Australian Government
Department of Health
Therapeutic Goods Administration

COVID-19 vaccine weekly safety report - 22-07-2021

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Vaccination against COVID-19 is the single most effective way to reduce severe illness and death from infection. Two COVID-19 vaccines (//www.tga.gov.au/covid-19-vaccines) are currently in use in Australia – AstraZeneca and Pfizer (Comirnaty). Like all medicines, the vaccines can have side effects (also known as adverse events). The overwhelming majority of these are mild and resolve within a few days. The Therapeutic Goods Administration (TGA) closely monitors suspected side effects. Importantly, adverse events reported to the TGA are often not caused by the vaccine itself. Learn more about causality (//www.tga.gov.au/about-daen-medicines#causality).

Learn about the TGA's COVID-19 vaccine safety monitoring and reporting (//www.tga.gov.au/covid-19-vaccine-safety-monitoring-and-reporting) activities or report a suspected side effect (//www.tga.gov.au/reporting-suspected-side-effects-associated-covid-19-vaccine).

Summary

- The most frequently reported suspected side effects associated with Comirnaty (Pfizer) and AstraZeneca COVID-19 vaccines continue to be events that were seen in the clinical trials, and are commonly experienced with many vaccines.
- Over the last week, four additional cases of blood clots with low blood platelets have been assessed as thrombosis with thrombocytopenia syndrome (TTS) likely to be linked to the AstraZeneca vaccine. When assessed using the UK case definition, one was confirmed and three were deemed probable TTS. This brings the total number of cases of TTS to 87 from 6.1 million doses of the AstraZeneca vaccine administered to date.
- Sadly two people with confirmed TTS following the first dose of the AstraZeneca vaccine died in the last week. One was a 44-year-old man from Tasmania and the other was a 48-year-old woman from Victoria. We extend our sincere condolences to their families and loved ones.
- In particular, we continue to closely monitor reports of immune thrombocytopenia (ITP) and Guillain-Barre Syndrome (GBS) following vaccination with the AstraZeneca vaccine, and myocarditis and pericarditis with the Pfizer (Comirnaty) vaccine.

Reported side effects for COVID-19 vaccines

Gathering reports of adverse events following immunisation (AEFI) is just the first step in determining whether the effect is related to the vaccine and whether a significant safety issue is involved. Learn more about how the TGA identifies and responds to safety issues (//www.tga.gov.au/tga-safety-monitoring-medicines#steps).

In the week of 12-18 July 2021 we received 1,177 AEFI reports for COVID-19 vaccines.

Large scale vaccination means that coincidentally some people will experience a new illness or die shortly after vaccination. The TGA reviews all deaths reported in people who have received the vaccination. We also monitor signals that may relate to vaccine safety to distinguish between coincidental events and possible side effects of the vaccine. Part of our analysis includes comparing natural expected death rates with observed death rates following immunisation. So far, the observed number of deaths reported after vaccination remains less than the expected number of deaths that would occur naturally, or from other causes, for that proportion of the population.

Since the beginning of the vaccine rollout to 18 July 2021, over 10.1 million doses of COVID-19 vaccines have been given. The TGA has received and reviewed 399 reports of deaths in people who have recently been vaccinated and found six that were linked to immunisation. These deaths were all related to the first dose of the AstraZeneca vaccine – five were TTS cases and one was a case of immune thrombocytopenia (ITP).

Total adverse event reports to 18 July 2021

4.1	41,406	10,125,533
Reporting rate per 1000 doses	Total AEFI reports received	Total doses administered
27,451	13,672	291

Total reports for AZ vaccine	Total reports for Comirnaty	Total reports for brand not specified

Reporting rates per 1000 doses by jurisdiction

Australian Capital Territory	3.4	New South Wales	2.9
Northern Territory	3.6	Queensland	3.8
South Australia	3.7	Tasmania	6.2
Victoria	5.5	Western Australia	3.7

Most commonly reported vaccine side effects

The most common adverse effects following immunisation reported to the TGA are predictable and have been observed with many other vaccines. They include headache, muscle pain, fever, chills and injection site reactions.

The most common reactions reported for the AstraZeneca COVID-19 vaccine in the week of 12-18 July 2021 were headache, fever, muscle pain, fatigue and chills.

