1. COVID-19 Vaccine AstraZeneca and thromboembolic events with concurrent low platelet counts

The Medicines and Healthcare products Regulatory Agency (MHRA) and the Government's independent expert advisory body, the Commission on Human Medicines (CHM), is conducting a thorough review of reports of extremely rare thromboembolic events including cerebral venous sinus thrombosis (CVST) occurring in conjunction with thrombocytopaenia following the AstraZeneca COVID-19 vaccine. This notification informs you of the current status of the review and treatment guidance and provides information on how to report suspected cases.

By 31st March 2021, MHRA had received Yellow Card reports of 79 cases of thromboembolic events with concurrent thrombocytopaenia following vaccination with COVID-19 Vaccine AstraZeneca, 44 cases of cerebral venous sinus thrombosis (CVST) with thrombocytopaenia and 35 cases of other major thrombotic events, including one arterial, with thrombocytopaenia. These cases occurred in 51 women and 28 men, aged from 18 to 79 years. The estimated number of doses of vaccine administered in the UK by 31st March was 20.2 million giving an overall case incidence of 4.4 per million doses.

All reports are being followed up for clinical details and 19 cases have had a fatal outcome. Some cases have positive platelet factor 4 (PF4) antibodies and elevated D-dimer. In reports where this information was provided, all cases occurred after a first dose of the vaccine.

The CHM has carefully considered all available data, noting the need for further clinical details on the case reports and that data are also lacking on the background rate of CVST, including during the pandemic because Covid infection has been associated with thrombotic events. The CHM has advised that the currently available evidence does not establish a causal association between the AstraZeneca COVID-19 Vaccine and these events, but investigations (epidemiological and mechanistic) need to continue. The CHM's advice remains that the overall benefits of the vaccines against COVID-19 continue to outweigh any risks in the vast majority of people, and that the evidence does not currently support excluding any age group from vaccination.

In view of the available data, COVID-19 Vaccine AstraZeneca is contraindicated in patients with a history of major venous and arterial thrombosis with thrombocytopenia.

COVID-19 Vaccine AstraZeneca should only be given to patients with a history of CVST, acquired or hereditary thrombophilia, heparin-induced thrombocytopenia, or antiphospholipid syndrome when the benefits outweigh any potential risks.

Because these events are extremely rare and a comparatively small number of second doses have been given, it is currently not known how frequently these events may occur following a second dose of the vaccine. As a precaution, anyone who experienced cerebral or other major blood clots occurring with low levels of platelets after their first vaccine dose of COVID-19 Vaccine AstraZeneca should not have their second dose.

Anyone who did not have these side effects should come forward for their second dose when invited.

COVID-19 vaccine advice in pregnancy remains that pregnant women should discuss with their healthcare professional whether the benefits of having the vaccine outweigh the risks for them, noting the extremely rare risk of thromboembolic events with concurrent thrombocytopaenia referred to above.

The MHRA recently confirmed that the evidence to date does not suggest that the COVID-19 Vaccine AstraZeneca causes venous thromboembolism without a low platelet count.

Treatment guidance

Further information is available from the British Society for Haematology guidance issued on thrombosis and thrombocytopaenia possibly occurring after vaccination with COVID-19 vaccines. This includes information on presentation and typical laboratory features, and treatment recommendations. The guidance also includes advice on recommended investigations for possible cases.

Advice for the public

While the MHRA continues to investigate these cases, as a precautionary measure anyone that develops symptoms after vaccination is advised to seek prompt medical advice, such as:

• shortness of breath, chest or persistent abdominal pain, leg swelling
• blurred vision, confusion or seizures
• unexplained pin-prick rash or bruising beyond the injection site

Furthermore anybody with new onset of severe or persistent headache that does not respond to simple painkillers starting four days or more after vaccination should speak to their doctor.

Reporting advice for healthcare professionals

Patients and healthcare professionals should continue to report any side effects from vaccines to the MHRA through the Coronavirus Yellow Card site https://coronavirus-yellowcard.mhra.gov.uk/

If you see a patient who has suspected venous or arterial thrombosis *together with* a low platelet count following vaccination, you should report this to the dedicated Coronavirus Yellow Card site so that this information can be used for the ongoing monitoring of vaccine safety. For such reports of blood clots, it is essential to provide information that is as detailed and accurate as possible, to assist with the assessment of these cases. Please report:

- any imaging used to confirm the diagnosis of the thromboembolic event
- platelet counts
- D-dimer tests
- any tests for platelet factor 4 antibody.
- concomitant medications

Ongoing monitoring and review of reports will continue and further updates will be given as appropriate.

If you have any questions or require further assistance or clarification, please contact yellow.card@mhra.gov.uk and the YC helpline number 0800 731 6789

Further information will be provided as this review progresses.

1.1.1 The MHRA advice can be accessed here