ChAdOx1-S vaccine

Approved indication: prevention of COVID-19

COVID-19 Vaccine AstraZeneca multidose vials containing 5 x 10^{11} viral particles in 5 mL

In March 2020, the World Health Organization declared that the COVID-19 outbreak was a pandemic. Since then, there have been over 114 million confirmed cases worldwide and over 2.5 million deaths resulting from SARS-CoV-2 viral infection (WHO coronavirus disease dashboard).[1] In response, many vaccines are being rapidly developed in an effort to prevent further disease.[2]

ChAdOx1-S (also known as the Oxford/AstraZeneca vaccine) is the second COVID-19 vaccine to be given provisional approval for use in Australia following the BNT162b2 Pfizer vaccine. ChAdOx1-S is a viral-vectored DNA vaccine that consists of a replication-deficient adenovirus which carries the gene encoding the SARS-CoV-2 spike protein. Following injection, the viral vector is taken up by immune cells, such as dendritic cells, and the gene is translated into the spike protein. These antigen-presenting cells show the spike protein to other immune cells, including B and T cells. This triggers the production of antibodies to the spike protein.

The provisional approval of this vaccine is based on short-term efficacy and safety data from four ongoing randomised controlled trials involving 23,848 people.[3] A phase I trial established early safety and immunogenicity of the vaccine (COV001 conducted in the UK)[4] and also included an efficacy cohort. Phase II and III trials (COV002 in the UK,[5] COV003 in Brazil and COV005 in South Africa) had an expanded enrolment to include a wider population that were more likely to be exposed to the SARS-CoV-2 virus (e.g. health workers).

Initial studies found that the vaccine elicited neutralising antibodies and cell-mediated responses to SARS-CoV-2.[4-6] Its efficacy is based on an interim analysis of the phase II/III studies (COV002, COV003).[3] Most of the 11,636 participants included in the interim analysis were 18–64 years old. Although the studies excluded people with severe comorbid illness or severe immunosuppression, mild comorbidity (e.g. obesity (BMI ≥30 kg/m^2), heart disease, respiratory conditions or diabetes) was permitted and accounted for 36% of those in the efficacy analysis.

Participants were randomised to the ChAdOx1-S vaccine or a control (meningococcal group A, C, W and Y conjugate vaccine), given by intramuscular injection. Those in the COVID-19 vaccine group received either two standard doses (5 x 10^{10} viral particles/injection) or a low dose (2.2 x 10^{10} viral particles/injection) followed by a standard dose. Because of logistical problems, the interval between doses varied from 4 to 26 weeks.

The primary efficacy outcome was protection against COVID-19 disease at least two weeks after the second dose in participants who had no previous evidence of SARS-CoV-2 infection. During the surveillance period, there were 30 cases of COVID-19 among those who received the vaccine and 101 cases among those who received the control. This equated to a vaccine efficacy of 70.4%. Vaccine efficacy was 59.3% in those who received two standard doses (the licensed vaccine regimen in Australia) and 90% in those who received a lower first dose followed by a standard second dose (see Table).[3]

In a subgroup analysis of those given two standard doses, vaccine efficacy tended to be higher when the duration between doses was longer (53.3% at <6 weeks, 51.1% at 6–8 weeks, 61% at 9–11 weeks and 79% at ≥12 weeks). The vaccine appeared to reduce

Table **Efficacy of the ChAdOx1-S vaccine against COVID-19 disease**[3]

COVID-19 vaccine dosing regimen*	Cases of COVID-19		Vaccine efficacy†
	ChAdOx1-S vaccine	Meningococcal vaccine	
Low dose followed by a standard dose, or two standard doses	30/5807	101/5829	70.4% (CI 54.8–80.6)
Low dose followed by a standard dose	3/1367	30/1374	90% (CI 67–97)
Two standard doses	14/1879	35/1922	59.3% (CI 25.1–77.9)

CI confidence interval

* Low doses contained 2.2 x 10^{10} viral particles/injection and high doses contained 5 x 10^{10} viral particles/injection. Doses were given 4–26 weeks apart.

