

The Australian Technical Advisory Group on Immunisation (ATAGI) advice on the AstraZeneca COVID-19 vaccine in response to new vaccine safety concerns

8 April 2021

Summary

- ATAGI notes further evidence of a rare but serious side effect involving thrombosis (clotting) with thrombocytopenia (low blood platelet count) following receipt of COVID-19 Vaccine AstraZeneca
- ATAGI recommends that the COVID-19 vaccine by Pfizer (Comirnaty) is preferred over COVID-19 Vaccine AstraZeneca in adults aged under 50 years. This recommendation is based on the increasing risk of severe outcomes from COVID-19 in older adults (and hence a higher benefit from vaccination) and a potentially increased risk of thrombosis with thrombocytopenia following AstraZeneca vaccine in those under 50 years.
- COVID-19 Vaccine AstraZeneca can be used in adults aged under 50 years where the benefits clearly outweigh the risk for that individual and the person has made an informed decision based on an understanding of the risks and benefits.
- 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.

Background – Thrombosis with thrombocytopenia syndrome and COVID-19 Vaccine AstraZeneca

ATAGI recommends that all adults are vaccinated against COVID-19. The COVID-19 pandemic is continuing to cause severe disease around the world, with many lives being lost. The Australian population remains vulnerable to COVID-19 and most Australians have not yet been vaccinated and are not immune.

ATAGI [advised on 25th March 2021](#) that there was a potential safety concern being investigated overseas, involving cases of thrombosis (blood clots) and thrombocytopenia (low blood platelet count) occurring after COVID-19 Vaccine AstraZeneca. On [2nd April 2021](#) ATAGI reported that a probable case had been reported in an Australian vaccine recipient, and issued an [updated advice for healthcare providers](#).

This ‘thrombosis with thrombocytopenia syndrome’ (TTS) is a newly described serious condition, with unusual blood clots in the brain (cerebral venous sinus thrombosis) or in other parts of the body, associated with low platelet levels. Some researchers have provisionally called this condition ‘vaccine induced prothrombotic immune thrombocytopenia’ (VIPIT). However, the causal relationship and exact mechanism leading to this condition is not yet understood. Some people have antibodies which activate platelets (anti-PF4 antibodies). These antibodies have been detected in another disorder triggered by the drug heparin, which has a similar presentation.

ATAGI and other Australian officials continue to consult with the WHO, UK, European and other regulatory agencies in countries where use of the AstraZeneca COVID-19 vaccine has been widespread. Further information from the UK and Europe is still emerging. The [European Medicines Agency \(EMA\) stated](#) on 7 April 2021 that a causal relationship between the AstraZeneca vaccination and thrombosis in combination with thrombocytopenia is plausible.

In the UK, where approximately 20.2 million doses of AstraZeneca COVID-19 vaccine have been administered, their regulatory agency, the [MHRA have advised](#) that the evidence of a link is stronger but more work is still needed.

ATAGI is aware of more cases of TTS being reported from other countries, and has reviewed all available data and research provided by AstraZeneca, as well as independent expert groups.

Some countries that are using the AstraZeneca COVID-19 vaccine have made precautionary decisions about pausing or limiting its use based on the potential risk of this serious adverse event. These decisions are also informed by the local risk for COVID-19, how much of the population is already immune from vaccination and in what age groups, and whether they have an alternative supply of vaccines.

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. This includes countries in our region such as those currently experiencing very serious outbreaks of COVID-19, such as Timor Leste, Papua New Guinea and others.

Key Considerations

The following information has been considered by ATAGI in relation to its new recommendations:

Local epidemiology

- While Australia currently has very low or no community transmission of COVID-19, this could change, particularly in the context of high global transmission rates, including of new variants of the virus. The risk of serious disease and death in Australia remains, even as borders controls and other measures continue.
- Although Australia has had few deaths from COVID-19 in young adults until now, large outbreaks in other countries have caused many thousands of deaths in young adults, indicating that the risk for serious outcomes exists across the age spectrum.

Vaccine availability and uptake

- The AstraZeneca vaccine is highly effective at reducing the risk of death or severe disease from COVID-19 across all adult age groups. At the present time, the AstraZeneca vaccine is the only vaccine option for reducing this risk for many Australians, since the global availability of alternative vaccines is highly constrained.
- ATAGI recognises this safety concern will likely impact on confidence in being vaccinated with AstraZeneca vaccine in all age groups.
- Until the Government can increase supply of COVID-19 vaccines other than AstraZeneca, overall coverage under Australia's COVID-19 vaccine program will likely be reduced. This will likely impact the time frame to which the Australian population is protected against COVID-19.
- In the short term, delays in vaccine uptake increase the vulnerability of the Australian population to outbreaks of COVID-19 and the attendant risk of death and serious morbidity, especially among older Australians.

