

Australian Technical Advisory Group on Immunisation (ATAGI)

Clinical guidance on use of COVID-19 vaccine in Australia in 2021 (v7.3)

Version 7.3

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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 Comirnaty (Pfizer), Spikevax (Moderna) and Vaxzevria (AstraZeneca) vaccines. Recent changes from previous versions of ATAGI Clinical guidance on use of COVID-19 vaccine in Australia in 2021 include:

- *ATAGI recommends a third primary dose of COVID-19 vaccine in severely immunocompromised individuals, to be given 2-6 months after their second dose. An mRNA vaccine (Comirnaty or Spikevax) is preferred for the third dose, but Vaxzevria is also acceptable.*

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 adolescents, and critical and high-risk workers, including defence, police, fire, emergency services, operators of critical infrastructure and others.
- Vaccination for protection against COVID-19 is currently recommended for all people aged ≥ 12 years.
- Comirnaty (Pfizer Australia Pty Ltd) is provisionally registered by the TGA in people aged ≥ 12 years and is given in a two-dose schedule. Short-term efficacy against symptomatic COVID-19 is about 95% from seven days after the second dose in people aged ≥ 12 years.
- Spikevax (Moderna Australia Pty Ltd) is provisionally registered in people aged ≥ 12 years and is given in a two-dose schedule. Short-term efficacy against symptomatic COVID-19 is approximately 94% from two weeks after the second dose in people aged ≥ 18 years, and similar in adolescents aged 12–17 years.
- Vaxzevria (AstraZeneca Pty Ltd) is provisionally registered in people aged ≥ 18 years and is given in a two-dose schedule. Short-term 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%.
- Severely immunocompromised individuals are recommended to receive a third^d dose of a COVID-19 vaccine, 2-6 months after their second dose. An mRNA COVID-19 vaccine (i.e. Comirnaty or Spikevax) is preferred for this third dose, but Vaxzevria is also acceptable in certain circumstances.
- The effectiveness of all 3 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 (heterologous) schedules using 2 different vaccines to complete the primary vaccination course are only recommended in special circumstances such as for those with serious vaccine-attributed adverse events after the first dose and in those who were partially vaccinated overseas with a brand not available in Australia.
- Vaxzevria is associated with a rare risk of thrombosis with thrombocytopenia syndrome (TTS). The risk of TTS is higher in younger adults than in older adults, and is higher after the first dose than the second. Comirnaty and Spikevax are not associated with a risk of TTS.
- mRNA vaccines (i.e., Comirnaty or Spikevax) are the preferred vaccines over Vaxzevria in people aged < 60 years, and in pregnant people. Vaxzevria continues to be recommended in people aged 18 to < 60 years when the benefits outweigh risks, including in outbreak settings.
- People aged ≥ 12 years who are pregnant are a priority group for vaccination. Either Comirnaty or Spikevax should be routinely offered to pregnant people at any stage of pregnancy. If a first dose of Vaxzevria was given before pregnancy and a second dose is due during pregnancy, it is preferable to give Comirnaty or Spikevax for the second dose, however Vaxzevria is not contraindicated.
- Comirnaty or Spikevax are 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 or Spikevax are recommended for the second dose for people in these groups who have received a first dose of Vaxzevria.

- Contraindications to Vaxzevria include anaphylaxis to a previous dose or to an ingredient; history of capillary leak syndrome; thrombosis with thrombocytopenia after a previous dose, or any other serious adverse event attributed to a previous dose.
- Contraindications to Comirnaty or Spikevax include anaphylaxis to a previous dose or to an ingredient of an mRNA COVID-19 vaccine, myocarditis and/or pericarditis attributed to a previous dose, or any other serious adverse event attributed to a previous dose.
- Precautions for COVID-19 vaccination 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 (relevant for Comirnaty and Spikevax) or polysorbate 80 (relevant for Vaxzevria), and a history of confirmed mastocytosis (a mast cell disorder) with recurrent anaphylaxis which requires treatment.
- Precautionary conditions specific to Comirnaty and Spikevax include a recent history of inflammatory cardiac illness within the past 6 months, e.g., myocarditis, pericarditis, endocarditis; acute rheumatic fever (i.e., with active myocardial inflammation) or acute rheumatic heart disease; or acute decompensated heart failure. People with these conditions **can still receive Comirnaty or Spikevax**; however consultation with a GP, immunisation specialist or cardiologist is recommended prior to vaccination to discuss the best timing of vaccination and to consider if any additional precautions are needed.
- 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 through the specified reporting mechanisms for your state or territory, or to the Therapeutic Goods Association (TGA).

Additional Resources

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

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](#)
- [Product Information for Spikevax available 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](#)
- [ATAGI clinical guidance on replacement doses for invalid primary courses of COVID-19 vaccines](#)
- [ATAGI Recommendations on the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised](#)

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 Moderna \(Spikevax\) vaccine](#)
- [After your Moderna \(Spikevax\) vaccine](#)
- [Information on COVID-19 Vaccine AstraZeneca](#)
- [After your AstraZeneca vaccine](#)
- [Patient information sheet on AstraZeneca COVID-19 vaccine and thrombosis with thrombocytopenia syndrome \(TTS\)](#)

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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. SARS-CoV-2 is a single-stranded RNA betacoronavirus in the same subgenus as the severe acute respiratory virus syndrome (SARS) virus, and is more distantly related to the Middle East respiratory syndrome (MERS) virus.¹

SARS-CoV-2 contains four main structural proteins: spike (S) glycoprotein, small envelope (E) glycoprotein, membrane (M) glycoprotein and nucleocapsid (N) protein.² 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.³

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.⁴

As of September 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.⁴ 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.⁵ 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-2.⁶ Some early surveillance data also suggests that it causes a higher rate of severe outcomes compared with other variants.^{7,8}

Immunogenicity and efficacy/effectiveness of current COVID-19 vaccines against some variant strains of SARS-CoV-2 is reduced compared with the ancestral strain. For the Delta variant, vaccine effectiveness of both Comirnaty and Vaxzevria against symptomatic infection has been reduced compared with the Alpha variant but is maintained against hospitalisation.⁹ 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%.¹⁰ The most common symptoms are fever and cough.¹¹ 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.¹² Findings were similar when results were adjusted for other risk factors.¹³ 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.¹⁴

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

COVID-19 is a vaccine preventable disease.

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.¹⁵ However, disease outbreaks continue to occur following virus introduction from international travellers and then transmission in the community.

In settings where there is no sustained SARS-CoV-2 community transmission, the initial focus of the vaccine program is to prevent importation of cases and demonstrate reciprocity to critical (particularly frontline) workers at highest risk of exposure to SARS-CoV-2.¹⁶ Subsequent priority groups include older adults, particularly those living in residential aged care or disability care facilities, Aboriginal and Torres Strait Islander peoples and those with medical risk factors for severe illness or death from COVID-19.

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. Key information from the Product Information is extracted below.

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

Spikevax (generic name Elasmoran or mRNA-1273)

Sponsor:	Moderna Australia Pty Ltd
Approved age for use:	≥12 years
Presentation:	Multi-dose vial without preservative, each vial containing 10 doses in 5 mL.
Volume/strength:	0.5 mL per dose
Schedule:	2 doses, 28 days apart
Administration route:	Intramuscular injection, preferably into deltoid muscle
Ingredients:	Each 0.5 mL dose contains 100 µg mRNA encoding the SARS-CoV-2 spike glycoprotein List of excipients: <ul style="list-style-type: none">- Heptadecan-9-yl 8-[2-hydroxyethyl-(6-oxo-6-undecoxyhexyl)amino]octanoate- Cholesterol- Distearoylphosphatidylcholine- 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)- Trometamol- Trometamol hydrochloride- Acetic acid- Sodium acetate trihydrate- Sucrose- Water for injection

Vaxzevria (previously 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, 4 to 12 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:
	- 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 ≥12 years to protect against COVID-19.

