EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

29 March 2021

COVID-19 vaccine safety update

VAXZEVRIA

AstraZeneca AB

Severe allergic reaction will be included in the product information as a known side effect.

A warning on very rare specific blood clot events has been included in the product information, while further investigations into a possible causal relationship with the vaccine are ongoing.

Vaccinated persons should seek immediate medical attention if symptoms of blood clotting and/or bleeding occur.

The benefits of Vaxzevria in preventing COVID-19 continue to outweigh the risks; and there are no recommended changes regarding the use of this vaccine.

Safety updates provide the outcomes of the assessment of emerging data since marketing authorisation for COVID-19 vaccines. The assessments are carried out by EMA's safety committee (Pharmacovigilance Risk Assessment Committee [PRAC]). The safety updates are published regularly at COVID-19 vaccines: authorised.

All published safety updates for Vaxzevria (previously known as COVID-19 Vaccine AstraZeneca) are available at Vaxzevria: safety updates.

This safety update is the first update after the marketing authorisation in the European Union (EU).

Since its marketing authorisation in the EU on 29 January 2021 until 25 March 2021, more than 10 million doses of Vaxzevria have been administered in the EU/EEA[1].

1. Updates on safety of Vaxzevria

At its meetings held 8 to 11 March, on 18 March and on 25 March 2021, PRAC assessed all new safety data emerging worldwide, including the latest Summary Monthly Safety Report[2] from the marketing authorisation holder, and concluded that the benefit-risk balance of Vaxzevria remains positive.

Specifically, the following was concluded by PRAC in relation to:

Anaphylaxis and other allergic reactions

Cases of suspected anaphylaxis (severe allergic reaction) have been reported for Vaxzevria from its use in vaccination campaigns. In particular, 41 cases reported to EudraVigilance (see section 3) from around 5 million vaccinations in the United Kingdom (UK) (data lock point: 16-February-2021) were assessed at the PRAC meeting held 8 to 11 March 2021[3].

Following PRAC assessment, anaphylaxis and other allergic (hypersensitivity) reactions will now be included in the EU product information as known side effects. The frequency of these side effects, for inclusion in the EU product information, could not yet be estimated. Anaphylaxis continues to be closely monitored.

Information on the clinical management of anaphylaxis is already available in the product information and does not require updating.

[1] The European Centre for Disease Prevention and Control (ECDC) collects these data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.
[2] Summary Monthly Safety Reports will be compiled by the marketing authorisation holders for COVID-19 vaccines to support timely and continuous benefit-risk evaluations. These reports complement the submission of Periodic Safety Update Reports (PSURs).
[3] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 8-11 March 2021.

Embolic and thrombotic events

Cases of embolic and thrombotic events (formation of blood clots in the blood vessels) have been reported for Vaxzevria from its use in vaccination campaigns.

Following discussions during and after its meeting held 8 to 11 March 2021, on 18 March 2021 PRAC conducted a preliminary assessment - involving experts in blood disorders - of the available evidence from case reports in EudraVigilance (see section 3), quality, clinical, pre-clinical and scientific literature data, and data from the marketing authorisation holder. PRAC concluded the following:

There was no evidence of a problem with manufacturing or product quality related to the vaccine batches specified in the case reports. This was based on a quality assessment carried out within the EU regulatory network. This included the information from the official medicines control laboratory release certificates. These comprise independent testing and checking of the manufacturer's key test results before release of any batch of COVID-19 vaccines to the EU/EEA market.

Overall, the number of cases of embolic and thrombotic events after vaccination reported to EudraVigilance (see section 3) in relation to the number of people vaccinated was lower than the rate of such events in the general population.

However, Vaxzevria could possibly be associated with very rare cases of specific embolic and thrombotic events in combination with low levels of blood platelets (thrombocytopenia) and related bleeding. These events include disseminated intravascular coagulation (DIC) (where blood clots occur in multiple blood vessels) and cerebral venous sinus thrombosis (CVST) (where blood clots in the brain's venous sinuses prevent blood from draining out of the brain).

In the reported cases, including some that resulted in death, these events occurred within 14 days after vaccination. They occurred mostly in people under 55 years of age, the majority of whom were women. However, these patient characteristics could reflect the higher proportion of such individuals offered Vaxzevria in vaccination campaigns. As part of the preliminary assessment, the number of cases reported were compared to rates for these events applicable to the general EU population before the SARS-Cov-2 pandemic. This comparison showed increased numbers in vaccinated people. Such imbalances in numbers of cases between the general and vaccinated populations were not visible for the older age groups.