Evidence regarding TTS

- The AstraZeneca vaccine appears likely to be causally-linked with a risk of this newly recognised thrombosis with thrombocytopenia syndrome.
- There is currently uncertainty in, and different reported rates of risk, for this adverse event.
- Studies have suggested it may occur in approximately 4 – 6 people in every one million people in the 4-20 days after the first dose of vaccine. However, higher rates have been reported in Germany and some Scandinavian countries.

- Some evidence suggests the risk of this condition occurring may be somewhat higher in people of a younger age, however a small number of cases have been reported in people of different ages (including older adults).
- While there have been more reports of TTS in women in some settings, this may be because more vaccine doses have been given to women. In one country the reported rate of TTS (number of cases adjusted for the number of men and women vaccinated) was similar in men and women.
- TTS can cause serious long term disability or death (with death occurring in approximately 25% of reported cases).
- So far no specific biological risk factors or pre-existing medical conditions have been found to modify (i.e. increase or decrease) the risk of TTS occurring after AstraZeneca vaccine.
- We do not yet know to what extent earlier recognition of this syndrome and improved treatments will improve patient outcomes. More cases can be expected to occur, albeit rarely.
- Comirnaty (the Pfizer COVID-19 vaccine) does not appear to carry a risk of TTS.

Benefit-to-risk assessment

- ATAGI consider that the individual benefit-to-risk balance of vaccination with COVID-19 vaccine AstraZeneca in Australia varies with age. The risk of ongoing health issues and death from COVID-19 is highest in older age groups, particularly rising from 50 years of age. By comparison, the rate, and thus possibility of disability and death from TTS may be higher in younger people. This age-specific benefit-to-risk balance is demonstrated in an [analysis from the UK](#).
- Younger people with certain underlying medical conditions are also at increased risk of severe outcomes from COVID-19, which affects their individual benefit-to-risk balance.
- ATAGI respects a person's choice to make an informed decision on whether to accept the risk of COVID-19 vaccination with the AstraZeneca vaccine. ATAGI recognise that it is difficult for people to assess their personal risk where there is uncertainty about the short and long term risk of severe COVID-19 in different age groups, and the evidence around benefit and risk of the AstraZeneca vaccine is changing quickly.
- In the context of the ongoing risk of COVID-19 in Australia, ATAGI considers that the benefit-to-risk balance is favourable for use of AstraZeneca vaccine in all older adult age groups.
- ATAGI also consider that population coverage under Australia's COVID-19 vaccine program will likely be impacted until such time that an increased supply of alternative safe and effective vaccines can be secured.

Recommendations

ATAGI recommends that:

1. At the current time, use of Comirnaty COVID-19 vaccine (Pfizer) is preferred over AstraZeneca COVID-19 vaccine in adults aged < 50 years who have not already received a first dose of AstraZeneca vaccine. This is based both 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 TTS with increasing age.
2. Immunisation providers should only give a first dose of AstraZeneca COVID-19 vaccine to adults aged < 50 years of age where benefit clearly outweighs risk for that individual's circumstances.
3. 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 50 years of age. People who have had blood clots associated with low platelet levels after their first dose of COVID-19 Vaccine AstraZeneca should not be given their second dose.

4. That the Department of Health further develop and refine resources for informed consent that clearly convey the benefits and risks of AstraZeneca vaccine for both immunisation providers and consumers of all ages.

This advice may be revised as more information becomes available or if the epidemiological situation changes, particularly if there is, or is likely to be significant community transmission.

ATAGI supports the Australian Government's ongoing efforts to procure more or bring forward the delivery of alternate COVID-19 vaccine brands to replace the use of AstraZeneca COVID-19 vaccine that would have been administered to persons under 50 years of age. Where possible, onshore manufacturing of alternative safe and effective vaccines should be considered.

ATAGI intends to review other current COVID-19 vaccine recommendations as soon as practicable. This includes recommendations on vaccination for those who have a past history of heparin induced thrombocytopenia (HIT), central venous sinus thrombosis (CVST), and/or have other thrombosis risk factors, and those who are pregnant.

Further data and outcomes of investigations from the UK, Europe and other countries will continue to be reviewed over the coming days to weeks. ATAGI recommendations may change as a result of this ongoing assessment of new and emerging evidence over coming days and weeks.

Definitions

- **Thrombosis with thrombocytopenia syndrome (TTS)** is a rare and new syndrome which has been reported after being given the AstraZeneca COVID-19 vaccine. It may be caused by this vaccine. The condition involves blood clots (occurring in body sites like the brain or abdomen) together with low platelet levels.
- **Thrombosis** is the formation of a blood clot, which prevents blood flowing normally through the body.
- **Thrombocytopenia** is a condition in which you have a low blood platelet count. Platelets (thrombocytes) are blood cells that help blood clot. Platelets stop bleeding by clumping and forming plugs in blood vessel injuries.