In Australia there has been 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
- 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.¹⁷

Older adults

Older age is by far the strongest risk factor associated with morbidity and mortality from COVID-19.^{10,13,18}

All Aboriginal and Torres Strait Islander people aged ≥ 12 years

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.¹⁹

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

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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 women and pregnant adolescents aged ≥ 12 years

Compared with 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 to 2.95) but with significant heterogeneity between studies ($I^2 = 71.2\%$), need for invasive ventilation (OR 2.59, 2.28 to 2.94² 0%).²⁰ Compared with 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, $I^2=96.2\%$).²⁰

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	
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 an eGFR of <44 mL/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	

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	
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
Poorly controlled blood pressure (defined as two or more pharmacologic agents for blood pressure control, regardless of readings)	
Those living with significant disability requiring frequent assistance with activities of daily living	Including Down syndrome, muscular dystrophy, traumatic brain and spinal cord injury, severe intellectual disability
Those with severe mental health conditions	Including schizophrenia and bi-polar disorder
Children with complex chronic disease	
Pregnant people	

Vaccine preference recommendations

Comirnaty or Spikevax are preferred over Vaxzevria in people aged <60 years. This is based on the higher risk and observed severity of thrombosis and thrombocytopenia syndrome (TTS), a rare adverse event associated with Vaxzevria, in people <60 years compared with those ≥ 60 , and the higher risk of severe disease with increasing age among those who get COVID-19. However, Vaxzevria can be used in adults aged < 60 years 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 Vaxzevria if they are unable to access Comirnaty or Spikevax.²¹

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

mRNA COVID-19 vaccines (Comirnaty or Spikevax) are also the recommended vaccines for pregnant women. Pregnant women who have already received a first dose of Vaxzevria can receive either an mRNA COVID-19 vaccine or Vaxzevria for their second dose, although an mRNA COVID-19 vaccine 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 Vaxzevria 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-19.²² 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.

A third primary dose of COVID-19 vaccine is recommended for people with severe immunocompromise.

People with severe immunocompromise are recommended to receive a third dose of COVID-19 vaccine 2-6 months after their second dose. Definitions of severe immunocompromise and recommendations on the use of

the third dose is available in the [ATAGI recommendations for the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised](#)

An mRNA COVID-19 vaccine (i.e. Comirnaty or Spikevax) is preferred for the third dose, since most studies of third doses of COVID-19 vaccine in immunocompromised populations have involved the use of mRNA vaccines. AstraZeneca can be used for the third dose for individuals who have received AstraZeneca for their first 2 doses if there are no contraindications or precautions for use, or if a significant adverse reaction has occurred after a previous mRNA vaccine dose which contraindicates further doses of mRNA vaccine (e.g., anaphylaxis, myocarditis). Immunogenicity studies in immunocompromised populations are limited and the population who are immunocompromised are clinically diverse. As there is no clear correlate of protection from immunogenicity data, translating findings from immunogenicity studies to predict anticipated protection against asymptomatic or symptomatic infection, hospitalisation, or severe disease is difficult. Post-vaccination antibody geometric mean titres have been generally lower among people with higher degrees of immunosuppression such as solid organ transplant and haematological malignancies²³⁻²⁸ and those with B cell depleting therapies (anti-CD20 monoclonal antibodies).²⁹⁻³¹ Early studies in small numbers (n=12-54) of people with HIV infection have shown antibody responses similar to healthy people.³²⁻³⁴ Fewer studies have evaluated T cell responses (cellular immunity) with some³⁵ finding reduced responses and others relatively preserved cellular immunity.

Some early pre-print vaccine effectiveness studies suggest that immunocompromising conditions may be associated with a reduction in protection against COVID-19 compared with immunocompetent individuals. This finding, however, has not been consistently demonstrated and these studies have some limitations. Overall, vaccine effectiveness against COVID-19 was around 70-90% in immunocompromised,³⁶⁻³⁹ compared with effectiveness of around 84-94% in the general population. One preprint study by Whitaker et al (2021)³⁹ examined both Comirnaty and COVID-19 Vaccine AstraZeneca in the United Kingdom to 13 June 2021 and estimated vaccine effectiveness in a general immunocompromised population against medically attended PCR-confirmed COVID-19 after 2 doses of Comirnaty at 73.0% (33.9-89.0%) and COVID-19 Vaccine AstraZeneca at 74.6% (18.7-92.1%) at least 4 weeks post vaccination.

Effectiveness studies^{38,39} in immunocompromised individuals confirm that it is essential to receive 2 doses of a COVID-19 vaccine, as protection may be suboptimal after a single dose; estimates have ranged from 4-43%³⁸⁻⁴⁰ in partially vaccinated immunocompromised individuals. These studies were conducted prior to the widespread dominance of the Delta variant and may reflect effectiveness against older strains.

For further information on the immunogenicity of COVID-19 vaccines in people with immunocompromise and on the safety and immunogenicity of a third dose, refer to [ATAGI Recommendations on the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised](#).

Adolescents aged ≥ 12 years

COVID-19 vaccination is recommended for all adolescents aged ≥12 years. Comirnaty and Spikevax are registered for use in people aged ≥ 12 years, while Vaxzevria is only registered for use in those aged ≥ 18 years. If Vaxzevria is inadvertently given as a first dose to a person aged < 18 years, Comirnaty or Spikevax should be used for the second dose. No further (i.e. third) dose is required.

Although the frequency of severe illness from COVID-19 is lower in adolescents (with approximately 4-7% experiencing severe outcomes) compared with adults, adolescents appear to have infection rates similar to adults.^{41,42} The SARS-CoV-2 Delta Variant of Concern (VOC) has demonstrated increased transmissibility across all age groups.⁴³ In many countries where the Delta variant has become the dominant circulating strain, including in Australia, and in the context of vaccinated older age groups, the median age of people with COVID-19 is falling with adolescents and children accounting for a higher proportion of cases. Overall hospitalisation rates for COVID-19 in the adolescent age group are higher than for other viral respiratory diseases such as influenza. In the USA, COVID-19 hospitalization rates in adolescents from October 2020 to April 2021 were 2.5–3.0 times higher than that for influenza-associated hospitalization rates from three recent influenza seasons.⁴⁴

Efficacy of COVID-19 vaccination has been demonstrated in adolescents. 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 to 100) from 7 days after the second dose, and an acceptable safety profile.⁴⁵ 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.

Similarly, a phase II/III trial of Spikevax which included 3732 adolescents aged 12 to 17 years found a vaccine efficacy against symptomatic COVID-19 in this age cohort of 92.7% (95% CI: 67.8 to 99.2%) from day 14 after dose 1 onwards, and an acceptable safety profile. No cases of COVID-19 with an onset of 14 days after dose 2 were reported in the vaccine group, and four cases occurred in the placebo group. The most common adverse event was injection site pain (92-93%), followed by fatigue (48-68%) and headache (45-70%).⁴⁶ Fever occurred in 12% of participants aged 12 to 17 years who received dose 2 of Spikevax. Within this age group, the frequency of these reactions was also generally similar among participants 12–15 years and those 16–17 years of age. Systemic adverse events were more common after the second dose. No vaccine-related serious adverse events were reported. Trials of Spikevax in younger cohorts are underway.

For further information refer to the [ATAGI recommendations on the use of COVID-19 vaccines in all young adolescents in Australia](#).

