

Australian Technical Advisory Group on Immunisation (ATAGI)

Clinical guidance on use of COVID-19 vaccine in Australia in 2021 (v6.0)

Version 6.0
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This clinical guidance is for COVID-19 immunisation providers and program staff and is updated based on currently available data. It provides recommendations on the use of the Comirnaty (Pfizer) COVID-19 vaccine and COVID-19 Vaccine AstraZeneca. Recent changes from previous versions of ATAGI Clinical guidance on COVID-19 vaccines in Australia include:

- *Comirnaty is recommended for children aged 12-15 years with medical conditions that increase their risk of severe illness; all Aboriginal and Torres Strait Islander children aged 12-15 and all children aged 12-15 years in remote communities as part of outreach vaccination programs.*
- *Additional medical conditions relevant to adolescents have been added to the list of 'Conditions associated with increased risk of severe COVID-19'.*
- *Mixed vaccination schedules are recommended in special circumstances, including in some returned travellers and in those who have had a serious vaccine-attributed adverse event following a first dose.*
- *Myocarditis and pericarditis have been rarely reported after Comirnaty. People who develop myocarditis or pericarditis after having Comirnaty should defer further doses of Comirnaty and discuss this with their treating doctor.*
- *People with a past history of inflammatory cardiac illness e.g., myocarditis, pericarditis, endocarditis; acute rheumatic fever; complex or severe congenital heart disease; acute decompensated heart failure or a history of cardiac transplant can receive Comirnaty, however consultation with a cardiologist is recommended as a precaution prior to vaccination.*
- *A history of capillary leak syndrome is a new contraindication to COVID-19 Vaccine AstraZeneca.*
- *Immune thrombocytopenia, Guillain Barré Syndrome and capillary leak syndrome have been reported after COVID-19 Vaccine AstraZeneca.*
- *Precautions are required for people with a history of confirmed mastocytosis with recurrent anaphylaxis. Patients with other mast cell disorders can be vaccinated without special precautions.*

Key points

- The overarching goal of Australia's COVID-19 vaccination program is to protect all people in Australia from the harm caused by SARS-CoV-2, through preventing serious illness and death, and, as much as possible, disease transmission.
- Delivery of vaccine has been prioritised initially for population groups at increased risk of exposure to SARS-CoV-2 or of severe COVID-19, or occupational groups critical to societal functioning. These are: quarantine and border workers; frontline healthcare workers; aged care and disability care staff and residents; older adults (initially ≥80 years with progression to lower age brackets); people aged ≥12 years with underlying medical conditions associated with an increased risk of severe COVID-19; Aboriginal and Torres Strait Islander adults and critical and high-risk workers, including defence, police, fire, emergency services and others.
- COVID-19 vaccine is current recommended for all people aged ≥ 16 years, and for the following groups:
 - Children aged 12-15 years with specified medical conditions that increase their risk of severe COVID-19
 - Aboriginal and Torres Strait Islander children aged 12-15 years
 - All children aged 12-15 in remote communities, as part of broader community outreach vaccination programs.
- Comirnaty (Pfizer Australia Pty Ltd) is provisionally registered by the TGA in people aged ≥12 years and is given in a two-dose schedule. Efficacy against symptomatic COVID-19 is about 95% after two doses.
- COVID-19 Vaccine AstraZeneca (AstraZeneca Pty Ltd) is provisionally registered in people aged ≥18 years and is given in a two-dose schedule. Efficacy against symptomatic COVID-19 ranges from about 62% to 73%, with the higher efficacy seen after a longer interval (12 weeks) between doses. Efficacy from day 22 after the first dose up until 12 weeks is about 73%.
- The effectiveness of both vaccines against symptomatic infection with the Delta strain of SARS-CoV-2 is reduced compared with earlier strains, however protection against hospitalisation is maintained.
- ATAGI recommends completing the vaccination course with the same vaccine. Mixed schedules are only recommended in special circumstances such as for those with serious vaccine-attributed adverse events after the first dose, or in those who were partially vaccinated overseas with a brand not available in Australia.
- COVID-19 Vaccine AstraZeneca is associated with a rare risk of thrombosis with thrombocytopenia syndrome (TTS). The risk of TTS appears higher in younger adults than in older adults, and is higher after the first dose than the second. Comirnaty is not associated with a risk of TTS.
- Comirnaty is the preferred brand over COVID-19 Vaccine AstraZeneca in people aged <60 years, and in pregnant people. COVID-19 Vaccine AstraZeneca continues to be recommended in people aged 18 to <60 years when the benefits outweigh risks, including in outbreak settings
- Comirnaty should be routinely offered to pregnant people at any stage of pregnancy, and to women who are breastfeeding or planning pregnancy.
- Comirnaty is recommended in people with a past history of certain precautionary conditions for COVID-19 Vaccine AstraZeneca; cerebral venous sinus thrombosis (CVST), heparin induced thrombocytopenia (HIT), idiopathic splanchnic (mesenteric, portal, splenic) vein thrombosis, and antiphospholipid syndrome with thrombosis. Comirnaty is recommended for the second dose for people in these groups who have received a first dose of COVID-19 Vaccine AstraZeneca
- Precautions to the use of both Comirnaty and COVID-19 Vaccine AstraZeneca include a history of generalised (non-anaphylactic) reaction to a prior dose or an ingredient, past anaphylaxis to medications/vaccines which may contain polyethylene glycol or polysorbate 80, and a history of confirmed mastocytosis with recurrent anaphylaxis which requires treatment

- Precautionary conditions specific to Comirnaty include a past history of inflammatory cardiac illness e.g., myocarditis, pericarditis, endocarditis; acute rheumatic fever; complex or severe congenital heart disease; acute decompensated heart failure or a history of cardiac transplant. People with these conditions **can still receive Comirnaty**, however consultation with a cardiologist is recommended prior to vaccination.
- Contraindications to COVID-19 Vaccine AstraZeneca include anaphylaxis to a previous dose or to an ingredient; thrombosis with thrombocytopenia after a previous dose; capillary leak syndrome, or any other serious adverse event attributed to a previous dose.
- Contraindications to Comirnaty include anaphylaxis to a previous dose or to an ingredient; myocarditis and/or pericarditis attributed to a previous dose, or any other serious adverse event attributed to a previous dose.
- Co-administration of a COVID-19 vaccine with other vaccines is not routinely recommended. A minimum 7-day interval is advised between administration of a COVID-19 vaccine and any other vaccine, including influenza vaccine. This interval can be shortened (including to same day administration) in special circumstances.
- Recording of COVID-19 vaccine administration in the Australian Immunisation Register (AIR) is mandatory.
- Notification of adverse events following immunisation should be made to the Therapeutic Goods Association (TGA) and through the specified reporting mechanisms for **your state or territory**.

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Freedom of Information Act 1982 (FOI) by the Department of Health and Aged Care.

Additional Resources

The following resources are available for providers and consumers:

Resources for providers

- [COVID-19 Vaccine training](#)
- [Information for providers: COVID-19 vaccination consent and FAQs](#)
- [Information for immunisation providers on thrombosis with thrombocytopenia syndrome \(TTS\) following COVID-19 vaccination](#)
- [Provider guide to COVID-19 vaccination of people with immunocompromise](#)
- [Consent form for COVID-19 vaccination](#)
- [Guidance on the use of multi-dose vials for COVID-19 vaccination](#)
- [Product Information for Comirnaty available at the Therapeutic Goods Administration \(TGA\) website](#)
- [Product Information for COVID-19 Vaccine AstraZeneca at the Therapeutic Goods Administration \(TGA\) website](#)
- [ATAGI clinical advice on use of a different COVID-19 vaccine as the second dose in special circumstances](#)
- [Primary Care Approach to Thrombosis with Thrombocytopenia Syndrome \(TTS\) after COVID-19 Vaccine AstraZeneca](#)
- [Joint ATAGI-CSANZ Guidance on Myocarditis and/or Pericarditis after mRNA COVID-19 Vaccines](#)

Shared decision guides

- [COVID-19 vaccination decision guide for women who are pregnant, breastfeeding, or planning pregnancy](#)
- [COVID-19 vaccination decision guide for frail older people, including those in residential aged care facilities](#)
- [COVID-19 vaccination decision guide for people receiving palliative or end-of-life care](#)
- [COVID-19 vaccination decision guide for people with immunocompromise](#)
- [COVID-19 vaccination – Weighing up the potential benefits against risk of harm from COVID-19 Vaccine AstraZeneca](#)

Resources for consumers

- [Preparing for COVID-19 vaccination](#)
- [Information on COVID-19 Pfizer \(COMIRNATY\) vaccine](#)
- [After your Pfizer \(COMIRNATY\) vaccine](#)
- [Information on COVID-19 Vaccine AstraZeneca](#)
- [After your AstraZeneca vaccine](#)
- [Patient information sheet on AstraZeneca COVID-19 vaccine and thrombosis with thrombocytopenia syndrome \(TTS\)](#)

Additional resources are available at www.health.gov.au, including 'easy read' and translated versions of patient fact sheets.

