Information for Immunisation Providers on Thrombosis with Thrombocytopenia Syndrome (TTS) following COVID-19 vaccination

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What has been updated:

ATAGI reinforce recommendations on use of COVID-19 vaccines following its review of vaccine safety data and benefits. ATAGI continues to closely monitor both the local and international data on thrombosis with thrombocytopenia syndrome.

Thrombosis with thrombocytopenia syndrome (TTS)

On 8 April 2021, the Australian Government received advice and recommendations from the Australian Technical Advisory Group on Immunisation (ATAGI) as to a link between the AstraZeneca vaccine and a very rare new adverse event called thrombosis with thrombocytopenia syndrome (TTS).

On 23 April 2021, ATAGI issued a statement reinforcing recommendations on use of COVID-19 vaccines following review of vaccine safety data and benefits. ATAGI made this statement after reviewing an additional three cases of TTS was confirmed by the TGA on 22 April 2021. ATAGI is meeting regularly to review emerging data on TTS.

The Department of Health is working to update information available on Government websites and in information sheets as fast as possible.

Please visit health.gov.au/covid19-vaccines regularly to stay up-to-date.

What is thrombosis with thrombocytopenia syndrome (TTS)?

This is a very rare, new and unexpected adverse event that appears to be causally linked with COVID-19 Vaccine AstraZeneca.

It involves thrombosis with thrombocytopenia, with onset of symptoms occurring around 4 to 28 days following vaccination. The sites of thrombosis in reported cases are unusual, varied and usually venous. Most cases reported to date have included cerebral venous sinus thrombosis (CVST) or thrombosis of the splanchnic (abdominal) circulation. Although very rare, TTS can
cause disability and even death, with a fatal outcome in about 19% of the cases reported in the UK.\textsuperscript{1,2}

No biological or other risk factors have been identified that predict who will develop TTS. It appears to be an idiosyncratic reaction. Cases have been reported in all ages and in both men and women.

In Australia, the rate of TTS is estimated to be about 6 cases per million people vaccinated with COVID-19 Vaccine AstraZeneca. But for those under 50 years of age, the rate is currently estimated to be higher, at about 20-40 people per million people vaccinated. These estimates are based on the small numbers of people who have been vaccinated in Australia but are similar to rates seen in some countries overseas. They will be updated as further information becomes available.

So far, almost all reported cases of thrombosis with thrombocytopenia syndrome have occurred after the first dose of COVID-19 Vaccine AstraZeneca. The risk of this syndrome occurring after the second dose is thought to be very low. ATAGI will be continuously reviewing international vaccine safety data to inform recommendations about the second AstraZeneca COVID-19 vaccine dose.

Based on what we know now, Comirnaty (Pfizer vaccine) is not associated with TTS.

**What is the ATAGI advice?**

ATAGI recommends:

1. **Comirnaty (Pfizer vaccine) is preferred over COVID-19 Vaccine AstraZeneca in adults aged <50 years.**
2. **The AstraZeneca vaccine can still be given to adults < 50 years if vaccine benefits are likely to outweigh the risk and the patient has provided informed consent.**
3. **Special situations**
   a. If the first dose of COVID-19 Vaccine AstraZeneca has already been given with no serious adverse events, such as TTS or anaphylaxis, COVID-19 Vaccine AstraZeneca can be given for the second dose.
   b. Comirnaty is the preferred vaccine for people with a past history of cerebral venous sinus thrombosis or heparin-induced thrombocytopenia. This is precautionary advice, based on a theoretical concern that these patients may have an increased risk of TTS. However, there is no evidence yet to suggest this is the case.
   c. There is no evidence that people with any other previous thromboembolic disorders or other clotting tendencies have an increased risk of this unique thrombosis with thrombocytopenia after vaccination. COVID-19 Vaccine AstraZeneca can be given to such patients.

This advice may be revised as more information about TTS becomes available, or if the epidemiological situation of COVID-19 in Australia changes, particularly if there is likely to be significant community transmission of SARS-CoV-2.
Counselling patients

Anyone 18 years and over can decide to have the AstraZeneca vaccine, with informed consent. The Department of Health has published a patient information sheet on TTS, which patients should be encouraged to read before vaccination with COVID-19 Vaccine AstraZeneca. The following guide will assist patients and providers to assess the benefits against risks of harm of vaccination for people of different ages: Weighing up the potential benefits against risk of harm of COVID-19 Vaccine AstraZeneca.

FAQs

1. What are the benefits and risks of vaccination with COVID-19 Vaccine AstraZeneca Vaccine for my patient?

The benefits of vaccination with COVID-19 Vaccine AstraZeneca are greater for some people, such as older adults (>50 years), people who have an increased risk of exposure to COVID-19 (e.g. through their occupation or upcoming overseas travel), and people who have medical comorbidities that increase their risk of severe illness from COVID-19.