Women and adolescents who are pregnant, breastfeeding or planning pregnancy

Pregnant people are a priority group for COVID-19 vaccination and should be routinely offered an mRNA COVID-19 vaccine (Comirnaty or Spikevax) at any stage of pregnancy.

mRNA vaccines (Comirnaty or Spikevax) are the preferred COVID-19 vaccines for people who are pregnant. This is based on the growing body of evidence supporting the safety of mRNA vaccines in pregnancy, while there are still very limited data on the safety of viral vector vaccines (such as Vaxzevria) in pregnancy. However pregnant women who cannot access an mRNA vaccine can consider vaccination with Vaxzevria if the benefits to the individual outweigh the potential risks. Pregnant women who received a first dose of Vaxzevria can receive either an mRNA COVID-19 vaccine (Comirnaty or Spikevax) or Vaxzevria for their second dose, although an mRNA vaccine is preferred.

Women who are breastfeeding or planning pregnancy are preferred to have an mRNA COVID-19 vaccine because of their age (i.e. mRNA vaccines are the preferred vaccines for all people under 60) and because post-marketing studies demonstrate safety of these vaccines in pregnancy. However, there are no theoretical safety concerns associated with the use of Vaxzevria specific to breastfeeding or planning pregnancy, and women in these groups who cannot access an mRNA COVID-19 vaccine should consider vaccination with Vaxzevria, particularly in outbreak settings.

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

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 with non-pregnant reproductive aged women²⁰ 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 (54% received Comirnaty, 46% received Spikevax), the adverse event profile was similar to that of non-pregnant women.^{47,48} 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 or Spikevax, and fewer than 5% after the second dose of Comirnaty, and 11.8% after the second dose of Spikevax. Fever of 39°C occurred in < 0.05% of pregnant participants after the first dose, and 0.5% after the second dose. The findings from this large study are supported by other smaller observational studies.⁴⁷⁻⁴⁹

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.⁵⁰ 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.⁵¹ In the clinical trial for Spikevax, 13 individuals were unknowingly pregnant or became pregnant during the trial, of which six received the vaccine.⁵² Information about the outcomes of their pregnancies is awaited. A phase 2/3 randomised controlled trial of Comirnaty in pregnant women is underway in the US.⁵³

A more recent (pre-print) study reported on this same cohort with updated data investigated 2456 women vaccinated with at least one dose of Comirnaty (53%) or Spikevax (47%) in the preconception period (up to 30 days prior to the first day of the last menstrual period) or during pregnancy before 20 weeks' gestation. It found the age-standardised cumulative risk of spontaneous abortion occurring at 6 to 19 weeks of gestation was 12.8% (95% CI: 10.8 to 14.8%). This rate was within the expected range of the reported background rate⁵⁴ in high income countries. The highest risk of spontaneous abortion was observed in weeks 8 and 9 of gestation, and this risk decreased markedly after week 13 of gestation, comparable to what is observed in the general population.

Animal studies of Comirnaty and Spikevax have not shown any negative effects on fertility or pregnancy.^{52,55-57} In humans, two studies have evaluated assisted reproductive therapy (ART) outcomes in the same couples before and after Comirnaty.^{56,57} Two other studies compared ART outcomes among those vaccinated with an mRNA COVID-19 vaccine, those previously infected with SARS-CoV-2 and those neither infected nor vaccinated.^{58,59} No adverse effects of vaccination on oocyte quality and retrieval, fertilisation rates, top-quality embryo rates, and sustained implantation rates were observed.

Evidence of vaccine effectiveness of mRNA COVID-19 vaccines in pregnant women is also emerging. A retrospective cohort study that included 15,060 pregnant women in Israel, including 7,530 who received Comirnaty, estimated effectiveness against PCR-confirmed SARS-CoV-2 infection from ≥ 28 days post vaccination to be 78% (95% CI 57 to -89%).⁶⁰

People with a past SARS-CoV-2 infection

People with SARS-CoV-2 infection can be vaccinated as soon as they have recovered from their acute illness or can defer vaccination for up to six months after onset of the SARS-CoV-2 infection.

Past infection reduces the risk of reinfection for at least 6 months.^{61,62} ⁶³ A 2-dose schedule is recommended in previously infected people and is safe and well tolerated.⁶⁴⁻⁶⁶

People who have prolonged symptoms from COVID-19 beyond six months after the initial illness can be vaccinated on a case-by-case basis. Laboratory testing to detect current or past infection with SARS-CoV-2 before vaccination is neither necessary nor recommended.

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 phase III trial of Spikevax, a small number of participants had evidence of current or prior SARS-CoV-2 infection based on RT-PCR or serology testing (n = 680).⁶⁷ Adverse reactions among this population occurred at lower or similar rates compared with individuals without prior SARS-CoV-2 infection and no specific safety

concerns were observed.⁵² A separate analysis of vaccine efficacy in this subgroup was not performed (only one previously infected individual in the placebo group subsequently developed COVID-19 in the study period).^{52,67} In the pooled analysis of phase II/III trials of Vaxzevria, 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.⁶⁸

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 a COVID-19 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.

Recommended schedule

Comirnaty and Spikevax

The recommended interval between two doses for Comirnaty is 21 to 42 days (3 - 6 weeks). The recommended interval between two doses for Spikevax is 28 to 42 days (4 - 6 weeks). This interval range allows time for logistical considerations, including supply and timing of access to vaccine at the individual and clinic levels, and is extrapolated from data on the intervals applied in clinical trials.

Longer intervals between first and second doses of Comirnaty or Spikevax, e.g., 8-12 weeks 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). This requires local decision-making taking into account information on supply, logistics and disease epidemiology.

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

Although Comirnaty and Spikevax 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.

ATAGI advises that the absolute minimum interval between the first and second dose for the second dose to be considered as acceptable and valid as fully vaccinated in the Australian Immunisation Register (AIR) is 14 days. Refer to the [Use of an additional COVID-19 vaccine dose as a replacement dose if the second dose was given less than 14 days after the first dose](#) section for further information.

Vaxzevria

The recommended interval between two doses of Vaxzevria 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.

In clinical trials, the timing of administration of Vaxzevria ranged from approximately 4 weeks up to 26 weeks. In a post-hoc analysis, vaccine efficacy following the second dose of Vaxzevria 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: 48.8 to 85.8).⁶⁹ 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 to 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 Vaxzevria is administered later than the recommended interval, no further doses are required.

ATAGI advises that the absolute minimum interval between the first and second dose for the second dose to be considered as acceptable and valid as fully vaccinated in the Australian Immunisation Register (AIR) is 14 days. Refer to the [Use of an additional COVID-19 vaccine dose as a replacement dose if the second dose was given less than 14 days after the first dose](#) section for further information.

Mixed (heterologous) schedules

Based on current evidence, ATAGI recommends using the same COVID-19 vaccine for the two doses of the primary course. Emerging data demonstrates that mixed schedules are immunogenic. They also have an acceptable safety profile in the small cohorts vaccinated with these heterologous schedules.⁷⁰⁻⁷³ These studies usually involve Vaxzevria as dose 1 and either Comirnaty or Spikevax as dose 2. One small randomised controlled trial investigated Comirnaty as first dose followed by Vaxzevria as the second dose.

Preprint data from a large Danish population cohort study investigated heterologous schedules (either Vaxzevria dose 1 and Comirnaty dose 2 or Vaxzevria dose 1 and Spikevax dose 2). It found these heterologous schedules led to good vaccine effectiveness against PCR-confirmed SARS-CoV-2 infection (88% [95% CI: 83 to 92%]) from day 14 after dose 2 onwards, and against COVID-19 related hospitalisation and death (VE estimated 100%; no confidence interval estimable due to no COVID-19 related hospitalisations or death seen after dose 2).⁷⁴ Larger studies and longer term follow up are required to confirm the safety of this approach.

