Australian Government
Department of Health
Therapeutic Goods Administration

COVID-19 vaccine weekly safety report - 01-07-2021

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Previous reports

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 – the AstraZeneca vaccine and the Comirnaty (Pfizer) vaccine. Like all medicines, the vaccines 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 vaccines generally.
- Five 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 United Kingdom (UK) case definition, two were confirmed and three were deemed probable TTS. This brings the total number of cases of TTS to 69 out of 4.8 million doses to date.

Reported side effects for COVID-19 vaccines

Gathering reports of adverse events following immunisation (AEFI) is just the first step in determining whether or not 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 21-27 June 2021 we received 1459 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 and monitors 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 27 June 2021, there have been over 7.3 million doses of COVID-19 vaccines administered. The TGA has received and reviewed 335 reports of deaths in people who have recently been vaccinated and found that two were definitely linked to vaccination. These were both TTS cases related to the AstraZeneca vaccine.

Total adverse event reports to 27 June 2021

4.6 Reporting rate per 1000 doses	33,807 Total AEFI reports received	7,374,666 Total doses administered
23,235 Total reports for AZ vaccine	10,314 Total reports for Comirnaty	263 Total reports for brand not specified

Reporting rates per 1000 doses by jurisdiction

Australian Capital Territory	4.0	New South Wales	3.4
Northern Territory	4.4	Queensland	4.4
South Australia	4.1	Tasmania	6.6
Victoria	5.8	Western Australia	4.0

Most commonly reported vaccine side effects

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

The most common reactions reported for the AstraZeneca COVID-19 vaccine in the week of 21-27 June 2021 were headache, muscle pain, fever, nausea and fatigue.

The most common reactions reported for the Comirnaty (Pfizer) COVID-19 vaccine in the week of 21-27 June 2021 were headache, dizziness, nausea, muscle pain, and lethargy.

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.

Thrombosis with thrombocytopenia syndrome (TTS)

The TGA and other medicines regulators around the world continue to closely monitor and investigate TTS. This 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.

On the 17 June, the Australian Technical Advisory Group on Immunisation (ATAGI) recommended (https://www.health.gov.au/news/atagi-statement-on-revised-recommendations-on-the-use-of-covid-19-vaccine-astrazeneca-17-june-2021) that Pfizer's Comirnaty vaccine be preferred over the AstraZeneca vaccine for those aged 16–60 years old. However, while Comirnaty is preferred for under 60s, the AstraZeneca vaccine remains approved by the TGA (and most other major regulators) for those 18 and over.

People under 60 years of age who have already received their first AstraZeneca dose should complete the two-dose schedule as the risk of TTS after the second dose is extremely low (1.6 cases per million second doses based on UK data). Updated reporting rates of TTS in Australia were published in a statement from ATAGI on 25 June 2021 (https://www.health.gov.au/news/atagi-update-following-weekly-covid-19-meeting-23-june-2021).

People under the age of 60 years can also have the AstraZeneca vaccine if they choose. Information is available to help people weigh up the benefits and risks of receiving the AstraZeneca vaccine (https://www.health.gov.au/sites/default/files/documents/2021/06/covid-19-vaccination-weighing-up-the-potential-benefits-against-risk-of-harm-from-covid-19-vaccine-astrazeneca_0.pdf). While TTS is very rare, some people may have concerns that they can discuss with their doctor. This is essential to allow people to make an informed choice about vaccination.

People should seek immediate medical attention if they develop any of the following symptoms after vaccination:

- severe or persistent headache or blurred vision
- 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 cases to date

Since last week's report, a further five 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 25 June-1 July 2021‡

New confirmed TTS	New probable TTS

New confirmed TTS	**New probable TTS**
Two new cases: • 52-year-old woman from WA • 59-year-old woman from Victoria	Three new cases: • 64-year-old woman from NSW • 77 and 83-year-old men 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 a consistent set of criteria, based on the case definitions established by the UK's Medicines and Healthcare products Regulatory Agency.

This takes the total Australian reports assessed as TTS following the AstraZeneca vaccine to 41 confirmed cases and 28 probable cases, with a total of 69 cases overall from approximately 4.6 million doses of the AstraZeneca vaccine.

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 involve clots in an unusual location, such as the brain or abdomen (Table 2). Of note, Tier 1 cases tend to have more serious outcomes than Tier 2 cases. Tier 1 cases were less common in older people. Approximately one quarter of cases were classified as Tier 1 in patients aged 60 years or older, compared to approximately half the case in people aged less than 60 years.

Based on the information we have, about half of the Tier 1 cases had clots in the brain (cerebral venous sinus thrombosis - CVST) and half had clots in the abdomen (splanchnic vein thrombosis). Of those with clots in the brain, around half also had another clot in the leg (deep vein thrombosis - DVT) or the lungs (pulmonary embolism - PE). The Tier 2 and unclassified TTS cases had only the more common clots like deep vein thrombosis or pulmonary embolism.

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	4	4	-	-
50-59	20	9	6	5
60-69	13	3	4	6
70-79	19	6	5	8
80+	11	3	4	4
All ages	**69** **(34 men, 35 women)**	26	20	23

† 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 44 days (Table 3). In some cases with a longer time to diagnosis, patients had experienced symptoms at an earlier stage but complicating factors, including symptoms from comorbidities, may have delayed a clear diagnosis. Approximately one in four TTS cases has required Intensive Care Unit (ICU) treatment, although all but three patients have since been released from ICU.