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The virus: SARS-CoV-2

The pandemic of coronavirus disease (COVID-19) is caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2), a virus first identified in December 2019. Bats appear to be the reservoir of SARS-CoV-2.¹ SARS-CoV-2 is a single-stranded RNA betacoronavirus in the same subgenus as the severe acute respiratory syndrome (SARS) virus, and is more distantly related to the Middle East respiratory syndrome (MERS) virus.²

SARS-CoV-2 contains four main structural proteins: spike (S) glycoprotein, small envelope (E) glycoprotein, membrane (M) glycoprotein and nucleocapsid (N) protein.³ Most COVID-19 vaccines target the spike protein, which contains two subunits: S1 and S2. S1 contains the receptor binding domain, which binds to the angiotensin converting enzyme 2 receptor on host cells, facilitating entry.⁴

Several SARS-CoV-2 variant strains have been identified. Some variants are associated with higher transmissibility and increased severity or duration of disease. These variants are classified as a Variant of Concern (VOC) or Variant of Interest depending on their attributes.⁵

As of July 2021, four VOCs have been identified: Alpha, first identified in the United Kingdom; Beta, first identified in South Africa; Gamma, first identified in Brazil, and Delta, first identified in India.⁵ These variants are more transmissible than the wild type of SARS-CoV-2, and they have become the predominant strains in their countries of origin and in other settings.⁶ The Delta variant has been shown to be more transmissible than other variants. In many countries, it has replaced Alpha as the dominant variant of SARS-CoV-2.⁷ Some early surveillance data also suggests that it causes a higher rate of severe outcomes compared to other variants.^{8,9}

Immunogenicity and efficacy/effectiveness of current COVID-19 vaccines against some variant strains of SARS-CoV-2 is reduced compared to the ancestral strain. For the Delta variant, vaccine effectiveness of both Comirnaty and COVID-19 Vaccine AstraZeneca against symptomatic infection has been reduced compared to Alpha but is maintained against hospitalisation.¹⁰ Refer to the **Vaccine Information** section for further information.

Clinically significant variations in the efficacy/effectiveness of different vaccines against these emerging strains will continue to be monitored to determine if any changes to vaccines or to vaccine policy are needed.

The disease: COVID-19

SARS-CoV-2 causes asymptomatic or mild disease in 81% of cases; severe illness (with dyspnoea, hypoxia or >50% lung involvement on imaging within 48 hours) in 14%; and critical illness in 5%.¹¹ The most common symptoms are fever and cough.¹² Other common symptoms include myalgia, headache, dyspnoea, sore throat, diarrhoea and nausea/vomiting. Loss of smell or taste and rhinorrhoea occur in fewer than 10% of cases.

Older age is an important risk factor for severe COVID-19, as shown in several international systematic reviews. In comparison with those aged <50 years, the risk of death from COVID-19 progressively increases throughout each decade of age, from about 2 times high for those aged 50–59 years to >10 times higher for those aged ≥80 years.¹³ Findings were similar when results were adjusted for other risk factors.¹⁴ In Australia, prior to the implementation of the COVID-19 vaccination program, the COVID-19 case fatality ratio increased substantially with age, from 0.6% in those aged 50–64 years, to 7.0% in those aged 65–79 years and 33.8% in those aged ≥80 years.¹⁵

Certain medical conditions are associated with an increased risk of severe illness from COVID-19. Refer to **Box 1** for a list of specified medical conditions.

There are certain occupational and environmental settings that may place individuals at higher risk of COVID-19 exposure either because of a higher risk of infected individuals being present and/or because the conditions enable rapid spread of the virus. These include healthcare facilities; aged care and disability care facilities; border and quarantine facilities; and some industries such as meat processing. Refer to the **Recommendations** section for further information.

Further information about COVID-19 is available in the [COVID-19 CDNA National Guideline for Public Health Units](#). Information about Australian epidemiology is available on the [Department of Health website](#), including regular epidemiological reports.

The COVID-19 vaccination program

The aim of the COVID-19 vaccination program in Australia is to reduce COVID-19 related harm by preventing serious illness and death, and, as much as possible, disease transmission. Information on COVID-19 vaccination program implementation in Australia is available on the [Department of Health website](#).

The epidemiology of COVID-19 is a key determinant informing the most appropriate use of COVID-19 vaccines, in addition to the characteristics and availability of COVID-19 vaccines.

In Australia, outbreak control measures (including contact tracing, testing and isolation; border control and quarantine; and physical distancing) have been successful in limiting the spread of COVID-19 in the community.¹⁶ However, sporadic disease outbreaks continue to occur following virus introduction from international travellers.

In settings where there is no sustained SARS-CoV-2 community transmission, the initial focus of a vaccine program is to prevent importation of cases and demonstrate reciprocity to critical (particularly frontline) workers at highest risk of exposure to SARS-CoV-2.¹⁷ Subsequent priority groups include older adults, particularly those living in residential aged care or disability care facilities, and those with medical risk factors for severe illness or death from COVID-19.

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Vaccine, doses and administration

The following COVID-19 vaccines have been provisionally approved for use in Australia. The [TGA website](#) provides access to the TGA-approved product information for each vaccine. Refer also to **Vaccine information** section for more details.

Comirnaty (generic name BNT162b2)

Sponsor:	Pfizer Australia Pty Ltd
Approved age for use:	≥12 years
Presentation:	Multi-dose vial without preservative, each vial containing 6 doses in 0.45 mL. Requires dilution with 1.8 mL of sterile 0.9% NaCl without preservative into each multi-dose vial.
Volume/strength:	0.3 mL (30 µg) per dose
Schedule:	2 doses, at least 21 days apart
Administration route:	Intramuscular injection into deltoid muscle
Ingredients:	Each 0.3mL dose contains 30 mcg mRNA encoding the SARS-CoV-2 spike glycoprotein List of excipients: <ul style="list-style-type: none"> ○ ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315) ○ 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159) ○ Distearoylphosphatidylcholine (DSPC) ○ Cholesterol ○ Potassium chloride ○ Monobasic potassium phosphate ○ Sodium chloride ○ Dibasic sodium phosphate dihydrate ○ Sucrose ○ Water for injections

COVID-19 Vaccine AstraZeneca

Sponsor:	AstraZeneca Pty Ltd
Approved age for use:	≥18 years
Presentation:	Multi-dose vial without preservative, each vial containing either 8 doses in 4 mL or 10 doses in 5 mL.
Volume/strength:	0.5 mL per dose
Schedule:	2 doses, 12 weeks apart (minimum interval 4 weeks apart)
Administration route:	Intramuscular injection into deltoid muscle
Ingredients:	Each 0.5 mL dose contains 5×10^{10} viral particles of ChAdOx1-S ^a List of excipients: <ul style="list-style-type: none"> ○ Histidine ○ Histidine hydrochloride monohydrate ○ Sodium chloride ○ Magnesium chloride hexahydrate ○ Disodium edetate (EDTA) ○ Sucrose ○ Ethanol absolute ○ Polysorbate 80 ○ Water for injection

a. Recombinant, non-replicating chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike glycoprotein

Recommendations

COVID-19 vaccination is recommended for all people aged ≥ 16 years to protect against COVID-19.

Additionally, ATAGI currently recommends that the following children aged 12-15 years be prioritised for vaccination:

- Children with specified medical conditions that increase their risk of severe COVID-19 [**Box 1**]
- All Aboriginal and Torres Strait Islander children aged 12-15 years
- All children aged 12-15 in remote communities, as part of broader community outreach vaccination programs that provide vaccines for all ages (≥ 12 years).

Recommendations for use in all other children aged 12-15 years will be made in updated advice within the coming months.

There is a limited supply of COVID-19 vaccines in the initial phases of the COVID-19 vaccination program. Therefore, vaccine allocation is being determined based on several factors, such as timing of supply, priority target groups and logistical considerations. The following population groups are prioritised initially:

People with occupational risk of exposure to SARS-CoV-2

People in certain occupations are at increased risk of being infected with SARS-CoV-2 and/or transmitting the virus to vulnerable people who have risk factors for severe illness. These include:

- frontline healthcare workers, who have a seven-fold increased risk of severe COVID-19 compared with non-essential workers (RR 7.42; 95% CI: 5.52–10.00)¹⁸
- quarantine and border workers
- aged care and disability care staff
- critical and high-risk workers including defence, police, fire and emergency services; certain laboratory staff; meat processing workers; and select others.