In the following special circumstances, an alternative brand (or an alternative platform i.e. mRNA versus non mRNA) may be recommended for the second dose:

- People with serious vaccine-attributable adverse events after dose 1 that warrant the use of an alternative vaccine brand for dose 2:
 - anaphylaxis to the first dose of a COVID-19 vaccine (note: anaphylaxis to a previous dose of an mRNA COVID-19 vaccine [Comirnaty or Spikevax] is a contraindication to further doses of either vaccine), OR
 - thrombosis with thrombocytopenia following the first dose of Vaxzevria, OR

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- Any other serious adverse event attributed to a previous dose of a COVID-19 vaccine (and without another cause identified) that:
 - has been reported to state adverse programs and/or the TGA, and
 - has been determined following review by, and/or on the opinion of, an experienced immunisation provider/medical specialist taking into account whether repeat vaccine doses would be associated with a risk of recurrence of the serious adverse event.*
- People with a precautionary condition for which the use of Comirnaty or Spikevax are recommended instead of Vaxzevria:
 - 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 any of the alternative brand is 4 to 12 weeks after the first dose, regardless of first dose brand. An interval longer than 12 weeks 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](#).

* Assessment of adverse events following immunisation requires detailed information on the event, a determination of the likelihood of a causal link with vaccination, as well as the severity of the condition. Serious adverse events are generally defined as those which require hospitalisation (e.g., thrombosis with thrombocytopenia following the first dose of Vaxzevria); are medically significant (e.g., immune thrombocytopenia purpura, myocarditis), are potentially life threatening (e.g., anaphylaxis) and/or result in persistent or significant disability (e.g., Guillain-Barre Syndrome). These reactions do not typically include expected local or systemic reactions known to occur within the first few days after vaccination. Attributing a serious adverse event to a previous dose of a COVID-19 vaccine may require discussion with the individual's GP, local immunisation service or relevant medical specialist.

Use of an additional COVID-19 vaccine dose as a replacement dose if the second dose was given less than 14 days after the first dose

A second dose of a COVID-19 vaccine administered <14 days after the first dose is considered an invalid dose. An additional COVID-19 vaccine dose should be administered as a replacement dose. The aim of this replacement dose is to attain a level of immune response that is comparable to that expected following completion of a two-dose primary course of a COVID-19 vaccine according to the recommended dosage and schedule.

The same COVID-19 vaccine brand should be used for the replacement dose to complete the primary vaccination course, unless there are special circumstances for indicating the use of an alternative vaccine. Refer to the [ATAGI clinical advice on use of a different COVID-19 vaccine as the second dose in special circumstances](#)).

The interval between the invalid second dose and the replacement dose is flexible, recommended at 4 to 12 weeks after the invalid second dose. Timing of the replacement dose warrants individual risk-benefit assessment, including consideration of risk of exposure to SARS-CoV-2. For example workers in healthcare, aged care, disability care, border and quarantine facilities may warrant vaccination with a replacement dose sooner. Other factors include local disease epidemiology, mandatory requirements for work (such as aged care or healthcare workers) and individual medical conditions associated with increased risk of severe COVID-19 (such as immunocompromise).

Noting that there are no direct clinical trial data on vaccines used in Australia regarding a second dose being administered at <14 days after the first dose, this replacement dose recommendation is based on first principles. It takes into consideration the small amount of preliminary data in trials where participants received a third dose of the vaccine albeit at different intervals, and the potential incremental benefits outweighing adverse effects with this replacement dose.

Third dose/booster dose vaccination

Additional or booster doses after completion of a two-dose primary course according to an acceptable schedule are not currently recommended.

Data on the real-world effectiveness and duration of protection from Comirnaty, Spikevax and Vaxzevria are emerging, 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. Moderna has released preliminary immunogenicity data indicating both a booster with the original Wuhan strain Spikevax vaccine and their booster formulation designed to target against the Beta variant of concern effectively increases neutralising antibody titres approximately six months following original vaccination.⁷⁵ The clinical significance of this is as yet unclear.

Contraindications

Contraindications to Vaxzevria 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 of Vaxzevria (and without another cause identified) that has been reported to state adverse programs and/or the TGA, and has been determined following review by, and/or on the opinion of, an experienced immunisation provider/medical specialist taking into account whether repeat vaccine doses would be associated with a risk of recurrence of the serious adverse event*

[#]Anaphylaxis to polysorbate 80, which is an excipient in Vaxzevria and is also included in many other vaccines, is rare.⁷⁶

Contraindications to Comirnaty or Spikevax are:

- anaphylaxis to a previous dose of an mRNA COVID-19 vaccine (Spikevax or Comirnaty) is a contraindication to further doses of either vaccine
- anaphylaxis to any component of the vaccine, including polyethylene glycol (PEG)[#]
- myocarditis and/or pericarditis attributed to a previous dose of either Comirnaty or Spikevax
- any other serious adverse event attributed to a previous dose of Comirnaty or Spikevax (and without another cause identified) that has been reported to state adverse programs and/or the TGA, and has been determined following review by, and/or on the opinion of, an experienced immunisation provider/medical specialist taking into account whether repeat vaccine doses would be associated with a risk of recurrence of the serious adverse event*

[#]Comirnaty and Spikevax contain polyethylene glycol (PEG), and it is possible that this component is implicated in anaphylaxis.^{77,78} However, anaphylaxis following PEG is reported to be extremely rare (37 case reports between 1977 and 2016).⁷⁷

* Assessment of adverse events following immunisation requires detailed information on the event, a determination of the likelihood of a causal link with vaccination, as well as the severity of the condition. Serious adverse events are generally defined as those which require hospitalisation (e.g., thrombosis with thrombocytopenia following the first dose of Vaxzevria); are medically significant (e.g., immune thrombocytopenia purpura, myocarditis), are potentially life threatening (e.g., anaphylaxis) and/or result in persistent or significant disability (e.g., Guillain-Barre Syndrome). These reactions do not typically include expected local or systemic reactions known to occur within the first few days after vaccination. Attributing a serious adverse event to a

previous dose of a COVID-19 vaccine may require discussion with the individual's GP, local immunisation service or relevant medical specialist.

Refer to [Adverse events section](#) for further information on anaphylaxis following COVID-19 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 and Spikevax, or polysorbate 80 in Vaxzevria)
- 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 alternative 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 Vaxzevria

Comirnaty or Spikevax are recommended instead of Vaxzevria 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 Vaxzevria, Comirnaty or Spikevax is recommended for the second dose. Refer to [Vaccine preference recommendations](#).

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** Vaxzevria:

- 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

People who develop **immune thrombocytopenia (ITP)** within 42 days after receiving Vaxzevria should consult a haematologist regarding whether to proceed with the second dose using the same or an alternative vaccine, and the timing of the second dose.

Precautionary conditions for Comirnaty and Spikevax

Vaccination with an mRNA COVID-19 vaccine should be **deferred** in people with active cardiac inflammation, or an alternative vaccine (e.g. Vaxzevria) considered in people aged ≥ 60 years. People who develop myocarditis and/or pericarditis attributed to a dose of Comirnaty or Spikevax should defer further doses of mRNA COVID-19 vaccines and discuss this with their treating doctor. Additional advice on second dose vaccination in this context will be provided in the near future. .

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

- Recent (i.e., within the past 6 months) inflammatory cardiac illness e.g., myocarditis, pericarditis, endocarditis
- Acute rheumatic fever (i.e., with active myocardial inflammation) or acute rheumatic heart disease
- Acute decompensated heart failure.

Comirnaty and Spikevax continue to be recommended for people with a history of most chronic cardiovascular conditions and **can be given** to people in the following groups without any specific precautions:

- Prior myocarditis, pericarditis or endocarditis (i.e. > 6 months prior to vaccination)
- Coronary artery disease
- Myocardial infarction
- Stable heart failure
- Arrhythmias
- Prior history of rheumatic heart disease (RHD)
- Kawasaki disease
- Congenital heart disease
- Cardiomyopathy
- Cardiac transplant
- People with implantable cardiac devices.

