

Information for clinicians – thrombosis with thrombocytopenia syndrome (TTS)

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This information is designed to provide healthcare workers in Queensland with an understanding of thrombosis with thrombocytopenia syndrome (TTS). Also known as Vaccine Induced Prothrombotic Immune Thrombocytopenia (VIPIT), Vaccine Associated Thrombosis Thrombocytopenia (VATT) and Vaccine Induced Immune Thrombotic Thrombocytopenia (VITT). It is intended as a guide only and does not replace sound clinical judgement.

As our accepted understanding of this syndrome is rapidly evolving, **do not** print this factsheet. Please refer to our [vaccine page](#) or [the Thrombosis and Haemostasis Society of Australia and New Zealand \(THANZ\)](#) for the latest advice.

Key messages

- A very small proportion of patients globally have developed thrombosis with thrombocytopenia syndrome following vaccination with COVID-19 Vaccine AstraZeneca.
- No specific risk factors have been identified and causality has not yet been proven.
- Prevalence is rare (1-2 per 100,000 in Australia) following a first dose of vaccine and very rare ([estimated](#) at 1.7 cases per million second doses).
- The benefits of COVID-19 vaccines outweigh the risk of TTS/VIPIT/VATT/VITT for most people, especially in a high-risk COVID environment.
- People who have had the first dose of COVID-19 Vaccine AstraZeneca without any serious adverse effects can be given the second dose, including adults under 50 years of age.
- Vaccination against COVID-19 should continue, with the Pfizer COVID-19 vaccine (Corminaty™) the preferred option in those under 60 years of age who have not yet received AstraZeneca.

What is the issue?

In late March 2021, potential safety concerns involving cases of thrombosis (blood clots) and thrombocytopenia (low blood platelet count) occurring after vaccination with COVID-19 Vaccine AstraZeneca were under investigation. On 2 April 2021 the Australian Technical Advisory Group on Immunisation (ATAGI) [reported](#) that a probable case had been reported in an Australian vaccine recipient, and issued [updated advice](#) for healthcare providers.

Since this time, it has emerged that a very small proportion of patients have developed thrombocytopenic thrombotic syndrome following a COVID-19 vaccination. Thrombosis with thrombocytopenia syndrome (TTS) is a rare and new syndrome and is different from other blood clotting conditions. It is triggered by the immune system's response to the COVID-19 Vaccine AstraZeneca. The condition involves blood clots occurring in body sites like the brain or abdomen, together with low platelet levels. The syndrome has some similarity to heparin induced thrombocytopenia (HIT).

Investigators in Europe have reported the detection of antibodies against platelet antigens PF4 as part of the immune stimulation post vaccination.

When should I suspect TTS/VIPIT/VATT/VITT?

The Thrombosis and Haemostasis society of Australia and New Zealand (THANZ) has released [a statement](#) which will be updated as more evidence becomes available. THANZ summarises the features of TTS/VIPIT/VATT/VITT (as of 29 June 2021) as:

- Onset 4-42 days after vaccination
- Thrombosis: predominant sites - cerebral venous sinus or splanchnic. Other VTE and arterial ischaemia also reported
- Thrombocytopenia or falling platelet count (platelets can be normal on presentation but drop within 4-6 hours)
- High D-Dimer (typically very high)
- Some patients are refractory to standard anticoagulation
- Response to Intravenous immunoglobulin (IVIG).

While the European Medicines Agency (EMA) has not identified any specific risk factors, such as age, gender or a previous medical history of clotting disorders for these very rare events, most cases of TTS/VIPIT/VATT/VITT described to date have been female and under 60 years of age. Males have also been affected, and it is believed the sex-adjusted rates are similar. Some cases report progression of thrombosis whilst on therapeutic heparin anticoagulation.

Patients presenting with organ specific symptoms of thrombosis (such as severe headaches unresponsive to simple analgesia, abdominal pain or respiratory symptoms) 4-42 days after vaccination should be reviewed carefully for signs of thrombosis or bleeding. Other neurological symptoms of cerebral vein thrombosis can include those of raised intracranial pressure such as visual changes, severe headache, seizures, focal neurological deficits, and general symptoms of encephalopathy including confusion.

As multiple sites have been involved (cerebral venous sinus, splanchnic, pulmonary embolism), **any patients presenting with symptoms of thrombosis shortly after vaccination should be considered carefully for TTS/VIPIT/VATT/VITT. As a precaution, patients with this suspected condition should NOT receive any heparin or platelet transfusions. These treatments may potentially worsen the clinical course.**

How do I investigate for TTS/VIPIT/VITT/VATT?

Please refer to the THANZ Advisory Statement [Suspected Vaccine Induced Immune Thrombotic Thrombocytopenia \(VITT\) / Vaccine Induced Prothrombotic Immune Thrombocytopenia \(VIPIT\) / THANZ Advisory Statement for Haematologists](#) for advice on screening and treatment (specialist consultation with haematology will be required). THANZ also advises that appropriate investigations should always be initiated based on the patient context. Do not delay the commencement of life-saving management while awaiting investigations. An [Adverse Event Following Immunisation \(AEFI\) form](#) should also be completed (see below).

THANZ recommends, if there are no contraindications, to treat all thrombotic events for patients who have recently received COVID vaccination (within the last 42 days), with a non-heparin anticoagulant (e.g. fondaparinux or DOAC - apixaban or rivaroxaban), even if TTS/VITT/VATT/VIPIT testing is negative. Consultation with a sub-specialist thrombosis haematologist is recommended.