Residents of aged care and disability care facilities

Aged care facilities have been the setting for a number of serious COVID-19 outbreaks in Australia.¹⁹

Older adults

Older age is by far the strongest risk factor associated with morbidity and mortality from COVID-19.^{11,14,20}

All Aboriginal and Torres Strait Islander people aged ≥ 12

Aboriginal and Torres Strait Islander people are at increased risk of severe illness and death from COVID-19 due to multiple factors, including a high prevalence of underlying chronic health conditions associated with severe COVID-19 and a greater likelihood of living in communities where social distancing cannot be practised.²¹

While the impact of COVID-19 on Aboriginal and Torres Strait Islander people to date has been mitigated by existing control measures (especially restriction of movement into communities), the factors above warrant prioritisation for vaccination.

People aged ≥ 12 with medical conditions that increase their risk of severe COVID-19

People aged ≥ 12 years with certain underlying chronic medical conditions, outlined in **Box 1**, are at increased risk of severe illness with COVID-19 and should be prioritised for vaccination, particularly older adults and those who have multiple comorbidities.

Pregnant people

Compared to non-pregnant women, pregnant women who contract COVID-19 have an increased risk of severe illness, including increased odds of intensive care admission (OR 2.13, 1.53 – 2.95; I² 71.2%), need for invasive ventilation (OR 2.59, 2.28 – 2.94, I² 0%) and need for extracorporeal membrane oxygenation (OR 2.02, 1.22 – 3.34, I² 0%).²³ Compared to pregnant women who did not have COVID-19, women who had COVID-19 during pregnancy may have a higher risk of stillbirth (OR 2.84, 95% CI 1.25 to 6.45), neonatal death (OR 2.77, 95% CI 0.92 to 8.37), need for admission to the neonatal intensive care unit (odds ratio 4.89, 95% CI 1.87 to 12.81, I²=96.2%).²³

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Box 1: Conditions associated with increased risk of severe COVID-19

Conditions	Notes
Immunocompromising conditions	
Haematological diseases or cancers	Including leukaemia, lymphoma or myeloma resulting in immunocompromise Recommend discussion with specialist regarding optimal timing of vaccination
Solid organ transplant recipients who are on immune suppressive therapy	Recommend discussion with specialist regarding optimal timing of vaccination
Bone marrow transplant recipients or chimeric antigen receptor T-cell (CAR-T) therapy recipients or those with graft host disease	Recommend discussion with specialist regarding optimal timing of vaccination
Non-haematological cancer	Diagnosed within the past 5 years or on chemotherapy, radiotherapy, immunotherapy or targeted anti-cancer therapy (active treatment or recently completed) or with advanced disease regardless of treatment
Survivors of childhood cancers	Nil
Chronic inflammatory conditions requiring medical treatments	Including: systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, ulcerative colitis, and similar who are being treated with disease modifying anti-rheumatic drugs (DMARDs) or immune-suppressive or immunomodulatory therapies. Generally not inclusive of people living with osteoarthritis, fibromyalgia, myalgic encephalomyelitis/chronic fatigue syndrome or similar non-immunocompromising inflammatory conditions.
Primary or acquired immunodeficiency	Including congenital causes of immunodeficiency and HIV/AIDS
Other underlying conditions	
Chronic renal (kidney) failure with a eGFR of <44mL/min	Does not include mild-moderate chronic kidney disease
Heart disease	Including ischaemic heart disease, valvular heart disease, cardiomyopathies and pulmonary hypertension, and complex congenital heart disease
Chronic lung disease	Including chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease and severe asthma (defined as requiring frequent hospital visits or the use of multiple medications). Does not include Mild or moderate asthma
Diabetes	Nil
Obesity	Defined for adults as severe obesity with BMI $\geq 40\text{kg/m}^2$; and for children as BMI $\geq 95^{\text{th}}$ percentile for age
Chronic liver disease	Nil
Chronic neurological conditions	Including stroke, dementia, multiple sclerosis, motor neurone disease, Parkinson's disease, cerebral palsy and epilepsy. Generally not inclusive of migraine or cluster headaches Generally not inclusive of migraine or cluster headaches
Poorly controlled blood pressure (defined as two or more pharmacologic agents for blood pressure control, regardless of readings)	Nil
Those living with significant disability requiring frequent	Including Down syndrome, muscular dystrophy, traumatic brain and spinal cord injury, severe intellectual disability

assistance with activities of daily living	
Those with severe mental health conditions	Including schizophrenia and bi-polar disorder
Children with complex chronic disease	
Pregnant people	Nil

Vaccine preference recommendations

Comirnaty is preferred over COVID-19 Vaccine AstraZeneca in people aged < 60 years. This is based on the higher risk and observed severity of thrombosis and thrombocytopenia syndrome (TTS) in people < 60 years compared to those ≥ 60. However, COVID-19 Vaccine AstraZeneca can be used in adults aged < 60 years if Comirnaty if the person has made an informed decision based on an understanding of the risks and benefits. In outbreak settings, adults <60 years of age should strongly consider COVID-19 Vaccine AstraZeneca if they are unable to access Comirnaty.

People of any age who have received their first dose of COVID-19 Vaccine AstraZeneca without any serious adverse events attributable to the first dose and without any new contraindications should receive a second dose of COVID-19 Vaccine AstraZeneca. This is supported by data indicating a substantially lower rate of TTS following a second COVID-19 Vaccine AstraZeneca dose in the United Kingdom (UK).

Comirnaty is also the recommended vaccine for pregnant women. [Pregnant women who have already received a first dose of COVID-19 Vaccine AstraZeneca can receive either Comirnaty or COVID-19 Vaccine AstraZeneca for their second dose, although Comirnaty is preferred.](#)

For those aged 60 years and above, the individual benefits of receiving a COVID-19 vaccine are greater than in younger people. The risks of severe outcomes with COVID-19 increase with age and are particularly high in older unvaccinated individuals. The benefit of vaccination in preventing COVID-19 with COVID-19 Vaccine AstraZeneca outweighs the risk of TTS in this age group and underpins its ongoing use in this age group.

Considerations for special populations

People who are immunocompromised

COVID-19 vaccine is recommended for people who are immunocompromised because of their increased risk of severe illness with COVID-19.²⁴ There are many causes and varying degrees of immunocompromise, and the risk of COVID-19 will vary according to the number and type of underlying conditions, medical management and other factors.

Currently, there are limited data on the safety and efficacy of COVID-19 vaccination for people who are immunocompromised. In principle there are no theoretical safety concerns for Comirnaty (a non-live vaccine) or COVID-19 Vaccine AstraZeneca (a non-replicating viral vector vaccine) in people who are immunocompromised, based on a general understanding of vaccine characteristics.

Early (preprint) evidence suggests a reduced immune response to vaccination with Comirnaty in people with cancer and solid organ transplant recipients.²⁵⁻²⁹ A small preprint study of 26 patients on biologic immunomodulatory medications for inflammatory bowel disease who received two doses of an mRNA COVID-19 vaccine showed that 22/26 patients achieved levels of antibody against the receptor binding domain (RBD) of the S-protein of SARS-CoV-2 that are comparable to convalescent plasma from recovered COVID-19 patients.³⁰

COVID-19 vaccine is also recommended for people with HIV. A small number of people (n=120) with stable HIV infection were recruited into the phase II/III trial for Comirnaty, and a cohort of people with stable HIV infection were recruited into a phase I/II trial of COVID-19 Vaccine AstraZeneca. Immunogenicity and safety data for these cohorts group are anticipated.^{31,32}

Before vaccination, people with immunocompromise should be counselled about the safety and efficacy of COVID-19 vaccine, and the limited available data in immunocompromised recipients. People with ATAGI Clinical Guidance on COVID-19 Vaccine in Australia_v6.0

immunocompromise who have been vaccinated should be advised to continue taking other protective measures against SARS-CoV-2.

For further information refer to the [COVID-19 vaccination decision guide for people with immunocompromise](#) and [Provider guide to COVID-19 vaccination in people with immunocompromise](#).

Children

COVID-19 vaccine is currently recommended for children aged 12-15 in the following groups:

- Those with specified medical conditions that increase their risk of severe COVID-19 [**Box 1**]
- All Aboriginal and Torres Strait Islander children aged 12-15 years
- All children aged 12-15 in remote communities, as part of broader community outreach vaccination programs that provide vaccines for all ages (≥ 12 years).

Recommendations for use in all other children in this age group will be made in updated advice within the coming months.

