6 October 2021

COVID-19 vaccine safety update

VAXZEVRIA

AstraZeneca AB

The safety of Vaxzevria is continuously monitored and safety updates are regularly provided to the public. This document outlines the outcomes from the assessment of emerging worldwide safety data carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (see section 1). It also contains high-level information from the reporting of suspected adverse reactions, which PRAC takes into account in its assessments (see section 2).

This safety update follows the update of 8 September 2021.

Main outcomes from PRAC's latest safety assessment

Immune thrombocytopenia (an autoimmune condition with low blood platelet levels) will be added to the product information as a side effect of Vaxzevria, together with a warning and advice about thrombocytopenic disorders.

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for Vaxzevria are available at Vaxzevria: safety updates.

Since its marketing authorisation in the European Union (EU) on 29 January 2021 until 30 September 2021, more than 68.7 million doses of Vaxzevria have been administered in the EU/EEA[1].

1. Updates on safety assessments for Vaxzevria

During its meeting held 27 to 30 September 2021, PRAC assessed new safety data (see section 2 'How safety is monitored').

Thrombocytopenia including immune thrombocytopenia (ITP)

Update to the Vaxzevria product information

PRAC finalised its assessment of cases reporting thrombocytopenia, including immune thrombocytopenia (ITP), after vaccination with Vaxzevria, taking into consideration discussions in the scientific literature[2]. Thrombocytopenia (low blood platelet levels) is a known common side effect of Vaxzevria[3].

ITP is a specific type of thrombocytopenia in which the immune system mistakenly targets blood cells called platelets that are needed for normal blood clotting (very low levels of blood platelets can be associated with bleeding and serious health problems).

PRAC assessed all available data and recommended updating the product information to include ITP as a side effect of Vaxzevria. The frequency category will be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported spontaneously by healthcare professionals

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.
[2] Simpson CR et al. First-dose ChAdOx1 and BNT162b2 COVID-19 vaccines and thrombocytopenic, thromboembolic and hemorrhagic events in Scotland. Nat Med. 27: 1290–1297;9 June 2021 (epub).; Pottegård A et al. Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study. Br Med J. 373: n1114; 5 May 2021 (epub).; Trogstad L et al. Association between ChAdOx1 nCoV-19 vaccination and bleeding episodes: large population-based cohort study. Research Square; 2021 (preprint).
[3] See safety update for Vaxzevria of 14 April 2021

or patients. Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

PRAC also agreed on a direct healthcare professional communication (DHPC) to raise awareness among healthcare professionals. Following agreement of the Committee for Medicinal Products for Human Use (CHMP) on the product information update and the DHPC, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holder according to an agreed communication plan. The DHPC will be available on a dedicated page on the EMA website and in the national DHPC registers of EU Member States[4].

Healthcare professionals should be aware that:

- cases of thrombocytopenia, including ITP, have been reported with Vaxzevria, typically within the first four weeks after vaccination;
- very rarely, these cases of thrombocytopenia presented with very low platelet levels (<20,000 per µL) and/or were associated with bleeding;
- some of these cases occurred in individuals with a history of ITP;
- cases with fatal outcome have been reported;
- if an individual has a history of a thrombocytopenic disorder, such as ITP, the risk of developing low platelet levels should be considered before administering the vaccine and platelet monitoring is recommended after vaccination.

Vaccinated individuals should:

- seek immediate medical attention if they experience unexplained bleeding or skin bruising or pinpoint round spots beyond the site of vaccination, appearing a few days after vaccination.

2. 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).

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes Monthly Summary Safety Reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled for at least the first six months of marketing (afterwards, pandemic summary safety reports may cover time periods

[4] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 27 - 30 September 2021

longer than a month). These reports complement the submission of Periodic Safety Update Reports (PSURs).

Case reports of suspected side effects

Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system. Healthcare professionals and vaccinated individuals are encouraged to report to their national competent authorities all suspected side effects individuals may have experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via EudraVigilance – European database of suspected drug reaction reports in all EU/EEA languages. Search for "COVID-19 VACCINE ASTRAZENECA (CHADOX1 NCOV-19)" to see all suspected side effect cases reported for Vaxzevria.

As of 30 September 2021, a total of 199,999 cases of suspected side effects with Vaxzevria were spontaneously reported to EudraVigilance from EU/EEA countries; 1,211 of these reported a fatal outcome[5,6]. By the same date, more than 68.7 million doses of Vaxzevria had been given to people in the EU/EEA[7].

These reports describe suspected side effects in individuals, i.e. medical events observed following the use of a vaccine. The fact that someone has had a medical issue or died after vaccination does not necessarily mean that this was caused by the vaccine. This may have been caused, for example, by health problems not related to the vaccination.

The EU regulatory network continuously monitors EudraVigilance to detect any new safety issues. EudraVigilance relies on individual healthcare professionals and patients to report their own experience. The monitoring detects unusual or unexpected patterns in the reports received for further investigation and risk assessment. EMA's detailed assessments take into

[5] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).
[6] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effects. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.
[7] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

account all available data from all sources to draw a robust conclusion on the safety of the vaccine. These data include clinical trial results, reports of suspected side effects in EudraVigilance, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

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.

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 EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

3. 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 had 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 all EU/EEA languages in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

The full product information with the summary of product characteristics and the package leaflet is also available in all EU/EEA languages.

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