† Defined as protection against COVID-19 disease at least two weeks after the second dose in participants who had no previous evidence of SARS-CoV-2 infection

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NEW DRUGS

COVID-19 hospitalisations compared to the control vaccine (0/6307 vs 9/6297 cases), measured 22 days after receiving a standard first dose.

Having one or more mild comorbidities at baseline did not appear to affect the protective efficacy of the vaccine (73.4%). Although the vaccine was immunogenic in people aged 65 years and older, vaccine efficacy could not be established as there were not enough cases of COVID-19 in this age group.

In a safety cohort of 12,021 vaccinated people, the most common adverse events were injection-site tenderness (>60%) and injection-site pain (>50%), fatigue and headache (>50%), myalgia and malaise (>40%), fever and chills (>30%), and arthralgia and nausea (>20%). Most reactions were mild to moderate in severity and resolved within a few days. Paracetamol appeared to reduce these reactions.[4] Adverse events were milder and less commonly reported after the second dose compared to the first dose. Older participants (≥65 years) reported fewer and less severe adverse events.

There were two serious adverse events in the vaccine group – one case of multiple sclerosis and one case of transverse myelitis. Both were thought unlikely to be related to vaccination. There were also two deaths in the vaccine group and four deaths in the control group. None were thought to be related to the vaccines received in the trial.

Vaccination should be postponed in those with acute severe febrile illness. Anaphylaxis can occur with any vaccine so emergency medical treatment and supervision should be available to manage anaphylactic reactions and observation for 15 minutes after vaccination is prudent. Caution is urged in people with thrombocytopenia, a bleeding disorder, or who are receiving anticoagulation therapy.

As with the BNT162b2 Pfizer vaccine, there are limited data on the use of this vaccine during pregnancy and lactation. Given the low level of community transmission in Australia, routine use of COVID-19 vaccines during pregnancy is not currently recommended by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists.[7] However, it states that vaccination may be considered in some groups with a high risk of complications from COVID-19. The guidelines also recommend that pregnant healthcare workers in an at-risk work environment should be allocated to lower risk duties, work from home or take leave of absence. If avoiding exposure is not possible, they should be offered vaccination. The Australian Department of Health has published a guide to help women making decisions about vaccination during pregnancy and breastfeeding.

The vaccine is supplied in multidose vials that should be stored in the refrigerator (2–8°C). Each vial contains ten 0.5 mL doses. Dilution of the vial is not required before administration. A separate sterile needle and syringe should be used for each patient. Opened vials should be discarded after six hours at room temperature and after 48 hours if stored in the refrigerator.

The vaccine should be given by intramuscular injection, preferably in the deltoid muscle. Two separate 0.5 mL doses should be given 4–12 weeks apart. The patient's name and the batch number of the vaccine must be recorded in the Australian Immunisation Register. Enhanced monitoring of adverse events following immunisation is in place for the COVID-19 vaccines at national and state and territory levels.[2] Training modules for vaccination providers have been developed by the Department of Health in partnership with the Australian College of Nursing to ensure COVID-19 vaccines are handled and administered safely.

This vaccine appears to be well tolerated and is effective at preventing COVID-19. Vaccine efficacy in older people and protection against variant SARS-CoV-2 strains is currently unclear. Follow-up data are limited so the duration of protection is also not yet known but clinical trials are ongoing. This vaccine is indicated for adults only.

Although the Australian Government's COVID-19 vaccination plan is for vaccines to be universally available, free and voluntary, they are initially being rolled out to priority groups including quarantine and border workers, frontline health workers, and staff and residents in aged care. Other vulnerable groups and high-risk workers are being targeted in later phases before the vaccine is rolled out to everyone.

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X manufacturer did not respond to request for data

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.