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HPRA DRUG SAFETY
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COVID-19 Vaccine AstraZeneca® – conclusion of EMA review of thromboembolic events following vaccination

The European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) has concluded its preliminary review of a signal of thromboembolic events in people vaccinated with COVID-19 Vaccine AstraZeneca® as of yesterday 18 March 2021.

The EMA concluded that the benefits of the vaccine in combating the, still widespread, threat of COVID-19 (which itself results in clotting problems and may be fatal) continue to outweigh the risks. Although the vaccine is not associated with an increase in the overall risk of blood clots (thromboembolic events) in those who receive it, the vaccine may be associated with very rare cases of blood clots associated with thrombocytopenia, including rare cases of Cerebral Venous Sinus Thrombosis (CVST). These are rare reports, with 18 cases of CVST and 7 cases of Disseminated Intravascular Coagulation (DIC) assessed as part of the EMA review. Approximately 20 million people in the UK and EEA had received the vaccine as of March 16 2021.

A causal link with the vaccine has not been established, but is possible, and will therefore be further analysed.

Overall, the number of thromboembolic events reported after vaccination, both in clinical trials before licensing and in reports after rollout of vaccination campaigns was lower than that expected in the general population, confirming that there is no increase in overall risk of blood clots.

The PRAC looked in detail at reports of DIC and CVST reported from across the EU, including 9 fatal cases. Most of these occurred in people under 55 and the majority were in women, although this may reflect the increased use within the EU of the vaccine in this population. Because these events are rare, and COVID-19 itself often causes coagulation disorders in patients, it is difficult to estimate a background rate for these events in people who have not had the vaccine. However, based on pre-COVID figures it was calculated that less than one reported case of DIC might have been expected by 16 March 2021 among people under 50 within 14 days of receiving the vaccine, whereas five cases had been reported. Similarly, on average 1.35 cases of CVST might have been expected among this age group whereas by 16 March 2021 there had been 12 cases reported. A similar imbalance was not visible in the older population given the vaccine.

Given the vaccine's proven efficacy in preventing hospitalisation and death from COVID-19, the PRAC concluded that the benefits of COVID-19 Vaccine AstraZeneca® outweighs the extremely small likelihood of developing DIC or CVST. However, given the findings, healthcare professionals and vaccine recipients should be aware of the remote possibility of developing such syndromes. Recipients should be advised to seek immediate medical attention should they develop symptoms as outlined below and should inform healthcare professionals of their recent vaccination.

While further analysis is ongoing, the product information for the vaccine will be updated to include more information on these risks. A direct healthcare professional communication (DHPC) will be sent to healthcare professionals and will also be published on the HPRA website.

There is no evidence of a problem related to specific batches of the vaccine.

Advice to healthcare professionals

- Healthcare professionals (HCPs) should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia following vaccination with COVID-19 Vaccine AstraZeneca®.
- HCPs should instruct those vaccinated to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg swelling, persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms including severe or persistent headaches and blurred vision after vaccination, or who experiences skin bruising (petechia) beyond the site of vaccination after a few days, should seek prompt medical attention.

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Key messages

Rare cases of thrombosis and thrombocytopenia, some presenting as mesenteric vein or cerebral vein/cerebral venous sinus thrombosis, have been reported in persons who had recently received COVID-19 Vaccine AstraZeneca®, mostly occurring within 14 days after vaccination. The number of these particular reported events exceeds those expected, and causality, although not confirmed, cannot therefore be excluded. There is no association with thromboembolic disorders overall.

The benefit-risk balance of the medicine remains positive, however, healthcare professionals should be alert to possible cases of thromboembolism, DIC or CVST occurring in vaccinated individuals and advise recipients as to the symptoms and signs that require immediate medical attention.

All reports of suspected adverse reactions should be reported to the HPRA via the available methods at www.hpra.ie/report.

Further information on the review is available on the EMA website and the HPRA website, as well as updated advice for patients and healthcare professionals in the product information.

Adverse reactions can be reported to the HPRA by members of the public, carers or healthcare professionals via www.hpra.ie/report. Reporting adverse reactions to the HPRA supports continuous monitoring of safe and effective use of COVID-19 vaccines. When reporting, as much information as is known should be provided, and where possible, the vaccine batch number should be included.

The HPRA cannot provide clinical advice on individual cases. Members of the public should contact their health care professional (their doctor or pharmacist) with any medical concerns they may have.

Current product information and updates to those documents, as well as safety communications and information on regulatory actions in relation to medicines are published on our website www.hpra.ie. You may register here with our website to receive notifications regarding alerts issued by the HPRA.

Correspondence/comments should be sent **by email only** to the Pharmacovigilance Section, Health Products Regulatory Authority, medsafety@hpra.ie.

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