The most common reactions reported for the Pfizer (Comirnaty) COVID-19 vaccine in the week of 12-18 July 2021 were headache, muscle pain, fatigue, dizziness and nausea.

Interpreting information on vaccine adverse event reports

We are aware that false claims are circulating based on misinterpretation of adverse event information published by the TGA and medicine regulators overseas. To improve transparency, the TGA makes adverse event reports publicly available 90 days after they are received in the Database of Adverse Event Notifications (DAEN (//www.tga.gov.au/database-adverse-event-notifications-daen)). When interpreting this information, it is important to understand that many of these events may not be caused by the vaccine.

The TGA encourages reporting of adverse events even if people are uncertain or only suspicious that it is related to a vaccine or medicine. This supports our scientists and health professionals to use the data to look for new safety signals. Reporting of adverse events, such as the death of anyone who has received a vaccine, is mandatory for health professionals in some states. It is therefore important to remember that the number of adverse events and deaths is not an indicator of the safety of the vaccines. Detailed investigation and expert review of individual case reports and the data are required to assess whether there is a link between an event and the vaccine.

It is important when looking for information about COVID-19 vaccines to consider whether the source of the information is credible. Useful websites such as 'COVID vaccines – is it true? (https://www.health.gov.au/initiatives-and-programs/covid-19-vaccines/is-it-true)' can address false claims and misleading rumours. Other reliable resources are listed at the end of this report.

Latest immunisation recommendations

COVID-19 outbreak

In light of a significant COVID-19 outbreak involving the Delta variant, the Australian Technical Advisory Group on Immunisation (ATAGI) continues to recommend that Pfizer's Comirnaty vaccine is preferred over the AstraZeneca vaccine for those aged 16–60 years old (https://www.health.gov.au/news/atagi-statement-on-use-of-covid-19-vaccines-in-an-outbreak-setting). ATAGI reinforces that the benefits of the AstraZeneca vaccine strongly outweigh the risks for people aged 60 and over and vaccination is very important in this group, particularly given the current outbreak.

With the current COVID-19 outbreaks, ATAGI has recommended that younger Australians who may not be able to get vaccinated immediately with Comirnaty assess whether to get the AstraZeneca vaccine. This should consider the protective benefits of vaccination to themselves and their contacts, who may be more vulnerable to serious disease or death from COVID-19, against the rare risk of a serious vaccine side effect.

Where there is a higher risk of contracting COVID-19, ATAGI also recommends getting the second AstraZeneca dose within 4–8 weeks after the first dose, rather than waiting 12 weeks, so full protection can be reached sooner.

Vaccination during pregnancy

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) and ATAGI recommend immunisation with the Comirnaty vaccine at all stages of pregnancy (https://www.health.gov.au/news/joint-statement-between-ranzcog-and-atagi-about-covid-19-vaccination-for-pregnant-women). This is due to the risk of complications from COVID disease for pregnant women and their unborn baby.

To date, no serious pregnancy-related safety concerns with the Comirnaty vaccine have been identified based on data from large numbers women overseas who have been vaccinated. After immunisation, protective antibodies have been found in cord blood and breastmilk. This suggests that vaccinating pregnant women may also offer protection to their infants after birth.

Women planning to become pregnant do not need to delay vaccination or avoid becoming pregnant after they have received the vaccination. Pregnant women are encouraged to discuss the timing of vaccination with their health professional. More details are given on the RANZCOG website (https://ranzcog.edu.au/statements-guidelines/covid-19-statement/covid-19-vaccination-information).

AstraZeneca COVID-19 vaccine

We continue to receive reports of side effects to the AstraZeneca vaccine. The reports are generally consistent with what is being observed internationally and most are expected side effects that we know occur after vaccination and resolve within a few days. To 18 July 2021, approximately 6.1 million doses of the AstraZeneca have been administered in Australia.

