

## PHS Health Protection Alert

Title	Description
<b>Event</b>	National incident in response to reports of thrombosis with thrombocytopenia following vaccination with the COVID-19 AstraZeneca vaccine
<b>Alert reference number</b>	2021/06
<b>Recipients of this alert</b>	Directors of Public Health, Health Protection Teams, Cell Leads, Scottish Government, Chief Medical Officers, NHS24, Immunisation Co-ordinators, FVCV PMO, FVCV Clinical Governance Group
<b>Alert status</b>	4. for action - monitoring, wider dissemination and specific measures to be taken by recipient
<b>Action required of initial recipients</b>	<ul style="list-style-type: none"> <li>• Cascade to others for action, as indicated</li> </ul>
<b>Date of issue</b>	07/04/2021
<b>Source of event information</b>	<p><a href="https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots">https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots</a></p> <p><a href="https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement">https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement</a></p>
<b>Contact</b>	Dr Claire Cameron <a href="mailto:p hs.immunisation@p hs.scot">p hs.immunisation@p hs.scot</a>
<b>Authorised by</b>	Dr Jim McMenamin, Incident Director for Covid-19
<b>HPZone context</b>	AstraZeneca Vaccine Safety

## Situation

**MHRA and JCVI have issued new advice on the safety of AstraZeneca COVID-19 vaccine. The benefits of vaccination continue to outweigh any risks but the MHRA advises careful consideration be given to people who are at higher risk of specific types of blood clots because of their medical condition. The JCVI recommends to offer alternative vaccines to adults under 30 without underlying health conditions.**

## Background

The AstraZeneca (AZ) COVID-19 vaccine was licensed for use in the UK on the 30th December 2020 and since the 4th January more than 20 million doses have been administered across the UK. The COVID-19 programme in the UK has been estimated to have prevented over 6,100 deaths in adults aged 70 years and older till the end of February with a vaccine effectiveness of a single dose against hospitalisation estimated at 80% both the Pfizer/BioNTech and the AZ vaccines (1).

As of 31st March, there have been 79 reports of thromboembolic events accompanied by thrombocytopenia, most notably a very rare and specific type of syndrome of blood clots in the cerebral veins, known as cerebral venous sinus thromboses (CVST) occurring together with low platelet counts across the UK. These have affected patients of all ages and genders. The cases are unusual because despite thrombocytopenia, there is progressive thrombosis, primarily venous, including cerebral venous sinus thrombosis and portal vein thrombosis, as well as the more usual presentations of deep vein thrombosis and pulmonary embolism. Arterial events have also been noted. Typical laboratory features include a low platelet count, very raised D-Dimer levels - above the level expected for venous thromboembolism (VTE) and inappropriately low fibrinogen. Antibodies to platelet factor 4 (PF4) have been identified and so this has similarities to heparin-induced thrombocytopenia (HIT), but in the absence of patient exposure to heparin treatment.

This is known to occur naturally although the underlying risk factors have not yet been fully established. The background rate of CVSTs is around 5-16 per million annually but there is currently limited data on the background rate of CVSTs with thrombocytopenia. It is currently estimated that the overall incidence following the AZ vaccine is around 4 per million first doses administered. Importantly thromboses are described in individuals with natural COVID-19 infection. More than a fifth of hospitalised patients with COVID-19 infection have evidence of blood clots, and the presence of these almost doubles the risk of death.

## Assessment

Based on a review of cases reported to the Yellow Card Scheme and the evidence of effectiveness of the COVID vaccines used in the UK to prevent serious complications and deaths from COVID-19 infection, the current MHRA advice remains that the overall benefits of the vaccine programme outweighs the extremely rare adverse events reported to date following the AZ vaccine.

The Joint Committee on Vaccination and Immunisation (JCVI) has assessed the overall risk benefit of the use of the AZ vaccine in the population. This is based on data presented by the MHRA on reported adverse events through the Yellow Card Scheme and benefits (in terms of deaths, ICU and hospital admissions averted) estimated by Public Health England. There appears to be a trend of increasing incidence of this condition with decreasing age amongst adults, with the highest incidence reported in the younger adult age groups. In contrast, the risks of serious disease associated with COVID-19 increases steeply with age, with the younger adults at the lowest risk of serious disease. Therefore, weighing the balance of benefits and risks, currently the JCVI has concluded that for adults under 30 years of age who are not in a clinical risk group, it is preferable to offer an alternative to the AZ vaccine if available.