Preliminary evidence suggests that children and adolescents have a lower susceptibility to SARS-CoV-2 compared to adults and play a lesser role in transmission at a population level.³³ Children and adolescents with COVID-19 are commonly asymptomatic or have mild or moderate symptoms. A systematic review that included data on illness severity in 1,475 children with COVID-19 reported asymptomatic infection in 15%, mild illness in 42%, moderate illness in 39%, severe illness in 2% and critical illness in 0.7%.³⁴

A rare but serious condition associated with COVID-19 in children is Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS), which can present with features similar to those of Kawasaki disease or toxic shock syndrome.³⁶

Severe illness from COVID-19 in children is uncommon but is more likely in those with certain pre-existing medical conditions.³⁷⁻³⁹ A phase II-III trial of Comirnaty which included 2260 adolescents aged 12 to 15 years found a vaccine efficacy against symptomatic COVID-19 in this age cohort of 100% (95% CI 75.3 – 100) from 7 days after the second dose, and an acceptable safety profile.⁴⁰ The most common adverse event was injection site pain (79-86%), followed by fatigue (60-66%) and headache (55-65%). Fever occurred in 20% of participants who received Comirnaty, and was slightly more frequent in those aged 12-15 (37%) than in those aged 16-25 (32%). Systemic adverse events were more common after the second dose. No vaccine-related serious adverse events were reported. Trials of Comirnaty and other COVID-19 vaccines in younger cohorts are underway.

People who are pregnant, breastfeeding or planning pregnancy

Pregnant people should be routinely offered Comirnaty at any stage of pregnancy. Pregnant women with COVID-19 have an increased risk of severe illness and adverse pregnancy outcomes. Women who are breastfeeding or who are planning pregnancy are also recommended to receive Comirnaty.

Comirnaty is the preferred COVID-19 vaccine for people who are pregnant, breastfeeding or planning pregnancy. There is a growing body of evidence supporting the safety of mRNA COVID-19 vaccines in pregnancy. There are still very limited data on the safety of viral vector vaccines (such as COVID-19 Vaccine AstraZeneca) in pregnancy. Pregnant women who received a first dose of COVID-19 Vaccine AstraZeneca can receive either Comirnaty or COVID-19 Vaccine AstraZeneca for their second dose, although Comirnaty is preferred.

Pregnant women with COVID-19 have a higher risk of intensive care admission (OR 2.13, 95% CI 1.53 - 2.95), invasive ventilation (2.59, 95% CI 2.28 - 2.94), need for extra corporeal membrane oxygenation (OR 2.02, 95% CI 1.22 - 3.34) and preterm birth (OR 1.47, 95% CI 1.14 – 1.91) compared to non-pregnant reproductive aged women²³ with COVID-19. Factors which increase the risk of severe illness and death from COVID-19 during pregnancy include increased maternal age, high body mass index and pre-existing co-morbidities. Infants born to mothers with COVID-19 are more likely to require admission to the neonatal intensive care unit (OR 4.89, 95% CI 1.87 – 12.81) versus those without COVID-19.

In a prospective cohort study of over 35,000 pregnant women who received an mRNA COVID-19 vaccine, the adverse event profile was similar to that of non-pregnant women.^{41,42} Pregnant women were slightly more likely to report injection site pain, and less likely to report generalised symptoms such as fever or tiredness. Fever of 38°C or above was reported by fewer than 1% of pregnant women after the first dose of Comirnaty, and fewer than 5% after the second dose. The findings from this large study are supported by other smaller observational studies.^{41,42}

The same study reported on pregnancy and neonatal outcomes in 827 women who received an mRNA COVID-19 vaccine in pregnancy, and did not identify any safety concerns.⁴³ Complications such as preterm delivery, stillbirth, small for gestational age infants and congenital anomalies occurred at a similar rate to what is seen in the general population. In the clinical trial for Comirnaty, 23 women became pregnant during the study period, of which 11 had received Comirnaty. Information about the outcomes of their pregnancies is awaited.⁴⁴ Animal studies of Comirnaty have not shown any negative effects on fertility or pregnancy. A phase 2/3 randomised controlled trial of Comirnaty in pregnant women is underway in the US.⁴⁵

[For further information refer to the Shared decision making guide for women who are pregnant, breastfeeding or planning pregnancy](#)

People with a past SARS-CoV-2 infection

Past infection with SARS-CoV-2 is not a contraindication to vaccination; however, it is recommended that vaccination be deferred for up to six months after the acute illness in those who have had PCR-confirmed SARS-CoV-2 infection. Evidence suggests that past infection reduces the risk of reinfection for at least 6 months.⁴⁶ Individuals who have prolonged symptoms from COVID-19 beyond six months can be vaccinated on a case-by-case basis.

In the phase II/III trial of Comirnaty, the vaccine was administered to a small number of people with serological evidence of previous SARS-CoV-2 infection. There were no specific safety issues reported among these individuals. A similarly high overall efficacy was shown when participants who had had previous SARS-CoV-2 infection were also included for analysis, but a separate estimate of efficacy for these individuals was not reported.

In the pooled analysis of phase II/III trials of COVID-19 Vaccine AstraZeneca, 718 participants (3%) were found to be seropositive, and the safety profile was consistent across participants with or without prior evidence of SARS-CoV-2 infection at baseline. Seropositive participants had increased anti-spike antibody responses after the first dose, but no further increase after the second.⁴⁷

Serological testing or other testing to detect current or previous infection with SARS-CoV-2 before vaccination is neither necessary nor recommended before vaccination.

Timing of administration of other vaccines, including influenza vaccine

The preferred minimum interval between receipt of a COVID-19 vaccine and any other vaccine, including influenza vaccine, is 7 days. A shorter interval (i.e., less than 7 days, including co-administration) is acceptable in the following settings:

- Increased risk of COVID-19 or another vaccine-preventable disease (e.g., COVID-19 outbreak, influenza outbreak, tetanus-prone wound)
- Logistical issues e.g., difficulty scheduling visits to maintain the 7-day interval

This also means that a person may be able to receive another vaccine in between their two doses of Comirnaty vaccine, if appropriate.

As with any other vaccine, vaccination should be deferred if the recipient is acutely unwell. If a person experiences a short term expected adverse event such as fever following vaccination, other vaccines should not be administered until the adverse event has resolved.

Co-administration or near administration (e.g. within days) of two or more vaccines can sometimes lead to a higher frequency of mild to moderate adverse events or make the attribution of potential adverse events to vaccination more challenging.

This advice is based on the current absence of data on the immunogenicity and safety of these vaccines when co-administered, and may change as further information becomes available.

If co-administration of an influenza vaccine and COVID-19 vaccine occurs, revaccination is not required for either vaccine. The patient should be informed of the possibility of an increased likelihood of common adverse effects and be asked to [report any untoward adverse events](#).

Co-administration of antipyretics/analgesics

Prophylactic use of paracetamol or ibuprofen is not recommended before receiving a COVID-19 vaccine. Antipyretics and analgesics can be taken after vaccination for management of vaccine-related side effects such as fever and myalgia, if required.

Variation of schedule

Comirnaty

The recommended interval between two doses of Comirnaty is at least 21 days. The minimum acceptable interval between the two doses is 19 days. It is recommended to complete the two-dose course within 6 weeks. This allows time for logistical considerations, including supply and timing of access to vaccine at the individual and clinic levels. These limits are based on the intervals between doses studied in clinical trials.

Shortening of the minimum acceptable interval may result in a sub-optimal immune response. If two doses have inadvertently been given at a shorter than the minimum acceptable interval, it is not currently recommended that a vaccine dose is repeated. This is because there are no data on administration of more than two vaccine doses given in close proximity in time, and there is still a likelihood of good protection in that individual.

Longer intervals between first and second doses may need to be recommended during program rollout if epidemiological considerations warrant a change (e.g. during an outbreak response to ensure available doses are provided as first doses to as many people as possible).

If the second dose of Comirnaty is administered later than the recommended interval, no further doses are required.

Although Comirnaty may provide partial protection against COVID-19 as soon as 12 days after the first dose, this protection is likely to be short lived. A two-dose course is recommended for optimal protection.

COVID-19 Vaccine AstraZeneca

The recommended interval between two doses of COVID-19 Vaccine AstraZeneca is 12 weeks. The minimum interval between doses is 4 weeks. Shortening the interval from 12 weeks to no less than 4 weeks between doses is acceptable and may be appropriate in certain circumstances, for example, imminent travel or anticipated risk of COVID-19 exposure. In an outbreak setting, ATAGI recommends an interval of 4 to 8 weeks between doses. If a dose has been inadvertently given before the minimum 4-week interval, it is not currently recommended that the vaccine dose be repeated.

In clinical trials, the timing of administration of COVID-19 Vaccine AstraZeneca ranged from approximately 4 weeks up to 26 weeks. In a post-hoc analysis, vaccine efficacy following the second dose of COVID-19 Vaccine AstraZeneca progressively increased with a longer interval between doses and appeared to be greatest when the interval was ≥ 12 weeks. Short-term efficacy from 3 weeks after the first dose, before the second dose and up to 12 weeks post vaccination was about 73% (95% CI: 48.79–85.76).⁴⁸ Also refer to the **Vaccine information** section for further information. Short term efficacy from 22 days until 90 days after a single dose was 76% (95%

CI: 59-3–85-9). The duration of protection after a single dose has not yet been established, and a second dose is recommended for optimal protection.