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, Spikevax and Vaxzevria 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.⁷⁹

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

mRNA COVID-19 vaccines

Clinical trial data – Comirnaty

In clinical trials, mild to moderate local and systemic adverse events within 7 days following vaccination were very common. Injection site pain was reported after both doses and more frequently in adolescents and young adults than in those >55 years of age (refer to **Table 1**).⁸⁰ Severe pain was reported in <1% of individuals within the broad age range of ≥ 16 years in the initial phase II/III trial,⁸⁰ and in 1.5% of adolescents 12 to 15 years compared with 3.5 % in young adults 16 to 25 years in a subsequent phase III trial.⁴⁵ Injection site redness and swelling occurred in <10% of all participants. These local reactions generally resolved within 1 to 2 days.^{45,80}

In both adolescents and adults, systemic adverse events were more common following the second dose of Comirnaty than the first dose (refer to **Table 1**)^{45,80} and generally resolved within a few days of vaccination.⁸¹ Adverse events were generally less frequent in adults aged >55 years than in those aged 16–55 years.⁸¹ Fatigue and headache were the most frequently reported systemic adverse events among adolescents 12-15 years and young adults 16 to 25 years (Table 1).⁴⁵

In the phase II/III trial of individuals ≥ 16 years, the median duration of follow-up for adverse events was 2 months after the second dose. Lymphadenopathy (swelling of the lymph nodes), though uncommon (<1%), was more common in vaccine recipients than in placebo recipients (64 cases [0.3%] versus 6 cases [<0.1%]⁸⁰) and is likely related to the expected immune response to the vaccine. The cases of lymphadenopathy (swelling of the lymph nodes) 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.⁸¹ However, this observed frequency was consistent with the expected background rate of Bell's palsy in the general population and thus may not have been caused by vaccination. There were no substantive differences in the frequency of adverse events overall observed in the clinical trial by sex, 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.⁸⁰

In the phase III study of individuals 12 to 25 years of age, safety data up to one month following dose 2 was reported. Lymphadenopathy was reported in 0.8% of vaccine recipients and 0.2% of placebo recipients⁴⁵ aged 12 to 15 years of age. There was no difference in reactogenicity by baseline SARS-CoV-2 status.⁴⁵

Table 1: Frequency of select common adverse events reported within 7 days following each dose of Comirnaty in phase II/III trial^{45,81}

	12 – 15 years of age		16 to 25 years of age		16–55 years of age		>55 years of age	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2
Injection site pain	86%	79%	83%	78%	83%	78%	71%	66%
Fever	10%	20%	7%	17%	4%	16%	1%	11%
Fatigue	60%	66%	60%	66%	47%	59%	23%	51%
Headache	55%	65%	54%	61%	42%	52%	25%	39%
Chills	28%	42%	25%	40%	14%	35%	6%	23%
Muscle pain	24%	32%	27%	41%	21%	37%	14%	28%
Joint pain	10%	16%	13%	22%	11%	22%	9%	19%

	12 – 15 years of age		16 to 25 years of age		16–55 years of age		>55 years of age	
Required paracetamol	37%	51%	32%	46%	28%	45%	20%	38%

Clinical trial data - Spikevax

In the phase III trial of Spikevax that included participants aged ≥ 18 years, adverse events in the first 7 days following vaccination were very common but generally mild to moderate and well tolerated.⁶⁷ Preliminary data on the safety of Spikevax in adolescents aged 12-17 years are available from the ongoing phase II/III trial. The adverse reaction profile was similar to that of participants aged ≥ 18 years.⁴⁶

Adverse reactions at the injection site were very common after both the first and second dose of the vaccine. Injection site pain was the most frequently reported and was more common in people aged 12 to 17 years and those aged 16 to 64 years than in people aged ≥ 65 years (**Table 2**).⁴⁶ Axillary lymphadenopathy within 7 days from vaccination occurred in 10% and 14% of vaccine recipients aged ≥ 18 years after the first and second doses, respectively. It was more common in adolescents aged 12-17 years, occurring in 23% and 21% of recipients, respectively. The mean duration of lymphadenopathy was 3 days after both dose 1 and dose 2.

Delayed-onset injection site reactions that started after the first 7 days, including pain, redness or swelling, occurred in 0.8% after the first dose, and 0.2% after the second dose in adults. These reactions resolved after a mean 4-5 days.⁶⁷

Systemic adverse reactions were more frequent after the second (79%) than the first dose (55%) of Spikevax, and more common in participants aged 18-64 years compared with those aged 65 years or over. The most frequently reported were fatigue, headache and myalgia, which were reported at similar rates among adolescents 12 to 17 years (**Table 2**).

Hypersensitivity-related adverse reactions were more common in adult vaccine recipients compared with placebo recipients (1.5% versus 1.1%). However, there were no anaphylactic or severe hypersensitivity reactions in close temporal relationship with the vaccine dose.

There was a small imbalance in the number of participants with Bell's palsy (3 in the vaccine arm on day 22, 28 and 32 versus 1 in the placebo arm on day 17). All cases were unrelated to the administration of either the vaccine or placebo. Two participants, both with a history of facial dermal filler cosmetic injection, experienced facial swelling within two days from vaccine receipt.

There were no reported differences in the occurrence of adverse reactions in this clinical trial by race, ethnicity, medical comorbidities, or prior SARS-CoV-2 infection.⁵²

Table 2: Frequency of select common adverse events reported within 7 days following each dose of Spikevax in phase III trial^{46,67}

	12 – 17 years of age		18-64 years of age		≥ 65 years of age	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2
Injection site pain	93%	92%	87%	90%	74%	83%
Lymph node swelling at the axilla	23%	21%	12%	16%	6%	9%
Fever	2.5%	12%	0.9%	17%	0.3%	10%
Fatigue	48%	68%	38%	68%	33%	58%

Headache	45%	70%	35%	63%	25%	46%
Chills	18%	43%	9%	49%	5%	31%
Myalgia	27%	47%	24%	62%	20%	47%
Arthralgia	15%	29%	17%	46%	16%	35%
Nausea/vomiting	10%	18%	9%	21%	5%	12%

Adverse events of mRNA COVID-19 vaccines reported in post-licensure use

Post-licensure surveillance is undertaken for all vaccines to identify signals for rare, population-specific events.

Reactogenicity

Injection site pain and systemic events such as fatigue, headache and muscle ache following Comirnaty have been commonly reported in routine use at similar or lower rates than reported in clinical trials. A small proportion of individuals have reported missing work, study or routine term duties for a short period following vaccination with Comirnaty (6.7% following dose 1 and 21.2% following dose 2⁸²).

Anaphylaxis

The observed rate of anaphylaxis after Comirnaty administration in the United States in early 2021 was 4.7 cases per million doses administered, and the rate of anaphylaxis after Spikevax administration in the same period was 2.5 cases per million doses, based on passive reporting to the Vaccine Adverse Event Report System (VAERS).⁸³ Most (89%) of cases after the administration of both mRNA vaccines occurred within 30 minutes of vaccination.⁸³

Myocarditis and pericarditis

Myocarditis and pericarditis (and combined myopericarditis) have been reported following vaccination with Comirnaty and Spikevax vaccine overseas^{84,85 86-88} and following Comirnaty in Australia.⁸⁹ The rate appears to be higher following the second dose and in younger males (aged < 30 years), including adolescents.⁹⁰ In an analysis of validated cases reported to the US Vaccine Adverse Events Reporting System (VAERS), 72% of cases occurring after dose 1, and 82% of cases occurring after dose 2 were in males.⁹¹ The highest reporting rates of myopericarditis were following the second dose of Comirnaty in males aged 16-17 (71.5 cases per million doses administered), followed by males aged 12-15 (42.6 per million). In males aged 18-24 the reporting rate was 37.1 per million following the second dose of Comirnaty and 37.7 per million following the second dose of Spikevax.