Thrombosis with thrombocytopenia syndrome (TTS)

> Early detection of TTS may help to prevent more serious complications developing. Guidance for health professionals is now available (https://www.health.gov.au/resources/publications/covid-19-vaccination-primary-care-approach-to-thrombosis-with-thrombocytopenia-syndrome-after-covid-19-astrazeneca-vaccine) which outlines when to suspect TTS, initial tests that can be performed in primary care and when to refer people for emergency care.
>
> People should seek immediate medical attention if they develop any of the following symptoms after vaccination:
>
> - severe or persistent headache, blurred vision, confusion or seizures
> - shortness of breath, chest pain, leg swelling or persistent abdominal pain
> - unusual skin bruising and/or pinpoint round spots beyond the site of vaccination.
>
> The most common time period for onset of TTS symptoms is 4–30 days after vaccination.

TTS is a rare event involving serious blood clots with a low blood platelet count. It is triggered by the immune system's response to the AstraZeneca vaccine and is different from other clotting conditions.

The latest rates of TTS in Australia were published in a statement from ATAGI on 15 July 2021. (https://www.health.gov.au/news/atagi-update-following-weekly-covid-19-meeting-14-july-2021)

While TTS is very rare, some people may have concerns that they can discuss with their doctor. 'Weighing up the potential benefits against risk of harm from COVID-19 Vaccine AstraZeneca' (https://www.health.gov.au/resources/publications/covid-19-vaccination-weighing-up-the-potential-benefits-against-risk-of-harm-from-covid-19-vaccine-astrazeneca) includes information to help people make informed decisions about vaccination.

Deaths related to TTS

Sadly, this week we were notified that two confirmed cases of TTS after the first dose of the AstraZeneca vaccine were fatal. One was in a 44-year-old man from Tasmania and the other was in a 48-year-old women from Victoria (this case was reported as probable TTS in last week's report (//www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-15-07-2021)). The TGA extends its sincerest condolences to their families and loved ones.

Since the beginning of the vaccine rollout in Australia, a total of five deaths from TTS have been reported out of 6.1 million doses of the AstraZeneca vaccine. All of them were related to a first dose of the vaccine.

TTS cases to date

Since last week's report, a further four reports of blood clots and low blood platelets have been assessed as confirmed or probable TTS likely to be linked to the AstraZeneca vaccine (Table 1).

Table 1: Newly confirmed and probable TTS cases for the week of 16-22 July 2021ǂ

New confirmed TTS	New probable TTS
One new case: • 44-year-old man from Tasmania	Three new cases: • 76 and 77-year-old men and a 79-year-old woman from NSW

‡As previously reported (//www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-10-06-2021), the TGA determines whether a report is likely to represent TTS by assessing cases against accepted criteria established by the UK's Medicines and Healthcare products Regulatory Agency.

One case reported last week as probable was reclassified to confirmed. This takes the total Australian reports assessed as TTS following the AstraZeneca vaccine to 87 cases (53 confirmed, 34 probable) from approximately 6.1 million vaccine doses.

We continue to investigate three probable TTS cases which appear to be related to the second dose. These cases, which have presented with less serious symptoms will be considered by an external panel of experts in the coming week to determine whether they are related to vaccination or not. UK data indicates that the risk of TTS after the second dose is extremely low (1.8 cases per million second doses (https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting)).

When assessed against the criteria used by the US Centers for Disease Control and Prevention (CDC) (https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-05-12/07-COVID-Shimabukuro-508.pdf), fewer than half of the cases reported to TGA are classified as Tier 1 cases which tend to have more serious outcomes. Tier 1 cases involve clots in an unusual location, such as the brain or abdomen (Table 2).

In Australia, severe cases of TTS appear to be more common in women in younger age groups. Nearly half of the TTS cases in women required treatment in intensive care. Cases meeting the criteria for Tier 1 were also twice as likely to occur in women compared to men. Four of the five deaths occurred in women aged 48 (two cases), 52 and 72-years-old. The other death was in a 44-year-old man, as reported above.

Table 2: Total confirmed and probable TTS cases to date by age and CDC classification

Age	Total cases	CDC classification†		
		Tier 1	Tier 2	Not classified
<30 years	1	-	1	-
30-39	1	1	-	-
40-49	6	6	-	-
50-59	22	10	7	5
60-69	19	6	6	7
70-79	26	7	7	12
80+	12	3	4	5
All ages	87 (41 men, 46 women)	33	25	29

† The US CDC classification is defined as:

- Tier 1 = clots in an unusual location (such as the brain or abdomen) and a low platelet count with or without antibodies that activate platelets (anti-PF4 antibodies)
- Tier 2 = clots found in common locations (such as the leg or lungs) and a low platelet count and anti-PF4 antibodies
- Not classified = case does not meet the criteria for Tier 1 or Tier 2 (for example clots in common locations with low platelet count but no evidence of anti-PF4 antibodies).