If the second dose of COVID-19 Vaccine AstraZeneca is administered later than the recommended interval, no further doses are required.

Mixed (heterologous) schedules

Based on current evidence, ATAGI recommends using the same COVID-19 vaccine for the two doses of the primary course. Emerging (preprint) data demonstrating that mixed schedules of Comirnaty and COVID-19 Vaccine AstraZeneca are immunogenic and have an acceptable safety profile in the small cohorts vaccinated.^{49,50} Larger studies and longer term follow up are required to confirm the safety of this approach.

In the following special circumstances, an alternate brand may be recommended for the second dose:

- People with serious vaccine-attributable adverse events after dose 1 that warrant the use of an alternate vaccine brand for dose 2:
 - anaphylaxis to the first dose of a COVID-19 vaccine
 - thrombosis with thrombocytopenia following the first dose of COVID-19 Vaccine AstraZeneca
 - any other serious adverse event attributed to the first dose of a COVID-19 vaccine (and without another cause identified) following expert review (typically by a jurisdictional immunisation specialist service or a relevant medical specialist).
- People with a precautionary condition for which the use of Comirnaty is recommended instead of COVID-19 Vaccine AstraZeneca:
 - history of cerebral venous sinus thrombosis (CVST)
 - history of heparin-induced thrombocytopenia
 - history of idiopathic splanchnic (mesenteric, portal, splenic) venous thrombosis
 - history of anti-phospholipid syndrome (APLS) with thrombosis.
- People given an incomplete course of a COVID-19 vaccine brand not available in Australia.

The recommended interval for administration of a second COVID-19 vaccine dose using an alternative brand is 4 to 12 weeks after the first dose. A longer interval is acceptable if the second dose cannot be administered during this time window. Further advice is available in [ATAGI clinical advice on use of a different COVID-19 vaccine as the second dose in special circumstances](#)

Repeat vaccination

Additional or booster doses beyond the two-dose course are not currently recommended.

Data on the real-world effectiveness and duration of protection from Comirnaty and COVID-19 Vaccine AstraZeneca are anticipated, including against current and emerging strains (variants) of SARS-CoV-2, and will inform future recommendations regarding the need for and timing of booster doses.

In the same way that the influenza vaccines are modified to protect against newly circulating strains each season, COVID-19 vaccines may in future be adapted to protect against SARS-CoV-2 variant strains.

Contraindications

Contraindications to COVID-19 Vaccine AstraZeneca are:

- anaphylaxis after a previous dose
- anaphylaxis to any component of the vaccine, including polysorbate 80
- history of capillary leak syndrome
- thrombosis with thrombocytopenia occurring after a previous dose
- any other serious adverse event attributed to a previous dose .

Contraindications to Comirnaty are:

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- anaphylaxis after a previous dose
- anaphylaxis to any component of the vaccine, including polyethylene glycol (PEG)
- myocarditis and/or pericarditis attributed to a previous dose
- any other serious adverse event attributed to a previous dose.

Anaphylaxis after COVID-19 vaccines

The observed rate of anaphylaxis after Comirnaty administration in the United States in early 2021 was 4.7 cases per million doses administered.⁵¹ 89% of cases occurred within 30 minutes of vaccination.⁵¹ Comirnaty contains polyethylene glycol (PEG), and it is possible that this component is implicated in anaphylaxis.^{52,53} However, anaphylaxis following PEG is reported to be extremely rare (37 case reports between 1977 and 2016).⁵²

Anaphylaxis to polysorbate 80, which is an excipient in COVID-19 Vaccine AstraZeneca and is also included in many other vaccines, is rare.⁵⁴ Anaphylaxis to COVID-19 Vaccine AstraZeneca is rare. The rate of reported anaphylaxis after COVID-19 Vaccine AstraZeneca in Australia appears similar to the overall rate for other vaccines.

Precautions

Specific allergies

The following individuals should be assessed for suitability for vaccination, if necessary in consultation with an allergist/immunologist or specialist immunisation clinic:

- people with immediate (within 4 hours) and generalised symptoms of a possible allergic reaction (e.g. urticaria/hives), without anaphylaxis, to a previous dose of a COVID-19 vaccine
- people with a generalised allergic reaction (without anaphylaxis) to any component of the COVID-19 vaccine to be administered (e.g. PEG in Comirnaty or polysorbate 80 in COVID-19 Vaccine AstraZeneca)
- people with a history of anaphylaxis to previous vaccines and/or multiple drugs (injectable and/or oral) where ingredients such as PEG or polysorbate 80 may conceivably be the cause
- people with a history of confirmed mastocytosis with recurrent anaphylaxis that requires treatment.

People in these categories may require vaccination in a facility with medical staff in attendance, observation for at least 30 minutes following administration of a COVID-19 vaccine dose, or vaccination with an alternate brand of COVID-19 vaccine. Refer to [ASCIA Guide: Allergy and COVID-19 Vaccination](#) for more information.

All other vaccine recipients, including those with a history of allergy; anaphylaxis to food, drugs, venom or latex; or allergic conditions, including asthma, atopic dermatitis (eczema) or allergic rhinitis (hay fever), should be observed for at least 15 minutes following administration of the vaccine at the clinic site in accordance with the current recommendations in the Australian Immunisation Handbook. It is important that all providers are trained in [anaphylaxis management](#).

For individuals suspected to have had an allergic reaction to their first dose of a COVID-19 vaccine, seek advice from the state/territory specialist immunisation service or a specialist allergist/immunologist. These individuals may need a clinical assessment prior to the second vaccine dose. Before and during each vaccination session, providers should check that up-to-date protocols, equipment, medicines and trained staff to manage anaphylaxis are available. Refer to the [Preparing for vaccination](#) section of the Australian Immunisation Handbook.

Precautionary conditions for COVID-19 Vaccine AstraZeneca

Comirnaty is recommended instead of COVID-19 Vaccine AstraZeneca in people of any age with:

- a history of cerebral venous sinus thrombosis (CVST)
- a history of heparin-induced thrombocytopenia (HIT)
- a history of idiopathic splanchnic (mesenteric, portal, splenic) thrombosis
- a history of antiphospholipid syndrome with thrombosis.

For people in the above groups who have received a first dose of COVID-19 Vaccine AstraZeneca, Comirnaty is recommended for the second dose.

People who develop immune thrombocytopenia (ITP) within 42 days after receiving COVID-19 Vaccine AstraZeneca should consult a haematologist regarding whether to proceed with the second dose using the same or an alternate vaccine, and the timing of the second dose.

Precautionary conditions for Comirnaty

People with a history of any of the following conditions **can receive Comirnaty** but advice should be sought from a cardiologist about the best timing of vaccination and whether any additional precautions are recommended:

- Inflammatory cardiac illness e.g., myocarditis, pericarditis, endocarditis
- Acute rheumatic fever
- People aged 12-29 years with dilated cardiomyopathy
- Complex or severe congenital heart disease including single ventricle (Fontan) circulation
- Decompensated heart failure
- Cardiac transplant recipients.

Vaccination should be deferred in people with ongoing cardiac inflammation, or an alternative vaccine (e.g. COVID-19 Vaccine AstraZeneca) considered in people aged ≥ 60 years. People who develop myocarditis and/or pericarditis after receiving Comirnaty should defer further doses and discuss this with their treating doctor.

For further information, refer to the [Joint ATAGI-CSANZ Guidance on Myocarditis and/or Pericarditis after mRNA COVID-19 Vaccines](#)

Acute illness

Vaccination should be deferred in people with an acute illness, including febrile illness (axillary temperature $\geq 38.5^{\circ}\text{C}$). This is a general precaution for all vaccines and will avoid potential misattribution of symptoms from the acute illness as being due to the vaccine or vice-versa.

People with bleeding disorders

People with bleeding disorders and people who are receiving anticoagulant therapy may develop haematomas at intramuscular injection sites. Before vaccination, the recipient should be informed about this risk. Comirnaty and COVID-19 Vaccine AstraZeneca should be administered by intramuscular injection. Subcutaneous administration is not recommended, as no data are available on the safety or immunogenicity of COVID-19 vaccines given via this route.

When administering an intramuscular injection to an individual with a bleeding disorder, a 23 or 25 gauge needle should be used, and firm pressure applied to the site without rubbing for at least 2 minutes.⁵⁵

For further information on how to safely administer vaccines intramuscularly to people with bleeding disorders, refer to the [Vaccination for people with bleeding disorders](#) section in the Australian Immunisation Handbook.

Adverse events

Comirnaty

In the phase II/III trial of Comirnaty, adverse events within 7 days following vaccination were very common but generally mild to moderate and well tolerated.