A causal link of DIC and CVST with the vaccine is not proven but cannot be excluded and requires further investigation.

People vaccinated with Vaxzevria should seek immediate medical attention if symptoms of blood clotting occur and inform healthcare professionals of their recent vaccination. Such symptoms include shortness of breath, chest or persistent abdominal pain, leg swelling, severe or persistent

headache, blurred vision, persistent bleeding, and skin bruising or round, pinpoint spots beyond the site of vaccination appearing after a few days.

The product information for Vaxzevria has been updated with this warning, and a direct healthcare professional communication (DHPC) has been sent out to raise awareness among healthcare professionals[4].

Based on all available data on embolic and thrombotic events, PRAC considered that the benefits of Vaxzevria in preventing COVID-19 and related death continue to outweigh the risks, and that this vaccine can be used while further data collection and assessment are ongoing[5].

Immune thrombocytopenia (ITP)

For all COVID-19 vaccines used in the EU, a specific PRAC assessment of immune thrombocytopenia (ITP, low blood platelet levels that can lead to bruising and bleeding) as a suspected side effect has been initiated. At this stage of the assessment, a causal association of ITP with any COVID-19 vaccine has not been established[6].

2. Other information for Vaxzevria

Vaxzevria (previously COVID-19 Vaccine AstraZeneca) is a vaccine that was authorised in the EU on 29 January 2021 for use in people aged 18 years and older to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death.

Vaxzevria contains an adenovirus that has been modified to carry molecules of DNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The spike protein does not cause COVID-19. The adenovirus cannot reproduce and does not cause viral disease.

Before Vaxzevria was granted an EU marketing authorisation, the efficacy and safety of the vaccine were assessed through pre-clinical studies and large clinical trials. More than 12,000 participants have been given the vaccine in clinical trials.

Like all medicines, this vaccine can cause side effects, although not everybody will experience them. The most common side effects known for Vaxzevria are usually mild or moderate and get better within a few days after vaccination.

More information on how Vaxzevria works and its use is available in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

[4] See DHPC 'COVID-19 Vaccine AstraZeneca: Risk of thrombocytopenia and coagulation disorders'.
[5] See EMA Public Health Communication of 18 March 2021.
[6] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 8-11 March 2021.

Information in all EU/EEA languages is available in the product information, which includes the summary of product characteristics and the package leaflet.

3. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on Vaxzevria is collected and promptly reviewed. This is in line with the pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

Collecting case reports of suspected side effects

The EU regulatory network continuously monitors reports of suspected side effects observed in vaccinated individuals. These case reports are collected and recorded in EudraVigilance, a system operated by EMA for managing and analysing information on suspected side effects of medicines.

Vaccinated individuals and healthcare professionals should report suspected side effects via the national reporting systems, which also contribute to EudraVigilance. For more information, see Reporting side effects. Information on how to report side effects in your Member State is available in the package leaflet and the list of national competent authorities.

You may visit EudraVigilance – European database of suspected drug reaction reports and search for "COVID-19 VACCINE ASTRAZENECA (CHADOX1 NCOV-19)" to see all suspected side effects reported for Vaxzevria in the EU/EEA. Please note that these reports describe suspected side effects in individuals, i.e. these events may not necessarily have been caused by, or be otherwise related to, the vaccine.

By 22 March 2021, 28 041 cases of suspected side effects reported for Vaxzevria from the EU/EEA had been included and monitored in EudraVigilance, relating to around 9.2 million doses administered[7].

Planned and ongoing studies

The company that markets Vaxzevria will continue to provide results from the main clinical trials, which are ongoing. It will also conduct additional studies to monitor the safety and effectiveness of the vaccine as it is used in vaccination campaigns and other clinical practice. For the list of planned and ongoing safety studies for Vaxzevria, see the risk management plan.

[7] See EMA Public stakeholder meeting: approval, safety monitoring and impact of COVID-19 vaccines in the EU on 26 March 2021.

A paediatric investigation plan (PIP) for Vaxzevria is in place. This describes how the company will collect data on the vaccine's efficacy and safety for its potential use in children.

In addition, EMA is coordinating observational studies in Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

European Medicines Agency
Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact
Telephone +31 (0)88 781 6000

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