EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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COVID-19 vaccines safety update

Comirnaty (BioNTech Manufacturing GmbH)
COVID-19 Vaccine Janssen (Janssen-Cilag International NV)
Nuvaxovid (Novavax CZ, a.s.)
Spikevax (Moderna Biotech Spain, S.L.)
Vaxzevria (AstraZeneca AB)

Marketing authorisation withdrawal

Vaxzevria was withdrawn from the EU market at the request of the company for commercial reasons. The withdrawal does not affect the information provided in this safety update.

The safety of authorised COVID-19 vaccines is continuously monitored, and updated information is regularly provided to the public.

Safety updates outline the outcomes from assessments of emerging worldwide safety data carried out mainly by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (section 1). They also outline how safety is monitored and contain high-level information on suspected adverse reaction reports, which PRAC takes into account in its assessments (section 2).

This safety update follows the update of 17 March 2022 and reflects the main assessment outcomes of the PRAC meetings held 4 to 7 April 2022.

EMA confirms that the benefits of all currently authorised COVID-19 vaccines continue to outweigh their side effects, given the risk of COVID-19 illness and related complications, including hospitalisation and death.

[1] This document was updated on 7 May 2024 to include a statement on the withdrawal of Vaxzevria.

Key messages from the latest safety assessments

No updates to the product information are currently recommended for any of the authorised COVID-19 vaccines.

1. Latest safety assessments

Auto-immune hepatitis (AIH)

No evidence for a causal relationship with Comirnaty or Spikevax

An assessment of whether vaccination with Comirnaty or Spikevax can cause auto-immune hepatitis (AIH) has been completed. PRAC has concluded that the currently available evidence does not support a causal association between the vaccines and this condition.

AIH is a serious chronic inflammatory condition in which the immune system attacks and damages the liver. Signs and symptoms of AIH vary from person to person and may include yellowing of the skin (jaundice), build-up of fluid in the legs (oedema) or belly (ascites) and gastrointestinal symptoms.

Further information can be found in the PRAC highlights of April 2022.

Corneal graft rejection (CGR)

Assessment started for Comirnaty, Spikevax and Vaxzevria

PRAC started an assessment of corneal graft rejection (CGR) to establish whether it may be a side effect of COVID-19 vaccines (Comirnaty, Spikevax and Vaxzevria). CGR occurs when the body's immune system mistakenly attacks the donor cornea (the transparent layer in front of the eye) that has replaced a damaged or diseased one.

The assessment follows a very small number of cases of CGR reported after vaccination with Comirnaty, Spikevax and Vaxzevria in the medical literature and EudraVigilance. 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.

Corneal transplantation is a relatively common procedure and although it generally has a high success rate, symptoms of rejection may occur in about 10% of corneal transplants.

PRAC will collect and assess all available data, including data from the marketing authorisation holders, to determine whether corneal graft rejection may be caused by Comirnaty, Spikevax or Vaxzevria. To date, no case reports have been received for COVID-19 Vaccine Janssen or Nuvaxovid.

Ongoing assessments of all EMA authorised vaccines have not raised any further safety concerns by PRAC.

Background information on the vaccines

Comirnaty (BioNTech Manufacturing GmbH)

The initial marketing authorisation for Comirnaty in the EU was issued on 21 December 2020. Information on how Comirnaty works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

About 598 million doses of Comirnaty in adults and 26.7 million doses of Comirnaty in children and adolescents (below 18 years of age) were administered in the EU/EEA from authorisation to 3 April 2022.[2]

COVID-19 Vaccine Janssen (Janssen-Cilag International NV)

The initial marketing authorisation for COVID-19 Vaccine Janssen in the EU was issued on 11 March 2021. Information on how COVID-19 Vaccine Janssen works is provided in the medicine overview (in all EU/EEA languages); full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages)

About 19.3 million doses of COVID-19 Vaccine Janssen were administered to adults in the EU/EEA from authorisation to 3 April 2022.[2]

[2] 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.