Cases have most often occurred about two weeks after vaccination, although the time to onset (or diagnosis) has ranged from one to 54 days (Table 3).

Table 3: Time to onset, treatment and outcomes for TTS cases*

Time to onset/ diagnosis (days)	Median (range)	12 (1-54)
Treated in ICU	At any point	26
	Currently	6
Outcome	Discharged	57
	In hospital	25

	Fatal	5

*Data is based on the most recent medical information available to the TGA

Immune thrombocytopenia (ITP)

The TGA is continuing to monitor reports of ITP. It is a type of thrombocytopenia or low platelet count. Thrombocytopenia has been included as a very rare adverse event in the Product Information for the AstraZeneca vaccine.

ITP occurs when the immune system mistakenly destroys platelets, which help blood to clot. It can occur after the immune system is activated, for example by a viral infection or vaccination, and has been reported with other vaccines. In many cases ITP is mild with up to a third of people having no symptoms at all, or only minor bruising. However, about 5% develop severe bleeding.

The risk of ITP associated with the AstraZeneca vaccine is still being investigated and characterised internationally (https://www.nature.com/articles/s41591-021-01419-1#:~:text=A%20prospective%20cohort%20analysis%20finds,is%20yet%20to%20be%20established.) and the TGA will report more information when it is known. ITP is difficult to diagnose because, unlike TTS, it does not have unique identifying features if it occurs after vaccination. There is no specific test that confirms ITP, so doctors rely on excluding other causes of thrombocytopenia. An alternative diagnosis often only becomes clear once more detailed patient information becomes available.

To 18 July 2021, the TGA has received 34 reports of suspected ITP following vaccination. These patients had an extremely low platelet count, and signs of thrombocytopenia including unusual bruising, a nosebleed and/or blood blisters in the mouth. These symptoms occurred in a timeframe that suggested they could be linked to vaccination and no other obvious cause was identified based on the information provided to TGA.

We encourage people to seek medical attention if they experience signs and symptoms that could suggest ITP, such as unusual skin bruising or clusters of small red or purple spots that do not lose their colour when pressed. Unusual bleeding is another sign, for example bleeding from the nose or mouth that is hard to stop, or blood in the urine or stools.

Guillain-Barre Syndrome (GBS)

The TGA has been closely monitoring reports of GBS since the beginning of the COVID-19 vaccine rollout as it has been associated with other types of immunisations such as influenza vaccines (https://academic.oup.com/cid/article/58/8/1149/355966).

A review by the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (EMA PRAC) on 5-8 July 2021 (https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-5-8-july-2021) was unable to either confirm or rule out a possible association with the vaccine. However, a warning has been added to the European Product Information (https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria-previously-covid-19-vaccine-astrazeneca#product-information-section) alerting health professionals to the signs and symptoms of GBS to ensure correct diagnosis and treatment.

GBS is a rare immune disorder in which the body's immune system attacks nerve cells. What causes it is not fully understood, but it often follows a viral infection or a bacterial type of gastroenteritis. GBS causes nerve inflammation and can result in pain, numbness, muscle weakness and difficulty walking. In many cases it resolves within months but can sometimes take up to two years.

To 18 July 2021, the TGA has received 61 reports of suspected GBS in people who have received the AstraZeneca vaccine. A possible link between GBS and the AstraZeneca vaccine remains under investigation and we are seeking expert advice on the results of a detailed evaluation.

We encourage people to seek medical attention if they experience symptoms that could suggest GBS. This includes weakness and paralysis in the hands or feet that can progress to the chest and face over a few days or weeks.

Up-to-date information about the expected side effects of the AstraZeneca COVID-19 vaccine can be found in the Consumer Medicine Information (https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/PICMI?OpenForm&t=cmi&q=COVID-19%20Vaccine%20AstraZeneca) (for consumers) and Product Information (https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/PICMI?OpenForm&t=PI&q=COVID-19%20Vaccine%20AstraZeneca&r=/) (for health professionals).

