Australian Government
Department of Health
Therapeutic Goods Administration

COVID-19 vaccine weekly safety report - 24-06-2021

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Previous reports

The Therapeutic Goods Administration (TGA) closely monitors suspected side effects (also known as adverse events) from the use of COVID-19 vaccines. 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 (//www.tga.gov.au/#section-544) 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 (//www.tga.gov.au/section-547) have been assessed as thrombosis with thrombocytopenia syndrome (TTS) likely to be linked to the AstraZeneca vaccine. When assessed using the UK case definition, three were confirmed and two were deemed probable TTS. However, following reassessment of a previously reported case as being unlikely to be TTS, there is only a net increase of four cases. This brings the total number of cases of TTS to 64.
- We are also monitoring reports of suspected myocarditis and pericarditis following vaccination with Comirnaty and suspected Guillain-Barre Syndrome following vaccination with the AstraZeneca vaccine. No causal association with either vaccine has been established at this stage.

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 14-20 June 2021 we received 2,018 AEFI reports for COVID-19 vaccines.

Since the beginning of the vaccine rollout to 20 June 2021, the TGA has received 318 reports of death in people who have recently been vaccinated.

Large scale vaccination means that coincidentally some people will experience a new illness or die shortly after vaccination. The TGA reviews all deaths reported after vaccination and monitors signals that may relate to vaccine safety. 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. To date, our review of cases and analysis of reporting patterns does not suggest that the vaccine caused these deaths, other than for the TTS cases.

Total adverse event reports to 20 June 2021

4.8	31,641	6,590,741
Reporting rate per 1000 doses	Total AEFI reports received	Total doses administered
21,799	9,592	253
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	4.1	New South Wales	3.5
Northern Territory	4.5	Queensland	4.7
South Australia	4.3	Tasmania	6.9
Victoria	6.1	Western Australia	4.1

Most commonly reported vaccine side effects

The AEFI most commonly reported to the TGA following COVID-19 vaccines are side effects that are observed with vaccines generally. They include headache, muscle and joint pain, chills and injection site reactions.

The most common reactions reported for the AstraZeneca COVID-19 vaccine in the week of 14-20 June 2021 were headache, fever, muscle pain, fatigue and chills.

The most common reactions reported for the Comirnaty (Pfizer) COVID-19 vaccine in the week of 14-20 June 2021 were headache, muscle pain, dizziness, fatigue and nausea.

Adverse events reported for Aboriginal and Torres Strait Islander people

When someone reports a suspected side effect to the TGA, we ask them to include patient ethnicity on the reporting form to help us identify any differences between particular populations. This information is not always given, so our data on ethnicity is not comprehensive. However, what we do receive gives us a useful indication of vaccine safety in different populations.

Since the beginning of the vaccine rollout to 20 June 2021, the reporting rate of side effects following vaccination of Aboriginal and Torres Strait Islander people is 3.1 reports per 1000 vaccine doses. This is slightly lower than for the total population (4.8 reports per 1000 vaccine doses), which may reflect incomplete reporting of ethnicity given that fewer than 20% of reports received by the TGA include information on ethnicity.

The nature of the side effects reported to the TGA for Aboriginal and Torres Strait Islander people are similar to the total population with the most common being headache, muscle and joint pain, fatigue, fever and chills, and lethargy.

Based on the information reported to the TGA, none of the TTS cases so far has been identified as being in an Aboriginal or Torres Strait Islander person.

Further information on adverse event reports in Aboriginal and Torres Strait Islander people is published in the ongoing AusVaxSafety survey (https://www.ausvaxsafety.org.au/safety-data/covid-19-vaccines).

AstraZeneca COVID-19 vaccine

We continue to receive reports of side effects to the AstraZeneca vaccine as it continues to be used in Australia. 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 17 June 2021, 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. Previously ATAGI recommended Comirnaty over the AstraZeneca vaccine for those aged 16–50 years old. ATAGI updated their recommendations due to emerging evidence in Australia of a higher risk and severity of TTS with the first AstraZeneca dose in the 50–59 year age group.

People aged 50–59 years old who have already received the first dose of the AstraZeneca vaccine should complete their two-dose schedule as the risk of TTS after the second dose is extremely low. For example, in the UK where many more AstraZeneca doses have been given, the risk of TTS (which includes confirmed, probable and possible cases) was estimated to be 1.5 cases per million with the second dose compared to 14.2 cases per million with the first dose.

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 and; review of additional clinical information has led to a previously reported probable case now being considered unlikely to be TTS. (Table 1).

Table 1: Newly confirmed and probable TTS cases for the week of 18-24 June 2021‡

New confirmed TTS	**New probable TTS**
Three new cases: • 51, 54 and 60-year-old women from NSW	Two new cases: • 59-year-old woman from Victoria • 95-year-old man 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.