Injection site reactions were very common (refer to **Table 1**). Injection site pain was reported with similar frequency after dose 1 and dose 2, and was more common in people aged 16 to 55 years (83% post dose 1 and 78% post dose 2) than in people aged >55 years (71% and 66 %, respectively). It also occurred at similar rates in people aged 12 to 15 years (86% post dose 1 and 79% post dose 2), and those aged 16-25 (83% and 78% respectively).⁴⁰ Injection site redness and swelling occurred in $<10\%$ of all participants. These local reactions

were generally mild to moderate, had a median onset on the day following vaccination, and resolved within 1 to 2 days.

Systemic adverse events were more common following the second dose of Comirnaty than the first dose (refer to **Table 1**). The median onset of systemic adverse events was 1–2 days after vaccine receipt, with resolution in a median of 1 day.⁵⁶ Adverse events were generally milder and less frequent in adults aged >55 years than in those aged 16–55 years. It also occurred at similar rates in people aged 12 to 15 years (e.g. fatigue 60% post dose 1 and 66% post dose 2; headache 55% post dose 1 and 65% post dose 2), and those aged 16–25 (fatigue 60% and 66%, respectively; headache 54% and 61% respectively).⁴⁰ Most adverse events were mild to moderate severity and did not affect daily activities. The reported rates of diarrhoea and vomiting did not differ between vaccine and placebo recipients.

The median duration of follow-up for adverse events was 2 months after the second dose. Lymphadenopathy, though uncommon (<1%), was more common in vaccine recipients than in placebo recipients (64 cases [0.3%] versus 6 cases [<0.1%]) and is likely related to the expected immune response to the vaccine. The cases of lymphadenopathy were generally mild to moderate and resolved after a median time of 10 days. There were four cases of Bell's palsy (acute peripheral facial paralysis) in the vaccination group (with onset at 3, 9, 37 and 48 days after a dose respectively), and no cases in the placebo group.⁵⁶ However, this observed frequency was consistent with the expected background rate of Bell's palsy in the general population and thus may not have a causal relationship to vaccination.

Rarely, myocarditis and pericarditis have been reported following vaccination with Comirnaty and other mRNA COVID-19 vaccines.^{57,58} Most reported cases have been mild, self-limiting and recovered quickly, although longer-term follow-up of these cases is ongoing. Cases have been reported predominantly after the second dose and predominantly in younger males (aged < 30 years).

There were no substantive differences in the frequency of adverse events overall observed in the clinical trial by age, sex, race, ethnicity or baseline SARS-CoV-2 status. There was no evidence of enhanced COVID-19 disease in vaccinated individuals who developed SARS-CoV-2 infection after completing vaccination, with only one severe case in the eight vaccine failures.⁵⁹

Anaphylaxis after Comirnaty has been reported rarely. Refer to **Contraindications** for further information.

Table 1: Frequency of select common adverse events reported within 7 days following each dose of Comirnaty in phase II/III trial⁵⁶

	12 – 15 years of age		16–55 years of age		>55 years of age	
			Dose 1	Dose 2	Dose 1	Dose 2
Injection site pain	86%	79%	83%	78%	71%	66%
Fever	10%	20%	4%	16%	1%	11%
Fatigue	60%	66%	47%	59%	23%	51%
Headache	55%	65%	42%	52%	25%	39%
Chills	28%	42%	14%	35%	6%	23%
Muscle pain	24%	32%	21%	37%	14%	28%
Joint pain	10%	16%	11%	22%	9%	19%
Required paracetamol	37%	51%	28%	45%	20%	38%

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COVID-19 Vaccine AstraZeneca

Thrombosis with thrombocytopenia syndrome

A newly identified, rare condition called thrombosis with thrombocytopenia syndrome (TTS) has been reported after COVID-19 Vaccine AstraZeneca in several countries including Australia, and appears to be causally linked to vaccination. TTS involves thrombosis *with* thrombocytopenia. The onset of symptoms is around 4 to 42 days post vaccination. The site of thrombosis varies, and reported presentations include cerebral venous sinus thrombosis (CVST), thrombosis in the splanchnic (mesenteric, portal, splanchnic) circulations, deep vein thrombosis, pulmonary embolism and arterial thrombosis. Although very rare, TTS can cause disability and even death, with a fatal outcome in about one fifth of the cases reported in the UK to date.⁶⁰

The overall estimated rate of TTS is around 1-2 cases per 100,000 doses administered, however this estimate is based on a relatively small number of cases, especially in young adults, reported in Australia to date and is therefore imprecise.⁶¹ The estimated rate is higher in younger adults (<60 years of age), therefore younger age appears to be a risk factor for TTS. No other specific risk factors have been identified. While some case series report more cases in women, others have found no difference by sex. There is no evidence that a past history of clots or of any clotting tendencies increases the risk of TTS, and people with the following conditions *can receive* COVID-19 Vaccine AstraZeneca:

- History of blood clots in typical sites
- Increased clotting tendency that is not immune-mediated
- Family history of blood clots
- History of ischaemic heart disease or stroke
- Current or past thrombocytopenia (low platelet count)
- Those receiving anticoagulation therapy

There is a theoretical concern that certain rare conditions may increase the risk of TTS, and therefore Comirnaty is recommended for people with a history of these conditions:

- Cerebral venous sinus thrombosis (CVST)
- Heparin-induced thrombocytopenia (HIT)
- Idiopathic splanchnic (mesenteric, portal, splenic) vein thrombosis
- Antiphospholipid syndrome with thrombosis.

The great majority of reported cases of TTS have been after the first vaccine dose. As of July 2021, 44 cases were reported out of 22.8 million second doses administered in the UK. This translates to a rate of 1.9 cases per million doses⁶⁰

TTS requires specific haematological investigations as part of the diagnostic workup.⁶² Antibodies to platelet factor 4 are reported in most, but not all, cases. For further information about TTS, refer to [Information for Immunisation Providers on Thrombosis with Thrombocytopenia Syndrome \(TTS\) following COVID-19 vaccination](#).

Other adverse events reported after COVID-19 Vaccine AstraZeneca

In the phase II/III trials of COVID-19 Vaccine AstraZeneca, adverse events reported within 7 days following vaccination were very common (86%) but the majority were mild or moderate.⁴⁷ Injection site tenderness (63.7%) and pain (54.2%) were the most commonly reported. Fatigue (53.2%) and headache (52.6%) were the most frequently reported systemic adverse events⁴⁷ (refer to **Table 2**).

Local or systemic solicited adverse events were most commonly reported on day 1 following vaccination. These reactions were generally mild to moderate and resolved within a few days. The most common systemic solicited adverse effects at day 7 were fatigue, headache and malaise.

Adults aged ≥ 65 years reported fewer local or systemic solicited adverse events, and fewer \geq grade 3 solicited adverse events, than younger adults.^{47,59} Most adverse events did not affect daily activities. Adverse events reported after the second dose were milder and less frequent than those after the first dose.

Reports on unsolicited adverse events were collected through to 28 days following a dose of the COVID-19 Vaccine AstraZeneca. Most of the unsolicited adverse events were mild to moderate in severity and consistent with adverse events commonly observed following vaccination with other vaccines.⁴⁷

In a combined interim analysis of four clinical trials, one case of transverse myelitis was reported in the vaccine arm, which occurred 14 days after dose 2.⁴⁸ This case was reviewed by an independent neurological committee and the likely diagnosis was revised to be idiopathic short segment spinal cord demyelination. Two additional cases of transverse myelitis were considered unlikely to be related to vaccination, with one case subsequently attributed to pre-existing but previously unrecognised multiple sclerosis, and the other case reported in the control group.

The first dose of COVID-19 Vaccine AstraZeneca has been found to be associated with a small risk of immune thrombocytopenia (ITP).⁶³ Two other serious but rare adverse events have been reported after COVID-19 Vaccine AstraZeneca, for which a causal association has not yet been confirmed. These are Guillain Barre syndrome and capillary leak syndrome.^{64,65}

Anaphylaxis after COVID-19 Vaccine AstraZeneca has been reported rarely. Refer to **Contraindications** for further information.

Table 2: Frequency of select common adverse events reported within 7 days following at least one dose of COVID-19 Vaccine AstraZeneca in phase II/III trial in people aged >18 years⁶⁶

	18–55 years		56–69 years		≥ 70 years	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2
Injection site pain	61%	49%	43%	34%	20%	10%
Injection site tenderness	76%	61%	67%	59%	49%	47%
Fatigue	76%	55%	50%	41%	41%	33%
Headache	65%	31%	50%	34%	41%	20%
Muscle pain	53%	35%	37%	24%	18%	18%
Fever	24%	0%	0%	0%	0%	0%

Reporting adverse events

All notifications of adverse events following immunisation should be made through the [usual reporting mechanisms](#).

The safety of COVID-19 vaccines will be actively monitored by the TGA as well as state and territory governments.