Most patients experienced symptoms within a week of vaccination (median 2-3 days).⁹¹ Most reported cases have required hospitalisation⁹⁰ but have responded well to treatment with a mild clinical course; longer-term follow-up of these cases is ongoing. Individuals who develop myocarditis or pericarditis after the first dose should defer the second dose and be referred to a cardiologist for further assessment and management.

For people with underlying cardiac conditions, refer to **Precautionary conditions for Comirnaty and Spikevax** above.

Any difference between the rate of myocarditis/pericarditis after Comirnaty compared with Spikevax that is statistically or clinically significant is still being examined. Vaxzevria has not been associated with an increased risk of myocarditis/pericarditis.

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

Vaxzevria

Clinical trial data

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In the phase II/III clinical trials of Vaxzevria, adverse events reported within 7 days following vaccination were very common (86%) but the majority were mild or moderate.⁶⁸ 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 events⁶⁸ (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 severe solicited adverse events, than younger adults.^{68,80} 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 Vaxzevria. Most of the unsolicited adverse events were mild to moderate in severity.⁶⁸

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, subsequently reclassified as idiopathic short segment spinal cord demyelination.⁶⁹ 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.

Table 3: Frequency of select common adverse events reported within 7 days following at least one dose of Vaxzevria in phase II/III trial in people aged >18 years⁹²

	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%

Adverse events identified in post-licensure use

Post-licensure surveillance is undertaken for all vaccines to identify signals for rare, population-specific events.

Reactogenicity

Systemic events such as fatigue, headache and muscle ache, along with injection site pain, have been commonly reported following Vaxzevria in routine use at similar rates to those reported in clinical trials. A small proportion of individuals have reported missing work, study or routine term duties for a short period following vaccination with Vaxzevria (17.6% following dose 1 and 5.3% following dose 2).⁸² Updated data, based on surveys of millions of Australian vaccine recipients, is regularly published by AusVaxSafety at <https://www.ausvaxsafety.org.au/safety-data/covid-19-vaccines>.

Anaphylaxis

Anaphylaxis to Vaxzevria is rare. The rate of reported anaphylaxis after Vaxzevria in Australia appears to be consistent with what is expected for other vaccines and has been reported to be less than 10 per million doses.⁹³ Anaphylaxis after Vaxzevria has been reported rarely. Refer to **Contraindications** for further information.

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Thrombosis with thrombocytopenia syndrome

Thrombosis with thrombocytopenia syndrome (TTS) a rare newly identified condition resulting in thrombosis with thrombocytopenia. The risk is higher in younger individuals with around 2.4 cases per 100 000 individuals less than 60 years of age,⁹⁴⁻⁹⁹ compared with 1.8 per 100 000 individuals \geq 60 years in Australia, following dose 1.¹⁰⁰ The risk in specific age-groups is provided in the guide, [COVID-19 vaccination – Weighing up the potential benefits against risk of harm from AstraZeneca -Vaxzevria](#). The risk is about 10 times lower following dose 2 and is estimated to be 1.8 per million second doses, based on data from the UK.¹⁰¹ The severity of TTS appears to be higher in younger women.¹⁰⁰

The onset of symptoms is usually around 4 to 42 days post vaccination. Thrombosis can occur at common sites (such as deep vein thrombosis or pulmonary embolism) or in more unusual locations (such as cerebral venous sinus thrombosis (CVST), thrombosis in the splanchnic (mesenteric, portal, splanchnic) circulations and arterial thrombosis). Early investigation (including full blood count and D-dimer) and clinical review, including in an emergency department as required, are important. Clinical outcomes have generally been better with early presentation and recognition of the symptoms and appropriate treatment. Symptoms and management are described in detail in the guide, [COVID-19 vaccination – Primary care approach to thrombosis with thrombocytopenia syndrome after COVID-19 AstraZeneca vaccine](#).

For people who developed TTS after the first dose of Vaxzevria, **an alternative vaccine, either Comirnaty or Spikevax, should be used for the second dose** if there are no contraindications to Comirnaty or Spikevax.

For people with underlying thrombotic conditions, refer to **Contraindications to Vaxzevria** and **Precautionary conditions for AstraZeneca** above.

Immune (idiopathic) thrombocytopenia

Immune (idiopathic) thrombocytopenia (ITP) has been reported following Vaxzevria. In Australia, one case has been causally linked to vaccination.⁸⁹ One study from Scotland suggested an association between Vaxzevria and ITP with an estimated risk of 1.13 cases per 100 000 doses.¹⁰²

Individuals should seek medical attention if they experience unusual bruising, petechiae or bleeding. People who develop ITP within 42 days after receiving Vaxzevria should consult a haematologist regarding whether to proceed with the second dose using the same or an alternative vaccine, and the timing of the second dose.¹⁰¹

Reported events under investigation

Post-marketing surveillance is undertaken for all vaccines to identify signals for rare, population-specific events. Medical events may be reported following vaccination but may not be causally related to the vaccine. Investigation and causality assessment is required to assess these reports. The conditions described below have been reported following vaccination but a causal relationship with the vaccine has not been established.

Capillary leak syndrome

Capillary leak syndrome has been reported rarely following AstraZeneca vaccine in the UK and Europe,¹⁰¹ including in people with a history of capillary leak syndrome. One case has been reported in Australia but a causal link with the vaccine could not be established.¹⁰³ Capillary leak syndrome is a rare but severe relapsing-remitting condition where capillary fluid leaks into surrounding tissues.

Vaxzevria is contraindicated in people with a past history of capillary leak syndrome.

Guillain Barre Syndrome

Cases of Guillain Barre Syndrome (GBS) have been reported following COVID-19 vaccine in Australia and overseas.^{104,105 98,106,107} . A causal relationship with vaccination has not yet been established.

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 to 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-2.⁸⁰ 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 to 99.7]).⁸⁰

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 to 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 to 99.9]) and in adults with at least one medical comorbidity or obesity (VE 95.3% [95% CI: 87.7 to 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 to 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.⁴⁵

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 to 98.8] versus 94.7% [95% CI: 85.9 to 98.6]⁸⁰).

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

Spikevax

There is an ongoing phase III trial of Spikevax that enrolled >30,000 individuals aged ≥18 years (mean age 51.4 years [range: 18 to 95 years]);¹⁰⁸ about a quarter were aged ≥65 years, and about one-fifth of adults aged 18–64 years had a medical condition with increased risk of severe COVID-19). Preliminary results of this trial to two months after the second dose, reported a vaccine efficacy of 94.1% (95% CI: 89.3 to 96.8%) in preventing symptomatic laboratory-confirmed COVID-19 in participants not previously been infected with SARS-CoV-2. All 30 severe COVID-19 cases occurred in the placebo group, resulting in a vaccine efficacy estimate of 100% (95% confidence interval unable to be estimated). One death due to SARS-CoV-2 infection occurred in the placebo group.

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Short-term vaccine efficacy against symptomatic laboratory-confirmed COVID-19, from 14 days after the first dose and prior to the second dose, was 92.1% (95% CI: 68.8 to 99.1%).

The duration of protection is yet to be determined. The phase I trial indicates that vaccine-induced antibodies lasted for at least 6 months after dose 2.¹⁰⁹

People aged ≥ 65 years

In the ongoing phase III trial, 24.8% of participants were aged 65 years or over.⁶⁷ In this subgroup, vaccine efficacy against symptomatic disease was estimated to be 86.4% (95% CI: 61.4 to 95.2%), as compared with 95.6% (95% CI: 90.6 to 97.9%) among patients aged 18-64 years.