Comirnaty (Pfizer) vaccine

Reports of side effects to the Comirnaty vaccine continue to be reported to the TGA and are consistent with what has been observed in the clinical trials and by other medicine regulators overseas. To 18 July 2021, approximately four million doses of the Comirnaty vaccine have been administered in Australia.

Myocarditis and pericarditis

A causal relationship of myocarditis (inflammation of the heart) and pericarditis (inflammation of the membrane around the heart) to the vaccine has not yet been established but is suspected. The TGA has worked with Pfizer to add a warning statement about these adverse events to the Consumer Medicine and Product Information for Comirnaty. This is in response to rare cases following vaccination in Australia and internationally.

These rare effects on the heart typically occur within 14 days of vaccination, particularly after the second dose of Comirnaty and more often in younger men. While cases are usually transient and resolve following rest, some patients require treatment in hospital.

The TGA continues to monitor myocarditis and pericarditis by analysing adverse event reports, working with international regulators and reviewing the medical literature. To 18 July 2021, we have received 66 cases of suspected myocarditis and/or pericarditis. We are evaluating these cases in line with internationally accepted criteria to assess whether or not they are myocarditis and/or pericarditis that is likely to be related to vaccination.

We know that myocarditis and pericarditis are much more common with COVID-19 infection and damage to the heart is frequently severe after infection. The benefits of protection against COVID-19 far outweigh the risks from these rare and transient side effects.

We encourage people to seek medical attention if they experience symptoms that could suggest myocarditis or pericarditis such as of chest pain, shortness of breath and palpitations.

Up-to-date information about Pfizer Comirnaty can be found in the Consumer Medicine Information (https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/PICMI?OpenForm&t=cmi&q=Comirnaty) (for consumers) and Product Information (https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/PICMI?OpenForm&t=pi&q=comirnaty) (for health professionals).

Useful links

Top 3 COVID-19 vaccine questions – Rapid COVID-19 tests, herd immunity and what causes the virus to change (https://www.health.gov.au/news/top-3-covid-19-vaccine-questions-rapid-covid-19-tests-herd-immunity-and-what-causes-the-virus-to-change)

Top 3 COVID-19 vaccine questions – COVID-19 vaccines and variants, and recent ATAGI advice about AstraZeneca doses – 16 July 2021 (https://www.health.gov.au/news/top-3-covid-19-vaccine-questions-covid-19-vaccines-and-variants-and-recent-atagi-advice-about-astrazeneca-doses)

COVID-19 vaccines: Frequently asked questions – 15 July 2021 (https://www.ncirs.org.au/covid-19/covid-19-vaccines-frequently-asked-questions)

COVID vaccines – is it true? 14 July 2021 (https://www.health.gov.au/initiatives-and-programs/covid-19-vaccines/is-it-true)

Latest recommendations from ATAGI on the use of COVID-19 vaccines during an outbreak – 13 July 2021 (https://www.health.gov.au/news/atagi-statement-on-use-of-covid-19-vaccines-in-an-outbreak-setting)

TGA COVID-19 vaccines hub (//www.tga.gov.au/covid-19-vaccines)

Australian Government Department of Health COVID-19 vaccines (https://www.health.gov.au/initiatives-and-programs/covid-19-vaccines) hub

AusVaxSafety (http://www.ausvaxsafety.org.au) (active surveillance activities and information)

COVID-19 vaccine symptom checker (https://www.healthdirect.gov.au/symptom-checker/tool/basic-details)

Database of Adverse Event Notifications (DAEN) (https://apps.tga.gov.au/PROD/DAEN/daen-entry.aspx)

Advice on COVID-19 vaccination during pregnancy – 9 June 2021 (https://www.health.gov.au/news/joint-statement-between-ranzcog-and-atagi-about-covid-19-vaccination-for-pregnant-women)

Comirnaty vaccine – phase III clinical trial (https://www.nejm.org/doi/full/10.1056/NEJMoa2034577?query=featured_home)

AstraZeneca vaccine – phase III clinical trial (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext)

URL: https://www.tga.gov.au/node/938717 (https://www.tga.gov.au/node/938717)