In the UK, the MHRA are reviewing all reported cases to the [COVID-19 Yellow Card scheme](#). In order to support the case reporting, clinical review and investigation, PHE has established an electronic clinical reporting scheme collecting patient identifiable information on all suspected cases across the UK, including Scotland. All health professionals are encouraged to [report any suspected case](#) with details of the clinical presentation, dates of vaccination, vaccine product received and any underlying conditions. A data sharing process has been agreed with the MHRA which means that professionals only need to report suspected cases once through this scheme.

While the detailed case review is ongoing, it is important to ensure all health professionals are alert to relevant symptoms which require further clinical review and investigation. As the recommended management of this presenting condition differs from the usual guidance, urgent advice is being cascaded to primary care to ensure GPs are on the alert for this syndrome. It is therefore recommended that an urgent full blood count be considered in any patient presenting more than 4 days and within 28 days of coronavirus vaccination with:

- New onset of severe headache, which is getting worse and does not respond to simple painkillers
- An unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness or seizures
- New onset of unexplained pinprick bruising or bleeding
- Shortness of breath, chest pain, leg swelling or persistent abdominal pain

If you have any clinical concerns, patients should be urgently referred to hospital and to appropriate specialist services for further assessment, particularly if the symptoms are unexplained and present in combination with thrombocytopenia. Further guidance for secondary care are available [here](#).

Mild flu-like symptoms, including headache, chills and fever remain one of the most common side effects of any COVID-19 vaccine. These generally appear within a few hours and resolve within a day or two.

In order to support the ongoing investigation led by the MHRA, a UK-wide national standard incident has been declared. This is being led by PHE as an incident response to support with:

- Case reporting and data collection
- Laboratory investigation of suspected cases including checking COVID antibody status
- Epidemiological investigation
- Communications – public and health professionals

Further information will be coming from Public Health Scotland and other agencies including PGDs and a new Green Book chapter.

## Recommendations

NHS Boards are asked to note the current information and guidance for primary and secondary care. NHS Boards are requested to cascade this briefing note to local primary and secondary care services to ensure colleagues are aware of the available guidance and how to report suspected cases.

An increase in calls requesting advice are expected. Immunisation teams are requested to note the current information and guidance and to cascade this briefing note which includes additional specific guidance developed for primary care with their local primary care teams. Additional resources will be published to support Immunisation teams in response to enquiries they may receive. Secondary care teams will find information [here](#).

COVID-19 immunisation services are asked to ensure that people receiving a COVID-19 vaccine are given the patient vaccination leaflet 'COVID-19 vaccination and blood clotting information leaflet', which should accompany the usual 'COVID-19 adult leaflet' before considering vaccination and then be given 'What to expect after vaccination' after vaccination and know to seek appropriate healthcare assistance if required. These resources have been updated to reflect that latest guidance. Primary care services should be aware of these symptoms and refer to secondary care as appropriate following assessment. Updated versions of the above leaflets will be available [here](#) from 8th April.

## References

(1) PHE monitoring of the effectiveness of COVID-19 vaccination [PHE monitoring of the effectiveness of COVID-19 vaccination - GOV.UK \(www.gov.uk\)](#); [COVID-19 vaccine linked to a reduction in transmission - News - Public Health Scotland](#); [Vaccine linked to reduction in risk of COVID-19 admissions to hospitals - News - Public Health Scotland](#)

## Sources of information

Coronavirus Yellow Card reporting site [Official MHRA side effect and adverse incident reporting site for coronavirus treatments and vaccines | Coronavirus \(COVID-19\)](#)

Public Health England: Thrombotic events with thrombocytopenia following immunisation to COVID-19 [https://cutt.ly/haem\\_AE](https://cutt.ly/haem_AE)

Guidance produced from the Expert Haematology Panel (EHP) focussed on syndrome of Thrombosis and Thrombocytopenia occurring after coronavirus Vaccination [Guidance produced from the Expert Haematology Panel \(EHP\) focussed on syndrome of Thrombosis and Thrombocytopenia occurring after coronavirus Vaccination | British Society for Haematology \(b-s-h.org.uk\)](#)

MHRA issues new advice, concluding a possible link between COVID-19 Vaccine AstraZeneca and extremely rare, unlikely to occur blood clots <https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots>

Use of the AstraZeneca COVID-19 vaccine: JCVI statement <https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement>

COVID-19 vaccination and blood clotting resources <https://www.gov.uk/government/collections/covid-19-vaccination-and-blood-clotting>

Blood Clotting following COVID-19 Vaccination - Information for Health Professionals <https://www.gov.uk/government/collections/covid-19-vaccination-and-blood-clotting>