Children aged <18 years

A phase II/III trial evaluating the safety and efficacy of Spikevax in adolescents aged 12 to 17 years old is currently ongoing,¹¹⁰ as is a phase II/III trial evaluating the vaccine efficacy among children aged 6 months to 11 years of age.¹¹¹

Regarding adolescents aged 12 to 17 years, interim results of the phase II/III trial⁴⁶ that recruited 3732 participants have been published. The efficacy analysis demonstrated vaccine efficacy of 92.7% (95% CI: 67.8 to 99.2%) in preventing symptomatic PCR-confirmed SARS-CoV-2 infection from day 14 after dose 1 onwards. No cases of COVID-19 with an onset of 14 days after dose 2 were reported in the vaccine group, and four cases occurred in the placebo group. Furthermore, the antibody response to Spikevax (measured by pseudotyped virus neutralisation assay) in this age group is similar to those aged 18 to 25 years, both in terms of antibody titre and in seroresponse rate.

People with specified medical conditions

The ongoing phase III trial enrolled individuals with stable medical conditions that put them at increased risk of severe COVID-19. An analysis of this subgroup demonstrated vaccine efficacy similar to the efficacy estimated in those without risk factors for severe disease (90.9% [95% CI: 74.7 to 96.7%] vs. 95.1% [95% CI: 89.6 to 97.7%]).

Vaxzevria

Phase II/III trials of Vaxzevria 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 to 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.⁶⁹ 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 Vaxzevria versus 101 among 5,829 who received the control vaccine).⁶⁹

Vaxzevria was demonstrated to have lower neutralisation activity against the Alpha variant than against a canonical (Victoria) lineage, however vaccine efficacy against the Alpha variant was preserved with VE 70.4% (95% CI 43.6 to 84.5), compared with VE 81.5% (95% CI 67.9 to 89.4) for the Victoria lineage.¹¹² 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 Vaxzevria compared with wild type. After 1 dose Vaxzevria, 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 to 71.73) in preventing symptomatic laboratory-confirmed COVID-19 in people aged ≥18 years who received two standard doses.¹¹³ This was based on 271 cases (74 among 7,201 who received Vaxzevria versus 197 among 7,178 who received the control vaccine).⁶⁹ Efficacy from day 22 after the first dose until up to 12 weeks post vaccination was 76.0% (59.3 to 85.9).⁶⁹

In clinical trials, the interval between the two doses of Vaxzevria 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 to 69.7), based on 218 cases.¹¹⁴ 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 to 69.9), 59.9% (95% CI 32.0 to 76.4), 63.7% (95% CI 28.0 to 81.7) and 81.3% (95% CI 60.3 to 91.2) respectively.¹¹⁵

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 Vaxzevria who were hospitalised, and 4 out of 4,455 in the control group.¹¹⁶

People aged ≥65 years

Fewer than 6% of participants included in the interim analysis were aged ≥65 years.⁶⁹ In this cohort there were only four and eight cases of COVID-19 in recipients of Vaxzevria 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.¹¹³ These small numbers preclude the assessment of the efficacy of Vaxzevria 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 Vaxzevria 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.^{117,118}

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 to 73.9).¹¹⁴

Vaccine effectiveness in post-licensure studies

The effectiveness of COVID-19 vaccines has been studied in vaccination programs in countries where they have been used since late 2020. Over this time, the distribution of variant strains in the location and during the period of study is a key consideration when interpreting results of studies on vaccine effectiveness.

Some key findings from selected major studies on effectiveness of the 3 vaccines currently available in Australia are summarised below. Results of other studies are generally consistent with these findings.

Vaccine effectiveness in the period prior to the dominance of the Delta variant

Comirnaty: In a study in Israel that included over 1.1 million people aged ≥16 years, conducted from 20/12/2020 to 1/2/2021 when the Alpha variant was predominant in Israel, the effectiveness of Comirnaty from 7 days after 2 doses was 87% (95% CI: 55 to 100) against COVID-19 hospitalisations and 92% (95% CI: 75 to 100) against severe disease.³⁷ Data on the duration of protection from the vaccine are not available yet.

Spikevax: In a US Mayo Clinic Health System study that included over 16,000 people aged ≥ 18 years and was conducted from 15/2/2020 to 20/4/2021, Spikevax was found to be 92% (95% CI: 82 to 97%) effective against PCR-positive SARS-CoV-2 infection from day 14 after dose 2.¹¹⁹ From seven days after the second dose, this vaccine was 86% (95% CI: 72 to 94%) effective against hospitalisation, and 100% (95% CI: 43 to 100%) against ICU admission.

Vaxzevria: In a population-based cohort study with more than 300,000 people aged ≥16 years in the UK, conducted from 1/12/2020 to 8/5/2021 when Alpha was predominant in the UK, effectiveness against PCR-ATAGI Clinical Guidance on COVID-19 Vaccine in Australia_v7.3

positive SARS-CoV-2 infection 21 days after 1 dose was 64% (95% CI: 55–70).⁶² Effectiveness against symptomatic infection was marginally higher than against asymptomatic infection. In a prospective population cohort study with 5.4 million people aged ≥18 years in Scotland, conducted from 8/12/2020 to 15/2/2021 when Alpha was predominant in the UK, effectiveness in the 28 to 34 days after 1 dose against COVID-19 hospitalisations was 94% (95%CI: 73 to 99).¹²⁰

Vaccine effectiveness against the Delta variant

For the Delta variant, studies in the UK, Qatar, USA and Canada have shown that the vaccine effectiveness of Comirnaty, Spikevax and Vaxzevria against symptomatic SARS-COV-2 infection with the Delta variant was lower compared with that due to the Alpha variant, but is maintained against hospitalisation.^{9,121} This lower effectiveness against symptomatic COVID-19 is more marked for dose 1.

Comirnaty: A cohort study in Scotland, conducted from 1/4/2021 to 6/6/2021 with >19,000 sequenced cases (7723 (39.5%) Delta variant cases), showed effectiveness against PCR-positive SARS-CoV-2 infection (irrespective of symptoms at the time of testing) was 30% (95% CI: 17 to 41) ≥28 days after dose 1 and 79% (95% CI: 75 to 82) ≥14 days after dose 2. When assessed against symptomatic infection, effectiveness estimates were 33% (95% CI: 15 to 47) and 83% (95% CI: 78 to 87) respectively.⁷

A test-negative case–control study in the UK, conducted from 26/10/2020 to 16/5/2021 with >19,000 sequenced cases (>4000 Delta variant cases), showed effectiveness against PCR-positive symptomatic disease after 2 doses was 88.0% (95% CI: 85.3 to 90.1) for Delta variant cases compared to 93.7% (95% CI: 91.6 to 95.3) for Alpha variant cases.¹²² After 1 dose, it was 35.6% (95% CI: 22.7 to 46.4) and 47.5% (95% CI:41.6 to 52.8), respectively.

A UK Study, conducted from 12/4/2021 to 4/6/2021 with 14,019 symptomatic cases with Delta showed effectiveness against hospitalisation after 2 doses was 96% (95% CI: 86 to 99) for Delta variant cases compared to 95% (95% CI:78 to 99) for Alpha variant cases.⁹ After 1 dose, it was 94% (95% CI: 46 to 99) and 83% (95% CI: 62 to 93), respectively.

