



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 April 2021

COVID-19 vaccine safety update

VAXZEVRIA

AstraZeneca AB

Very rare, potentially serious, events of unusual blood clots in combination with low blood platelet levels have been confirmed as a new side effect of Vaxzevria.

There are no recommended changes to the product information regarding how to use this vaccine; Vaxzevria is effective in preventing COVID-19.

Safety updates provide information about the assessments of emerging worldwide 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 are available at [Vaxzevria: safety updates](#).

This safety update follows the last update of 29 March 2021.

Since its marketing authorisation in the the European Union (EU) on 29 January 2021 until 9 April 2021, almost 17 million doses of Vaxzevria have been administered in the EU/EEA¹.

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.

1. Updates on safety of Vaxzevria

At its meeting held 6 to 9 April 2021, PRAC assessed the following in relation to:

Embolic and thrombotic events with a focus on thrombosis with thrombocytopenia

PRAC continued its assessment of cases of embolic and thrombotic events (blood clots obstructing blood vessels) reported for Vaxzevria from its use in vaccination campaigns, taking into account advice from an ad hoc expert group including haematologists, neurologists and epidemiologists, convened by EMA on 29 March 2021².

PRAC's investigation included an in-depth review of cases of embolic and thrombotic events and thrombocytopenia (low levels of blood platelets) reported from clinical trials and vaccination campaigns to EudraVigilance (see section 3). In its review, PRAC paid special attention to the information on the sex, age, risk factors, COVID-19 diagnosis (if available), and the time to onset and outcome of the reported events. The investigation also included an observed-to-expected analysis and a scientific literature review.

Taking into account all available evidence and advice, PRAC concluded that a causal relationship between vaccination with Vaxzevria and very rare cases of thrombosis together with thrombocytopenia, sometimes accompanied by bleeding, is plausible. The reported thromboses with thrombocytopenia include venous thrombosis, also in unusual sites such as cerebral venous sinus thrombosis (CVST) (where blood clots in the brain's venous sinuses prevent blood from draining out of the brain) and splanchnic vein thrombosis (which involves one or more veins in the abdomen [belly]), as well as arterial thrombosis. Although such side effects are very rare, the reported case numbers exceeded what is seen in the general population. The majority of these cases occurred within 14 days after vaccination and mostly in women under 60 years of age; some cases had a fatal outcome. Based on the available data, no specific risk factors were identified³.

PRAC agreed that the product information for Vaxzevria should be updated with this assessment and specify thrombocytopenia as a new common side effect (occurring in less than 1 in 10 persons) and thrombosis in combination with thrombocytopenia as a new very rare side effect (occurring in less than 1 in 10,000 persons).

In clinical trials, thrombocytopenia was mainly described as a mild to moderate decrease in the platelet count ($>100,000$ Pt/mm³) measured by

² See [EMA Public Health Communication of 25 March 2021](#) and [31 March 2021](#)

³ See [EMA Public Health Communication of 7 April 2021](#)

laboratory testing and was not associated with any clinical signs or symptoms. A transient but sometimes profound fall in platelet counts has also been reported after immunisation with other vaccines⁴.

Regarding thrombosis in combination with thrombocytopenia, the allocated frequency category 'very rare' is the category with the lowest frequency defined for regulatory labelling of any side effect in a product information. From vaccination campaigns, 62 cases of CVST and 24 cases of splanchnic vein thrombosis were reported in EudraVigilance (see section 3) from around 25 million people vaccinated with Vaxzevria in the EU/EEA and the United Kingdom (data lock point: 22 March 2021)⁵.

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. This information was already included in the [product information](#) in March 2021.

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia and inform vaccinated people accordingly. A further direct healthcare professional communication (DHPC) has been sent out to raise awareness among healthcare professionals.

A number of studies will be put in place to identify the exact pathophysiological mechanism for these embolic and thrombotic events and to estimate their frequency more precisely.

The use of Vaxzevria should be in accordance with official national recommendations.

Capillary leak syndrome

PRAC assessed five suspected cases of capillary leak syndrome (fluid leaks from smaller vessels with rapid fall in blood pressure and tissue swelling) reported to EudraVigilance (see section 3) from the EU/EEA and the United Kingdom (UK) relating to about 34 million vaccine doses administered by 4 April 2021 in both these territories⁶. PRAC requested the marketing authorisation holder to review data from all pre-clinical, clinical trial, post-authorisation and scientific literature sources for

⁴ Wise RP, Bonhoeffer J, Beeler J, Donato H, Downie P, Matthews D, Pool V, Riise-Bergsaker M, Tapiainen T, Varricchio F; Brighton Collaboration Thrombocytopenia Working Group. Thrombocytopenia: case definition and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2007;25: 5717-5724.

⁵ See [Meeting Highlights from the Pharmacovigilance Risk Assessment Committee \(PRAC\) 6-9 April 2021](#)

⁶ For the latest UK data, see [Coronavirus vaccine – weekly summary of Yellow Card reporting](#)

further assessment by PRAC. At this stage of the assessment, a causal relationship of this syndrome with Vaxzevria has not been established⁷.

Anaphylaxis and other hypersensitivity reactions

PRAC assessed new information for the known side effect anaphylaxis (severe allergic reaction) and for other suspected hypersensitivity reactions (allergic reactions) reported for Vaxzevria. PRAC requested further data reviews from the marketing authorisation holder for assessment by PRAC.

Information on the clinical management of anaphylaxis is already available in the [product information](#).

Pain, urticaria and influenza-like symptoms

PRAC is keeping up-to-date the [risk management plan](#) in relation to an ongoing review of clinical trial data by the [Committee for Medicinal Products for Human Use](#) (CHMP) assessing whether pain in the extremity (limb), abdominal (belly) pain, urticaria (raised, red and itchy skin rash) and influenza-like symptoms may be side effects of Vaxzevria.

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.

⁷ See [Meeting Highlights from the Pharmacovigilance Risk Assessment Committee \(PRAC\) 6-9 April 2021](#)

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.

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 suspected side effects](#). Information on how to report in your Member State is available in the [package leaflet](#) and via 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.

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 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