Vaccine information

Vaccine efficacy in clinical trials

Comirnaty

A phase II/III trial of Comirnaty is ongoing with >43,000 individuals aged ≥ 12 years enrolled. An interim analysis, with an observation period of 2 months post dose 2, reported vaccine efficacy (VE) of 95.0% (95% CI: 90.3–97.6) in preventing symptomatic laboratory-confirmed COVID-19 in people aged ≥ 16 years (median age 52 years, range 16–89 years for vaccine recipients) without evidence of prior infection with SARS-CoV-2.⁴⁸ There is also evidence of VE against severe illness, although the estimate is imprecise due to the lower number of people overall who developed severe disease (VE 88.9% after first dose [95% CI: 20.1–99.7]).⁵⁹

No data are currently available to assess efficacy for prevention of asymptomatic infection, although serological data are awaited. The duration of protection has not been determined.

In this interim analysis, short-term VE after a single dose was 52.4% (95% CI: 29.5–68.4), with protective effect observed starting 12 days after dose 1.

People aged ≥ 65 years

Sub-group analyses demonstrated similarly high efficacy in adults aged ≥ 65 years (VE 94.7% [95% CI: 66.7–99.9]) and in adults with at least one medical comorbidity or obesity (VE 95.3% [95% CI: 87.7–98.8]).⁴⁹

Children aged <16 years

Preliminary results of an ongoing study involving more than 2000 adolescents aged 12–15 years showed that VE against COVID-19 occurrence at least 7 days after dose 2 in participants with or without evidence of previous infection was 100% (95%CI 78.1-100) with no cases in the vaccine arm. After dose 1 and before dose 2, 3 COVID-19 cases were noted (within 11 days after dose 1) among vaccine recipients, compared with 12 cases among placebo recipients (VE:75% (95% CI: 7.6 to 95.5)). No cases of severe COVID-19 were observed in this age cohort. The neutralising antibody response after 2 doses was higher among those aged 12–15 years compared with those aged 16–25 years.⁴⁰

People with specified medical conditions

This ongoing phase II/III trial also includes participants with well-controlled chronic medical conditions. An interim sub-analysis of data on those with some specified medical conditions showed a similar VE to those without such conditions (95.3% [95% CI: 87.7–98.8] versus 94.7% [95% CI: 85.9–98.6])⁵⁹.

Data on safety, immunogenicity or efficacy of Comirnaty in people living with stable HIV have not yet been published.

COVID-19 Vaccine AstraZeneca

Phase II/III trials of COVID-19 Vaccine AstraZeneca are ongoing with >57,000 individuals aged ≥ 18 years enrolled. An interim analysis of pooled data was conducted as of 4 November 2020 from two ongoing randomised, blinded, controlled trials: a phase II/III study, COV002, in adults aged ≥ 18 years in the UK and a phase III study, COV003, in adults aged ≥ 18 years in Brazil. This analysis showed the overall VE was 70.4% (95% CI: 54.8–80.6) in preventing symptomatic laboratory-confirmed COVID-19 in people aged ≥ 18 years 15 or more days after the second dose in the primary efficacy study population.⁴⁸ The median duration of follow up from 15 or more days after the second dose was 48 days. This was based on 131 cases (30 among 5,807 who received COVID-19 Vaccine AstraZeneca versus 101 among 5,829 who received the control vaccine).⁴⁸

COVID-19 Vaccine AstraZeneca was demonstrated to have reduced neutralisation activity against the B.1.1.7 variant than against a canonical (Victoria) lineage, however vaccine efficacy against B.1.1.7 was preserved with VE 70.4% (95% CI 43.6 – 84.5), compared to VE 81.5% (95% CI 67.9 – 89.4) for the Victoria lineage.⁶⁷ No efficacy data has been published on the VE against the Delta variant. Sera neutralisation studies show 4.3-fold

reduction in neutralisation of Delta after 2 doses of COVID-19 Vaccine AstraZeneca compared to wild type. After 1 dose COVID-19 Vaccine AstraZeneca, the sera barely inhibited Delta.

Number of doses and interval between the 2 doses

Updated analysis of pooled data as of 7 December 2020 reported a VE of 63.09% (95% CI: 51.81–71.73) in preventing symptomatic laboratory-confirmed COVID-19 in people aged ≥ 18 years who received two standard doses.⁶⁸ This was based on 271 cases (74 among 7,201 who received COVID-19 Vaccine AstraZeneca versus 197 among 7,178 who received the control vaccine).⁴⁸ Efficacy from day 22 after the first dose until up to 12 weeks post vaccination was 76.0% (59.3–85.9).⁴⁸

In clinical trials, the interval between the two doses of COVID-19 Vaccine AstraZeneca ranged from approximately 4 weeks up to 26 weeks. Among participants who received two standard recommended doses at an interval of 4 to 12 weeks, the overall VE for prevention of symptomatic laboratory-confirmed COVID-19 was 59.5% (95% CI: 45.8–69.7), based on 218 cases.⁶⁹ The VE varies with dose interval. The VEs for prevention of symptomatic laboratory-confirmed COVID-19 more than 14 days after the second dose with intervals of < 6 weeks, 6–8 weeks, 9–11 weeks and ≥ 12 weeks between the first and second dose were 55.1% (95% CI 33.0 – 69.9), 59.9% (95% CI 32.0 – 76.4), 63.7% (95% CI 28.0 – 81.7) and 81.3% (95% CI 60.3 – 91.2) respectively.⁷⁰

There were very few people with severe disease and hospitalisation in the interim analysis of clinical trials to assess VE against these outcomes. In the population who received two standard doses, there were 0 out of 4,440 participants who received COVID-19 Vaccine AstraZeneca who were hospitalised, and 4 out of 4,455 in the control group.⁷¹

People aged ≥ 65 years

Fewer than 6% of participants included in the interim analysis were aged ≥ 65 years.⁴⁸ In this cohort there were only four and eight cases of COVID-19 in recipients of COVID-19 Vaccine AstraZeneca and of control vaccine, respectively. However, there were no cases of COVID-19 hospitalisation, severe disease or COVID-19 deaths among trial participants aged ≥ 65 years.⁶⁸ These small numbers preclude the assessment of the efficacy of COVID-19 Vaccine AstraZeneca in this age group at this time. Participants aged ≥ 65 years who received two doses showed SARS-CoV-2 specific neutralising antibody levels comparable with those in serum samples from people who had recovered from COVID-19 (convalescent sera).

Additional information on the efficacy of COVID-19 Vaccine AstraZeneca in adults aged ≥ 65 years is anticipated from a phase III clinical trial underway in the USA and South America (NCT04516746) with over 30,000 participants, including at least 25% of participants aged ≥ 65 years.^{72,73}

People with specified medical conditions

An interim sub-analysis of data on people with specified medical conditions in the Phase II/III trials showed VE in this group was similar to that in people without such conditions. A total of 2,068 (39.3%) participants had at least one pre-existing comorbidity (defined as a BMI ≥ 30 kg/m², cardiovascular disorder, respiratory disease or diabetes). A pooled data analysis (as of 7 December 2020) showed that participants who had one or more comorbidities had a VE of 58.3% (95% CI: 33.6–73.9).⁶⁹

Vaccine effectiveness in post-licensure studies

Comirnaty

The effectiveness of Comirnaty has been studied in vaccination programs in countries such as Israel, USA, Canada and the UK.

In a study in Israel that included over 1.1 million people aged ≥ 16 years, effectiveness of Comirnaty from 7 days after 2 doses was 87% (95% CI: 55–100) against COVID-19 hospitalisations and 92% (95% CI: 75–100) against severe disease.⁷⁴ Data on the duration of protection from the vaccine are not available yet.

In a large population-based cohort study in the UK that included about 375,000 participants aged ≥ 16 years, overall effectiveness of Comirnaty against PCR-positive SARS-CoV-2 infection was 67% (95% CI: 61–72) 21 ATAGI Clinical Guidance on COVID-19 Vaccine in Australia_v6.0

days after dose 1 and 72% (95% CI: 64–79) after dose 2. When assessed against asymptomatic and symptomatic infection, two-dose effectiveness estimates were 52% (95% CI: 34–64) and 91% (95% CI: 83–95), respectively. During the period of this study, the, Alpha (B.1.1.7) variant of SARS-CoV-2 predominated in the UK.

Large population studies have also been done in the UK in period when the Delta variant has become dominant. Overall effectiveness of Comirnaty against PCR-positive SARS-CoV-2 infection irrespective of symptoms at the swab test was 30% (95% CI: 17-41) \geq 28 days after dose 1 and 79% (95% CI: 75-82) \geq 14 days after dose 2. When assessed against symptomatic infection, effectiveness estimates were 33% (95% CI: 15-47) and 83% (95% CI: 78-87) respectively.⁸ Another study examined hospitalisation caused by Delta in the UK, vaccine effectiveness estimates were 94% (95% CI: 46-99) after dose 1 and 96% (95% CI: 86-99) \geq after dose 2.¹⁰

COVID-19 Vaccine AstraZeneca

Effectiveness data for COVID-19 Vaccine AstraZeneca are available from studies mainly in the UK. In a population-based cohort study in the UK, COVID-19 Vaccine AstraZeneca had 64% (95% CI: 55–70) effectiveness against PCR-positive SARS-CoV-2 infection 21 days after the first dose.⁷⁵ Effectiveness against symptomatic infection was marginally higher than against asymptomatic infection.

