out are now becoming available. A study in the United Kingdom showed that in adults  $\geq 70$  years vaccinated from early January 2021, vaccine effectiveness for the BNT162b2 (Pfizer BioNTech) reached 61% (95% CI 51-69%) from 28-34 days after the first dose of vaccination then plateaued. Following two doses of vaccine, effectiveness increased to 85-90%. With the AZ vaccine, vaccine effects were seen from 14-20 days after the first dose of vaccination reaching an effectiveness of 60% (95% CI 41-73%) from 28-34 days and further increasing to 73% (95% CI 27-90%) from day 35 onwards. The findings of a clinical trial among 32,449 participants across trial sites in the United States, Peru and Chile showed that in participants aged 65 years and over, the AZ vaccine had an efficacy of 85%.

## How does the efficacy of the AZ vaccine against the South African variant compare with those of other vaccines?

Data on the efficacy against variant B.1.351 first detected in South Africa is available for three vaccines, Janssen, Novavax and AZ, and some data on neutralizing antibody against the B.1.351 variant induced by the Pfizer BioNTech and Moderna vaccines.

In a multi-continent trial of the Janssen vaccine, an efficacy of 72% against moderate or severe disease was observed in the United States and 57% in South Africa where 95% of cases had the B.1.351 variant. Efficacy against severe or critical disease was 85% in the United States and 82% in South Africa. Interim results from the Novavax trial showed 96% efficacy against symptomatic COVID-19 against the ancestral strain, 86% against the B.1.1.7 variant first detected in the United Kingdom, and 60% against the B.1.351 variant. Insufficient data are available to assess protection against severe disease or death. In addition to the efficacy data summarized above, laboratory studies show that the antibodies induced by the Pfizer BioNTech and Moderna vaccines are less effective against the B.1.351 variant as compared to the ancestral strains.

Preliminary analyses from a Phase 1/2a trial (COV005) on AZ in South Africa indicate a marked

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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, including from animal studies, 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 AZ vaccine according to the WHO SAGE Prioritization Roadmap even if variants are present in a country. 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.

### If a country has reported variants, should the AZ vaccine still be used? What decision making steps should countries use?

WHO currently recommends the use of the AZ vaccine according to the WHO SAGE Prioritization Roadmap, even if virus variants are present in a country. Countries should assess the risks and benefits taking into consideration their epidemiological situation, including the extent of circulating variants. To stop the spread of new variants and support decision making on vaccination strategies, countries need to improve surveillance, including genomic analysis, to detect the prevalence of different virus strains.

The primary objective of any COVID-19 vaccination strategy should be to protect high risk individuals against severe disease, hospitalisation and death, and protect hospitals and health facilities from being overwhelmed. Many African countries have limited capacity for critical care. If infections rise due to the new COVID-19 variants, there could be a higher proportion of severely ill patients requiring hospitalization, including in intensive care units. The emphasis should be on starting vaccination as early as possible with available vaccines.

### How are WHO and vaccine manufacturers responding to the situation?

WHO, Vaccine manufacturers, regulators, and scientists worldwide are working to identify and understand COVID-19 variants and their consequences. Both new COVID-19 vaccines and new versions of existing COVID-19 are under development that take into consideration the emergence of variants and their consequence on vaccine efficacy.