Specific risk factors for TTS have not yet been determined. Younger adults appear to have a higher risk of TTS compared to older adults. There is no evidence to suggest that people with a history of clotting tendencies have an increased risk of TTS, however, it is a very rare condition and this has not been formally studied yet.

2. What should I advise people with a history of blood clots or clotting tendencies?

No medical risk factors for TTS have yet been identified. Reassuringly, in countries where COVID-19 Vaccine AstraZeneca has been extensively used, there does not appear to be an increased occurrence of other clotting conditions (i.e. thrombosis unaccompanied by thrombocytopenia) following vaccination.

Comirnaty is preferred for people with a history of cerebral venous sinus thrombosis (CVST) or heparin induced thrombocytopenia (HIT) at any age, because of theoretical concerns that these conditions may increase their risk of TTS.

For adults over 50 years of age who have a history of other types of blood clots, the benefits of vaccination are considered to outweigh the risk of TTS. There is no evidence that people with clotting conditions are at increased risk of developing TTS or becoming more unwell if they get it. Vaccination with COVID-19 Vaccine AstraZeneca is recommended. This is based on the increased risk of serious illness from COVID-19 in this age group.

ATAGI will continue to monitor evidence on TTS and will update its advice if any new risk factors are identified.

3. If my patient chooses to go ahead with AstraZeneca vaccine, what should we look out for?

Refer patients to the list of symptoms to monitor for, provided in the patient information sheet on TTS, summarised in the section below. Patients should be advised to present for
medical advice if they develop any severe, persistent symptoms after vaccination. Patients should be advised the onset of TTS is around 4 to 28 days following vaccination.

4. What else should I consider?

Some additional benefits of vaccination can be considered when counselling patients

- The potential indirect benefit of vaccination to others, e.g. household members who have risk factors for severe COVID-19.
- The ongoing potential for new incursions of SARS-CoV-2 into Australia, which could lead to new outbreaks.
- The potential for a delay in accessing an alternate brand of COVID-19 vaccine.

As with any vaccine, consent should be recorded by the vaccine provider.

Identification and referral of suspected cases

Any patient with concerning signs or symptoms potentially related to TTS following receipt of COVID-19 Vaccine AstraZeneca should be referred to an emergency department for assessment and investigation, including consultation with a haematologist. Based on reported cases to date, the timing of greatest risk is around 4 to 28 days after vaccination.

Concerning signs or symptoms include:

- New onset of severe persistent headache which does not improve with simple analgesia
- Signs and symptoms of raised intracranial pressure or focal neurological deficits or seizures
- Signs or symptoms suggestive of thrombosis in other anatomical locations (e.g. abdominal pain suggestive of thrombosis in the splanchnic circulation, or chest pain suggestive of pulmonary embolism)
- Signs suggestive of clinically significant thrombocytopenia, such as petechial rash or bleeding, or bruising not at the vaccine injection site that cannot be explained

Blood clots such as DVT or PE occur commonly in the population in the absence of vaccination, at an annual rate of about 1 per 1000 people. Some of the blood clots that occur will occur after AstraZeneca COVID-19 will be coincidental and not causally related to the vaccine. Providers should refer to clinical guidance from THANZ on investigation and management of anyone who presents with the above symptoms suggestive of thrombosis or thrombocytopenia after vaccination, and seek expert haematologist input as needed.

Initial investigations should include:

- Full blood count (to look for thrombocytopenia)
- D-dimer
- Fibrinogen (can be lower than expected)
- Imaging as clinically indicated (for example brain CT or MRI for CVST).

If screening tests suggest thrombosis with thrombocytopenia (low platelets <150x10⁹/L together with elevated D-dimer (at least 5 x upper limit of normal), a haematologist or haemostasis-
thrombosis specialist should be consulted to advise on further investigations (including a HIT screen). Also seek advice from your state or territory specialist immunisation services or health department.

Further information is available from the Thrombosis & Haemostasis society of Australia and New Zealand:

- [Advisory statement](https://www.thanz.org.au/documents/item/577)
- [Blood test request form](https://www.thanz.org.au/documents/item/579)

**CAUTION:** Patients with this suspected condition should NOT receive any heparin or platelet transfusions. These treatments may potentially worsen the clinical course.


Where can patients aged under 50 access the Pfizer vaccine?

The COVID-19 vaccination program has been modified in light of the ATAGI advice. More Pfizer vaccination sites will become available around the country in line with increasing supplies. You can check your eligibility and where to get a vaccine using the [eligibility checker](https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting).

**Further information for providers**


**References**