What does this mean for the vaccine rollout?

The risk-versus-benefit assessment for the use of AstraZeneca COVID-19 vaccine will be different for Australia compared to other countries, such as those with widespread transmission and very serious outbreaks.

The risk of serious disease and death in Australia remains, even as border controls and other measures continue. The COVID-19 Vaccine AstraZeneca is highly effective at reducing the risk of death or severe disease from COVID-19.

At the current time:

- Use of Pfizer COVID-19 vaccine is preferred over COVID-19 Vaccine AstraZeneca in adults under 60 years of age who have not already received a first dose of AstraZeneca vaccine. This is based on the increased risk of complications from COVID-19 with increasing age (and thus increased benefit of vaccination), and the potentially lower, but not zero, risk of thrombosis with thrombocytopenia syndrome with increasing age.
- COVID-19 Vaccine AstraZeneca can be used in adults aged under 60 years where the benefits are likely to outweigh the risks for that individual and the person has made an informed decision based on an understanding of the risks and benefits.
- People who have had their first dose of COVID-19 Vaccine AstraZeneca without any serious adverse effects can be given their second dose. This includes adults under 60 years of age. People who have had blood clots associated with low platelet levels or anaphylaxis after their first dose of COVID-19 Vaccine AstraZeneca should not be given their second dose.

The [TGA and ATAGI also advise](#) that the following groups of people **can** receive COVID-19 Vaccine AstraZeneca:

- people with a past history of venous thromboembolism in typical sites, such as deep vein thrombosis or pulmonary embolism
- people with a predisposition to form blood clots, such as those with Factor V Leiden, or other non-immune thrombophilic disorders
- people with a family history of clots or clotting conditions
- people currently receiving anticoagulant medications
- people with a history of ischaemic heart disease or cerebrovascular accident
- people with a current or past history of thrombocytopenia.

Comirnaty (Pfizer) is recommended for people aged 16 years and above with:

- a past history of cerebral venous sinus thrombosis (CVST)
- a past history of heparin-induced thrombocytopenia (HIT)
- a past history of idiopathic splanchnic (mesenteric, portal and splenic) venous thrombosis
- anti-phospholipid syndrome with thrombosis
- people with contraindications to COVID-19 Vaccine AstraZeneca, i.e.
 - anaphylaxis to a previous dose of COVID-19 Vaccine AstraZeneca or to an ingredient of the vaccine
 - thrombosis with thrombocytopenia occurring after the first dose of COVID-19 Vaccine AstraZeneca
 - other serious adverse events attributed to the first dose of COVID-19 Vaccine AstraZeneca.

Second dose risks of TTS/VIPIT/VATT/VITT

[UK data](#) suggest that the risk of TTS is much lower with a second dose, with 15 cases reported to date out of 9.0 million second doses of COVID-19 Vaccine AstraZeneca given. This translates into an estimated rate of 1.7 case per million doses.

ATAGI reinforces that people of any age who have had their first dose of COVID-19 Vaccine AstraZeneca without any serious adverse events can receive the second dose.

Risk benefit discussion

If Pfizer COVID-19 vaccine is contraindicated or not available, discuss risks and benefits for the individual as per below and in addition to the above. If a consumer wishes to proceed, then proceed with informed consent.

- If an individual cannot access Pfizer vaccine for any reason, do they have risk factors which might increase their exposure to COVID-19 in the workplace, their environment or at home? What is their risk of severe disease? They may also have individual reasons for not wishing to access the AstraZeneca vaccine and self-perceived risk which should be explored and discussed. Please refer to our [Decision Support Guide](#) for assistance with this process or the Australian Government's [Weighing up the potential benefits against risk of harm from COVID-19 Vaccine AstraZeneca](#). Additional patient materials are provided below.
- The aim of the current vaccination program is primarily around preventing severe disease for individuals who contract COVID-19.
- We respect a person's choice to make an informed decision on whether to accept the risk of COVID-19 vaccination with the COVID-19 Vaccine AstraZeneca.

Reporting a TSS/VIPIT/VATT/VITT Adverse Event Following Immunisation (AEFI)

An Adverse Event Following Immunisation (AEFI) is a serious, uncommon or unexpected event following immunisation. Under the *Public Health Act 2005* and the COVID-19 Vaccination Code, COVID-19 vaccine service providers are required to report any adverse events following immunisation directly to Queensland Health. Common side effects such as headache and fatigue are to be expected and do not need to be reported.

A patient is only considered to have thrombosis with thrombocytopenia syndrome if they have blood clotting AND a low platelet count, occurring between 4-42 days after a COVID-19 vaccination.

Click here to complete an [Adverse Event Following Immunisation \(AEFI\) form](#).

For your patients

- [Patient information on thrombosis with thrombocytopenia syndrome](#)
- [TTS explained video](#)

Recommended reading

- [Australian Technical Advisory Group on Immunisation \(ATAGI\) statement 8 April 2021 and 22 April](#)
- [Therapeutic Goods Administration](#)
- [Weighing up the potential benefits against risk of harm from COVID-19 vaccine AstraZeneca](#)
- [Suspected Vaccine Induced Immune Thrombotic Thrombocytopenia \(VITT / Vaccine Induced Prothrombotic Immune Thrombocytopenia \(VIPIT\) / THANZ Advisory Statement for Haematologists](#)
- [Australian Government's information for immunisation providers.](#)