Studies in the UK, USA, Qatar and Canada reinforce these results. Effectiveness against PCR-confirmed infection ranges from 79-93%, symptomatic disease ranges from 83-93%, severe disease ranges from 75-97% after dose 2.¹²¹

Spikevax: A test-negative case–control study in Canada was conducted from 14/12/2020 and 30/05/2021 (with Delta gaining prominence in May 2021). It studied >400,000 symptomatic cases and showed that effectiveness against PCR-positive symptomatic disease ≥21 days after dose 1 was 70% (95% CI: 52 to 81) for Delta variant cases compared to 84% (95% CI: 80 to 86) for Alpha variant cases. Effectiveness against hospitalisation or death ≥21 days after dose 1 was 95% (95% CI: 67 to 99) for Delta variant cases compared to 80% (95% CI:74 to 85) for Alpha variant cases.¹²¹

Studies in the USA and Qatar reinforce these results. Effectiveness against PCR-confirmed infection ranges from 76-86%, severe disease ranges from 81-100% after dose 2.^{123,124}

Vaxzevria: A cohort study in Scotland, conducted from 1/4/2021 to 6/6/2021 with >19,000 sequenced cases (7723 (39.5%) Delta cases), showed the effectiveness against PCR-positive SARS-CoV-2 infection irrespective of symptoms at the swab test was 18% (95% CI: 9 to 25) ≥28 days after dose 1 and 60% (95% CI: 53 to 66) ≥14 days after dose 2. When assessed against symptomatic infection, effectiveness estimates were 33% (95% CI: 23 to 41) and 61% (95% CI: 51 to 70) respectively.⁷

A test-negative case–control study in the UK, conducted from 26/10/2020 to 16/5/2021 with >19,000 sequenced cases (>4,000 Delta cases), showed that effectiveness against PCR-positive symptomatic disease after 2 doses was 67.0% (95% CI: 61.3 to 71.8) for Delta variant cases compared to 74.5% (95% CI: 68.4 to 79.4) for Alpha variant cases.¹²² After 1 dose, it was 30.0 (95% CI: 24.3 to 35.3) and 48.7 (95% CI: 45.2 to 51.9), respectively.

Another UK Study, conducted from 12/4/2021 to 4/6/2021 with 14,019 symptomatic cases with Delta showed that effectiveness against hospitalisation after 2 doses was 92% (95% CI:75 to 97) for Delta variant cases

compared to 86% (95% CI: 53 to 96) for Alpha variant cases.⁹ After 1 dose, it was 71% (95% CI 51 to 83) and 76% (95% CI 61 to 85), respectively

Studies in the UK, India and Canada reinforce these results. Effectiveness against PCR-confirmed infection ranges from 60-67%, against symptomatic disease ranges from 61-71% and against severe disease ranges from 77-92% after dose 2.^{125,126}

Regional differences in the vaccine roll out may have confounded the estimates of vaccine effectiveness (e.g., different vaccine intervals used over time and/or across different countries the world). Emerging data is constantly being monitored to inform future recommendations.

Vaccine effectiveness against SARS-CoV-2 transmission

Data from studies in the UK shows that both Comirnaty and Vaxzevria 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 to 57%) for Vaxzevria and 49% (95%CI:41 to 56%) for Comirnaty.¹²⁷ 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.¹²⁸

Preliminary data from Finland also suggest that there is an indirect effect of both Comirnaty and Spikevax on close contacts of vaccine recipients.¹²⁹ Among healthcare workers, vaccine effectiveness against PCR-confirmed infection in their unvaccinated household contacts was 43% (95% CI: 22 to 58%) 10 weeks after the first vaccine dose. The Alpha variant was the dominant strain in Finland at the time of this study.

The National Institute of Allergy and Infectious Diseases (NIAID) in the USA is currently undertaking a clinical trial evaluating the effect of Spikevax on transmission.¹³⁰

There are no published studies so far that assessed the effectiveness of COVID-19 vaccine in preventing onward transmission from breakthrough cases of the Delta variant strain.

Vaccine effectiveness in older adults

In a single-centre case–control study in Bristol in the UK,¹³¹ vaccine effectiveness against hospitalisation among adults aged ≥80 years from 14 days after dose 1 was 71% (95% CI: 36–95) for Vaxzevria and 79% (95% CI: 47 to 93) for Comirnaty.¹³¹

Other UK studies have reported the effectiveness of a first dose of *either* Comirnaty or Vaxzevria at 76% (95% CI: 68 to 82) against overall SARS-CoV-2 infection in people aged ≥75 years and 81% (95% CI: 65 to 90) against hospitalisation in people aged ≥80 years.^{62,120,132} Additionally, among long term care facility residents aged ≥65 years, vaccine effectiveness against PCR-confirmed SARS-CoV-2 infection, regardless of the presence of symptoms, was estimated to be 62% (95% CI: 23 to 81%), with no difference between Vaxzevria and Comirnaty.¹³²

A test-negative study in Ontario, Canada with more than 300,000 participants was conducted from 14/12/2020 to 19/4/2021 when Alpha was predominant in Ontario. It found effectiveness for the mRNA vaccines (Comirnaty and Spikevax) against PCR-confirmed symptomatic disease to be 40% (95% CI: 29 to 49) ≥14 days after Dose 1 and 94% (95% CI: 87 to 97) ≥7 days after Dose 2 for adults aged ≥70 years.¹³³

VE data available for two doses of Vaxzevria are still limited because of the 12-week interval between the two doses used in vaccination programs.⁶²

Transporting, storing and handling vaccines

Comirnaty

Comirnaty vaccine vials have a shelf life of 9 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 vial puncture and dilution, the vials and the prepared syringes with the vaccine dose 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](#).

Spikevax

The shelf life of Spikevax is 7 months frozen at -25°C to -15°C and in its original carton, protected from light. Spikevax vials cannot be stored on dry ice or at temperatures below -50°C. Frozen vials can be thawed at 2°C to 8°C in a refrigerator in 2.5 hours, or at room temperature (15°C to 25°C) in one hour. Thawed vials should not be re-frozen. Refer to the product information for more detailed guidance regarding thawing of vials.

Spikevax is a white to off-white liquid, and is available in multi-dose vials of 5 mL containing 10 doses of 0.5 mL. Spikevax does not contain a preservative. Dilution is not required. The vial should be swirled gently after thawing and before each withdrawal, but should not be shaken. Providers should confirm that the syringe containing the dose is not cold to touch prior to administration to minimize discomfort from receiving an injection of a chilled product.

Once thawed, the shelf life of an unpunctured vial is 30 days in a refrigerator (2°C to 8°C) protected from light, of which 12 hours can be used for transportation; and 24 hours in storage at 8°C to 25°C. Thawed vials can be handled in room light conditions.

Chemical and physical stability has been shown with storage of Spikevax for 19 hours at 2°C to 25°C after initial puncture. However, since this vaccine contains no antimicrobial preservatives, ATAGI recommends that opened vials should preferably be stored at 2°C to 8°C, and the cumulative storage time of opened vials at 2°C to 25°C should not exceed 6 hours. Additionally, as much as possible, pre-drawn doses kept at room temperature should be used within an hour to minimise any remote potential risk of infection.

Vaxzevria

Vaxzevria does not need to be stored in a freezer and hence does not need to be thawed. It is stored in a refrigerator at 2°C to 8°C. The shelf life of Vaxzevria is 6 months at 2°C to 8°C.

In Australia, Vaxzevria is supplied in multi-dose vials, with either 8 doses in 4 mL or 10 doses in 5 mL. Unopened multi-dose vials are to be stored at 2°C to 8°C and in the outer carton, to protect from light. Dilution is not required.

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 Vaxzevria 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.¹³⁴

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 Comirnaty, Spikevax and Vaxzevria 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.

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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 Spikevax, the median onset of systemic adverse events was 0-1 days following vaccination for the majority of participants (70.2%), and symptoms continued for about 3 days on average.⁶⁷ For Vaxzevria, 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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