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

Time to onset/ diagnosis (days)	Median (range)	12 (1-44)
Treated in ICU	At any point†	18
	Currently	3
Outcome	Discharged	51
	In hospital	16
	Fatal	2

*Data is based on the most recent medical information available to the TGA
†Last week's report had an error in the ICU data. Three patients that were in ICU were not included in the total for patients that received ICU treatment at any point. This has been corrected above.

The TGA has sadly been advised by its UK counterpart, the Medicines and Healthcare products Regulatory Agency (MHRA) (https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency), of the death of a woman in the UK five weeks after receiving her first dose of the AstraZeneca vaccine in Australia.

While some of her symptoms, imaging results and pathology tests suggested TTS, the woman had another very serious and recent underlying health condition and UK authorities have ordered a post-mortem to assess whether this condition, along with the impact of long plane and car travel from Australia to the UK, had a role in her death.

Her family has requested privacy, and we pass on our condolences to them at this sad time.

It is not known whether she was an Australian citizen or permanent resident.

Immune thrombocytopenia (ITP)

The TGA is closely monitoring reports of immune thrombocytopenia (ITP) and investigating whether there may be a link with the AstraZeneca vaccine. This is in light of cases reported to the TGA and a recent Scottish study suggesting a small increase in the risk of ITP (1 in 100,000 vaccinated people) (https://www.nature.com/articles/s41591-021-01408-4#article-info).

To 27 June 2021, the TGA has received 36 cases of suspected ITP in people who had received the AstraZeneca vaccine and two cases in people who received the Comirnaty vaccine. Although many of these individuals have recovered or are recovering, one person who had received the AstraZeneca vaccine sadly died. The TGA has convened an external Vaccine Safety Investigation Group of clinical experts and consumer representatives to review this fatality and assess whether it could have been related to the vaccine. The TGA will report on the outcome of this investigation when it becomes available. We extend our sincerest condolences to the individual's family and loved ones.

ITP is a rare bleeding disorder which occurs when the immune system mistakenly destroys platelets, which help blood to clot. It causes minor bruising in some people but others may develop severe bleeding. ITP can occur after the immune system is activated, for example by a viral infection or vaccination, and has been reported with other vaccines for hepatitis B, measles, mumps, rubella and influenza.

Capillary leak syndrome

Cases of capillary leak syndrome following immunisation with the AstraZeneca vaccine have been reported overseas (https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting). Two of these eight cases had a history of capillary leak syndrome. This is a very rare but severe relapsing-remitting condition where fluid from small blood vessels (capillaries) leaks into surrounding tissues. It is not well understood what triggers a relapse.

The TGA received one case of a patient who died from multi-organ failure but had signs of capillary leakage reported previously (//www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-10-06-2021). Although there was a temporal link with the vaccine, an expert Vaccine Safety Investigation Group was unable to establish a causal link as other causes could not be ruled out.

The TGA is in discussions with the sponsor about including information on capillary leak syndrome in the Product Information as a precautionary measure.

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

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.

Myocarditis and pericarditis

The TGA continues to monitor reports of myocarditis (inflammation of the heart) and pericarditis (inflammation of the membrane around the heart) following a safety concern in the US (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html) and Israel (https://www.gov.il/en/departments/news/01062021-03).

To 27 June 2021, the TGA has received 26 cases of suspected myocarditis or pericarditis. During this time, approximately 2.9 million Comirnaty doses have been given. Eight of the TGA reports were in men and 18 were in women. One of the men was 18 years old and another was 23 years old, while the others were aged 41–72 years. The women were aged 23–47 years old. At the time of reporting, the majority of individuals had recovered or were recovering.

Overseas cases of myocarditis and pericarditis have mostly been in young men after the second Comirnaty dose. As we have limited experience of Comirnaty in this age group and after the second dose, the TGA is considering international evidence in our ongoing investigation of this issue.

On 23 June 2021, a review by the US CDC's Advisory Committee on Immunization Practices advised that myocarditis and pericarditis following the Comirnaty vaccine (https://www.hhs.gov/about/news/2021/06/23/statement-following-cdc-acip-meeting-nations-leading-doctors-nurses-public-health-leaders-benefits-vaccination.html) are extremely rare side effects which are usually mild. The US Food and Drug Administration (FDA) has since added a warning to the product information. (https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-june-25-2021)

The TGA is actively considering the need for updates to the approved Product Information, and has sought advice from the Advisory Committee on Vaccines on this issue.

We know that myocarditis and pericarditis are much more common with COVID-19 infection and the risks to the heart can be more severe in this context. The benefits of protection against COVID-19 far outweigh these rare and generally mild 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. Typically these have occurred within seven days of vaccination, particularly after the second dose of Comirnaty.

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

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)

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

The latest from ATAGI – published 25 June 2021 (https://www.health.gov.au/news/atagi-update-following-weekly-covid-19-meeting-23-june-2021)

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

Top 3 COVID-19 vaccine questions – Delta variant, vaccination and breastfeeding, and more vaccine types (https://www.health.gov.au/news/top-3-covid-19-vaccine-questions-delta-variant-vaccination-and-breastfeeding-and-more-vaccine-types)

URL: https://www.tga.gov.au/node/938437 (https://www.tga.gov.au/node/938437)