A prospective cohort study in Scotland found effectiveness of COVID-19 Vaccine AstraZeneca against COVID-19 hospitalisations was 94% for the first dose in 28 to 34 days after vaccination.⁷⁶

Large population studies have also been done in the UK in period when the Delta variant has become dominant. Overall effectiveness of COVID-19 Vaccine AstraZeneca against PCR-positive SARS-CoV-2 infection irrespective of symptoms at the swab test was 18% (95% CI: 9-25) \geq 28 days after dose 1 and 60% (95% CI: 53-66) \geq 14 days after dose 2. When assessed against symptomatic infection, effectiveness estimates were 33% (95% CI: 23-41) and 61% (95% CI: 51-70) respectively.⁸ Another study examined hospitalisation caused by Delta in the UK, vaccine effectiveness estimates were 71% (95% CI: 51-83) after dose 1 and 92% (95% CI: 78-97) \geq after dose 2.¹⁰

Vaccine effectiveness against SARS-CoV-2 transmission

Data from studies in the UK shows that both Comirnaty and COVID-19 Vaccine AstraZeneca are effective in preventing onward transmission of the virus to close contacts in case of breakthrough infections. In one study among the UK general population the effectiveness against transmission from breakthrough infections to household contacts from 21 days after the first dose was 47% (95% CI :37-57%) for COVID-19 Vaccine AstraZeneca and 49% (95%CI:41-56%) for Comirnaty.⁷⁷ Another UK study reported that among healthcare workers, who predominantly had received Comirnaty, vaccination was associated with a 30% (95% CI: 22–37) reduction in transmission of SARS-CoV-2 to household contacts.⁷⁸

Vaccine effectiveness in older adults

In a single-centre case–control study in Bristol in the UK,⁷⁹ vaccine effectiveness against hospitalisation among adults aged \geq 80 years from 14 days after dose 1 was 71% (95% CI: 36–95) for COVID-19 Vaccine AstraZeneca 79% (95% CI: 47– 93) for Comirnaty ⁷⁹ .

Other UK studies have reported effectiveness of first dose of *either* Comirnaty or COVID-19 Vaccine AstraZeneca of 76% (95% CI: 68–82) against overall SARS-CoV-2 infection in people aged \geq 75 years and 81% (95% CI: 65–90) against COVID-19 hospitalisation in people aged \geq 80 years.^{75,76}

VE data available for two doses of COVID-19 Vaccine AstraZeneca are still limited because of the 12-week interval between the two doses used in vaccination programs.⁷⁵

Transporting, storing and handling vaccines

Comirnaty

Comirnaty vaccine vials have a shelf life of 6 months at -90°C to -60°C. Vials can be stored at domestic freezer temperatures (-25°C to -15°C) for up to 2 weeks and can be returned to -90°C to -60°C within the original shelf life. Frozen vials should be thawed at 2°C to 8°C. A carton of 195 vials would require 3 hours to thaw. Frozen vials can also be thawed at room temperature (up to 30°C) for 30 minutes, for immediate use. Once thawed, the vaccine should not be re-frozen. Refer to the product information for more detailed guidance regarding thawing of vials.

After thawing, the shelf life is 31 days at 2°C to 8°C. Undiluted vaccine vials can be stored at up to 30°C for 2 hours (including thawing time). After dilution, vials must be kept at 2°C to 30°C and used within 6 hours from the time of dilution (not including the 2-hour maximum window for storage of an undiluted vial at up to 30°C). Do not freeze the diluted vaccine. ATAGI recommends that, when possible, pre-drawn doses kept at room temperature be used within an hour to minimise any remote potential risk of infection.

Comirnaty is presented in a multi-dose vial containing 0.45 mL of undiluted vaccine and must be reconstituted by diluting with 1.8 mL of sterile 0.9% sodium chloride. The vaccine does not contain a preservative. Do not use bacteriostatic 0.9% sodium chloride. The total quantity after dilution will be 2.25 mL. Do not shake the vial. It is preferable to administer vaccine doses immediately after dilution.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

For additional information refer to the National Vaccine Storage Guidelines [Strive for 5](#).

COVID-19 Vaccine AstraZeneca

The shelf life of COVID-19 Vaccine AstraZeneca is 6 months at 2°C to 8°C.

In Australia, COVID-19 Vaccine AstraZeneca is supplied in multi-dose vials, with either 8 doses in 4 mL or 10 doses in 5 mL. Dilution is NOT required.

Unopened multi-dose vials are to be stored at 2°C to 8°C and in the outer carton, to protect from light.

After first opening, chemical and physical in-use stability has been demonstrated from the time of vial puncture to administration for no more than 6 hours at room temperature up to 30°C, or no more than 48 hours in a refrigerator at 2°C to 8°C. The vial can be re-refrigerated, but after first opening the cumulative storage time at room temperature must not exceed 6 hours, and the total cumulative storage time must not exceed 48 hours.

Although there are data supporting stability of vaccine doses after withdrawal into a syringe for up to 6 hours at room temperature (as reflected in the Astra Zeneca vaccine product information [PI]), ATAGI recommends that, when possible, pre-drawn doses kept at room temperature be used within an hour to minimise any remote potential risk of infection.

For additional information refer to the National Vaccine Storage Guidelines [Strive for 5](#).

Transporting doses for home visits

When transporting COVID-19 Vaccine AstraZeneca or Comirnaty for a home visit, there are two options:

1. Where possible, transport the vial at 2-8°C and not exceeding the total maximum storage period of 6 hours and draw up the dose at the site of administration
2. A pre-drawn dose in a syringe can be transported if it can be appropriately stored (protecting from light and maintaining the cold chain) and can be administered as soon as practicable and not exceeding the total maximum storage period of 1 hour if at room temperature, and within 6 hours if at 2-8°C).

Recording vaccination

It is mandatory to record every administered dose of COVID-19 vaccine on AIR.

This will assist in ensuring that the correct vaccine and interval are used for the second dose, and in identifying patients who are due for a second dose. This will also allow verification or provision of evidence of completion of COVID-19 vaccination, if required.

For more information, refer to the Services Australia website: [AIR for health professionals](#).

Serological testing for immunity

Testing for anti-spike antibodies or neutralising antibodies to demonstrate immunity against SARS-CoV-2 in vaccinated individuals is not recommended. An immune correlate of protection has not yet been established for SARS-CoV-2 infection.⁸⁰

Impact of vaccination on future COVID-19 testing

Receipt of a COVID-19 vaccine will not affect the results of nucleic acid (PCR) testing or rapid antigen testing for diagnosis of SARS-CoV-2 infection.

Since both Comirnaty and COVID-19 Vaccine AstraZeneca encode the spike protein of SARS-CoV-2, vaccination may affect any subsequent serological diagnostic testing and result in detection of antibody to the spike protein, but will not affect the results of anti-nucleocapsid antibody testing.

Isolation or testing for COVID-19 following adverse events

Testing for SARS-CoV-2 infection or implementing (non-medically recommended) isolation of someone who develops symptoms of fever, headache, fatigue or other systemic symptoms within and lasting for <48 hours after receipt of a COVID-19 vaccine is not necessarily required. If a vaccine recipient develops typical vaccine-related adverse events (refer to **Adverse events** section) and there is complete absence of respiratory symptoms (including loss of smell), it is more likely that they have an expected vaccine response. However, vaccine-induced protection is not immediate, and it is possible that SARS-CoV-2 could be contracted within several days before or after vaccination (this would not constitute vaccine failure).

Local public health guidance should be followed irrespective of a history of vaccination. Criteria for SARS-CoV-2 testing vary and depend, in part, on local epidemiology and outbreak management.

For Comirnaty, the median time of onset of systemic adverse events was 1–2 days after vaccine receipt, with resolution in a median of 1 day. For COVID-19 Vaccine AstraZeneca, local or systemic solicited adverse events were most commonly reported on day 1 following vaccination, and generally resolved within a few days.

Post-exposure prophylaxis

COVID-19 vaccines are not recommended for post-exposure prophylaxis use, as no data are available to support such use. The median incubation period for SARS-CoV-2 is 5–6 days (with a range of 1 to 14 days in most people) and vaccination after exposure is unlikely to generate sufficient immunity within this period to prevent infection in a previously unvaccinated exposed individual.

However, local public health authorities may recommend prioritising COVID-19 vaccination for certain populations related to local outbreaks or settings with community transmission of COVID-19. For latest information refer to the CDNA [National guidelines for public health units](#) on COVID-19.

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