One previously reported case from South Australia was reclassified from confirmed to probable following revised clinical information being provided to the TGA. This takes the total Australian reports assessed as TTS following the AstraZeneca vaccine to 39 confirmed cases and 25 probable cases, with a total of 64 cases overall from approximately 4.2 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 them 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.

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 other 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 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	18	8	4	6
60-69	12	3	4	5
70-79*	18	6	5	7
80+	10	3	4	3
All ages	64 **(32 men, 32 women)***	25	17	22

† 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).

* Please note last week's report had two minor errors that have been corrected in the above. They related to the number of cases in men and women, and a 69-year-old patient was incorrectly included in the 70-79 year old age group.

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 five 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	14
	Currently	5
Outcome	Discharged	43
	In hospital	19
	Fatal	2

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

Updated reporting rates of TTS in Australia were published in a statement from ATAGI published on 17 June 2021 (https://www.health.gov.au/news/atagi-statement-on-revised-recommendations-on-the-use-of-covid-19-vaccine-astrazeneca-17-june-2021). Compared to information published by the UK's medicine regulator (https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting), the fatality rate is lower in Australia (3% in Australia compared to 18% in the UK).

While TTS is very rare, it is appreciated that some people may have concerns that they can discuss with their doctor. This is essential to allow people to make an informed choice.

Anyone who has been vaccinated 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.

Guillain-Barre Syndrome (GBS)

To 20 June 2021, the TGA has received 38 reports of suspected Guillain-Barre Syndrome (GBS) following approximately 4.2 million doses of the AstraZeneca vaccine. GBS is a rare immune disorder that 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. GBS can occur following an infection or other immunisations such as the influenza vaccines.

A causal link between GBS and the AstraZeneca vaccine has not been confirmed in Australia or overseas and it is unclear if these cases are related to vaccination or occurred coincidentally. GBS is currently being assessed by the Pharmacovigilance Risk Assessment Committee in Europe (https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-3-6-may-2021) and the TGA will report on this investigation when more information is available. We continue to monitor and investigate Australian reports of GBS along with other serious adverse event reports that relate to the nervous system. Part of this investigation will look more closely at whether these suspected cases meet the clinical criteria for GBS, and will compare the number of observed cases to those expected generally for different age groups and time points following vaccination.

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.

Side effects with first and second doses of the Comirnaty vaccine

Data from an ongoing survey of Australians after they receive a COVID-19 vaccine (AusVaxSafety (https://www.ausvaxsafety.org.au/safety-data/covid-19-vaccines)) suggests that side effects are more common after the second dose of Comirnaty compared to the first dose. In the survey, 37% of respondents said they had a reaction to the first dose compared to 60% after the second dose. This reflects what was found in the clinical trials of Comirnaty (https://www.nps.org.au/australian-prescriber/articles/bnt162b2-vaccine-for-prevention-of-covid-19), with a higher proportion of people experiencing expected vaccine side effects such as fatigue, headache, muscle and joint pain and fever after the second dose than after the first dose. Interestingly, the opposite was found in trials of the AstraZeneca vaccine (https://www.nps.org.au/australian-prescriber/articles/chadox1-s-vaccine-for-prevention-of-covid-19) with side effects being less common after the second dose.

In the AusVaxSafety survey, the most common reactions with both Comirnaty doses were injection site pain, fatigue, headache and muscle aches. These are known and expected side effects of vaccines generally and mostly resolve within a day or two.

A similar pattern of reporting for Comirnaty is also observed in our database at the TGA with more reports of side effects with the second dose (4.2 per 1000 doses) compared to the first dose (3.1 per 1000 doses). The most common side effects reported to the TGA are similar to those seen in the AusVaxSafety survey.

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 reports of a signal for a possible 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) in young men. Almost all cases were considered mild and resolved within a few days. A causal link to the vaccine has not yet been established but international regulators are investigating this.

Myocarditis and pericarditis often occur following a viral infection and most cases are mild with no long-term effects. Severe cases may cause damage to the heart muscle although this is very rare.

Since last weeks' report (13–20 June 2021), the TGA has received four new reports – three reports of suspected myocarditis and one report of suspected pericarditis following immunisation with the Comirnaty vaccine. These reports will be considered as part of TGA's ongoing investigation.

We encourage people to report symptoms that could suggest myocarditis or pericarditis such as chest pain, shortness of breath and palpitations, 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 17 June 2021 (https://www.health.gov.au/news/atagi-statement-on-revised-recommendations-on-the-use-of-covid-19-vaccine-astrazeneca-17-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 – AstraZeneca for under 60s, over 60s, and side effects (https://www.health.gov.au/news/top-3-covid-19-vaccine-questions-astrazeneca-for-under-60s-over-60s-and-side-effects)

Top 3 COVID-19 vaccine questions – New ATAGI advice, second doses and Pfizer access (https://www.health.gov.au/news/top-3-covid-19-vaccine-questions-new-atagi-advice-second-doses-and-pfizer-access)

URL: https://www.tga.gov.au/node/938385 (https://www.tga.gov.au/node/938385)