Nuvaxovid (Novavax CZ, a.s.)

The initial marketing authorisation for Nuvaxovid in the EU was issued on 20 December 2021. Information on how Nuvaxovid works is provided in the medicine overview (in all EU/EEA languages); full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

About 149,000 doses of Nuvaxovid were administered to adults in the EU/EEA from authorisation to 3 April 2022.[2]

Spikevax (Moderna Biotech Spain, S.L.)

The initial marketing authorisation for Spikevax in the EU was issued on 06 January 2021. Information on how Spikevax works is provided in the medicine overview (in all EU/EEA languages). Full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

About 153 million doses of Spikevax in adults and 1.9 million doses of Spikevax in children and adolescents (below 18 years of age) were administered in the EU/EEA from authorisation to 03 April 2022.[2]

Vaxzevria (AstraZeneca AB)

The initial marketing authorisation for Vaxzevria in the EU was issued on 29 January 2021. Information on how Vaxzevria works is provided in the medicine overview (in all EU/EEA languages); full information on the vaccine, including all identified side effects and advice on how to use it, is available in the product information (in all EU/EEA languages).

About 69 million doses of Vaxzevria were administered to adults in the EU/EEA from authorisation to 03 April 2022.[2]

2. How safety is monitored

Before COVID-19 vaccines were granted EU marketing authorisation, the efficacy and safety of the vaccines were assessed in pre-clinical studies and large clinical trials.

All relevant new information emerging worldwide on the vaccines since marketing authorisation is collected and promptly assessed. 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).

EMA's detailed assessments take into account available data from all sources to draw robust conclusions on the safety of the vaccines. These data include clinical trial results, reports of suspected side effects, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

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 in the first months of marketing. Afterwards, summary safety reports may cover time periods longer than a month or may not be necessary anymore. Summary safety reports complement 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).

As of 3 April 2022, EudraVigilance contained the following:

- Comirnaty: a total of 699,605 cases of suspected side effects spontaneously reported from EU/EEA countries; 7,637 of these reported

a fatal outcome[3,4] (by the same date about 625 million doses of Comirnaty had been given to people in the EU/EEA[2]);

- COVID-19 Vaccine Janssen: a total of 45,947 cases of suspected side effects spontaneously reported from EU/EEA countries; 308 of these reported a fatal outcome[3,4] (by the same date, about 19.3 million doses of COVID-19 Vaccine Janssen had been administered to people in the EU/EEA[2]);
- Nuvaxovid: a total of 170 cases of suspected side effects spontaneously reported from EU/EEA countries; none of these reported a fatal outcome[3,4] (by the same date, about 149,000 doses of Nuvaxovid had been administered to people in the EU/EEA[2]);
- Spikevax: a total of 193,037 cases of suspected side effects spontaneously reported from EU/EEA countries; 994 of these reported a fatal outcome[3,4] (by the same date, about 155 million doses of Spikevax had been given to people in the EU/EEA[2]);
- Vaxzevria: a total of 266,091 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,512 of these reported a fatal outcome[3,4] (by the same date, about 69 million doses of Vaxzevria had been given to people in the EU/EEA[2]).

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.

Planned and ongoing studies

The companies that market COVID-19 vaccines continue to provide results from ongoing clinical trials. They also conduct additional studies to monitor

[3] 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).

[4] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effect. 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.

the safety and effectiveness of the vaccines as they are used in vaccination campaigns and other clinical practice. For the list of planned and ongoing safety studies with COVID-19 vaccines, see the respective risk management plan: Comirnaty, COVID-19 Vaccine Janssen, Nuvaxovid, Spikevax, and Vaxzevria.

A paediatric investigation plan (PIP) is in place for each authorised COVID-19 vaccine: Comirnaty, COVID-19 Vaccine Janssen, Nuvaxovid, Spikevax, and Vaxzevria. The PIP describes how the company will collect data on the vaccine's efficacy and safety for its potential use in children. Two vaccines, Comirnaty and Spikevax, are authorised for 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.

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