EUROPEAN MEDICINES AGENCY
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COVID-19 vaccines safety update

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

Marketing authorisation withdrawals

Vaxzevria and COVID-19 Vaccine Valneva were withdrawn from the EU market at the request of the marketing authorisation holders for commercial reasons.

The withdrawals do 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 8 September 2022 and reflects the main assessment outcomes of the PRAC meeting held 26 to 29 September 2022.

[1] This document was updated on 1 December 2023 and 7 May 2024 to include statements on the withdrawal of COVID-19 Vaccine Valneva and Vaxzevria, respectively.

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.

Key messages from the latest safety assessments

For Jcovden, an update to the product information has been recommended to add facial paralysis (temporary facial drooping), including Bell's palsy, as a rare side effect (i.e. occurring in less than 1 in 1,000 persons).

1. Latest safety assessments

Comirnaty (BioNTech Manufacturing GmbH)

There are no safety updates for Comirnaty.

About 665 million doses of Comirnaty, including about 55.6 million doses in children and adolescents (below 18 years of age), were administered in the EU/EEA from authorisation to 28 August 2022.[2]

The initial conditional 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).

COVID-19 Vaccine (inactivated, adjuvanted) Valneva (Valneva Austria GmbH)

There are no safety updates for COVID-19 Vaccine (inactivated, adjuvanted) Valneva.

[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.

By 28 August 2022, COVID-19 Vaccine (inactivated, adjuvanted) Valneva had not yet been used in the EU/EEA[3]; however, use may have started after this date.

The initial, standard marketing authorisation for COVID-19 Vaccine (inactivated, adjuvanted) Valneva in the EU was issued on 24 June 2022. Information on how COVID-19 Vaccine (inactivated, adjuvanted) Valneva 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).

Jcovden (Janssen-Cilag International NV)

Facial paralysis

Update to the product information

PRAC concluded an assessment for Jcovden with a recommendation to update the product information by adding facial paralysis (temporary facial drooping, usually one-sided), including Bell's palsy, as a side effect. Based on clinical trial data, this side effect was considered to be rare (i.e. occurring in less than 1 in 1,000 persons).

About 19.4 million doses of Jcovden in adults were administered in the EU/EEA from authorisation to 28 August 2022.[3]

The initial conditional marketing authorisation for Jcovden (previously COVID-19 Vaccine Janssen) in the EU was issued on 11 March 2021. Information on how Jcovden 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).

Nuvaxovid (Novavax CZ, a.s.)

There are no safety updates for Nuvaxovid.

[3] 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.

About 271,000 doses of Nuvaxovid in adults, and none in adolescents (below 18 years of age), were administered in the EU/EEA from authorisation to 28 August 2022.[4]

The initial conditional 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).

Spikevax (Moderna Biotech Spain, S.L.)

Urticaria

Assessment ongoing

An assessment of the potential hypersensitivity reaction urticaria (hives [raised, red and itchy skin rash]) with Spikevax remains ongoing.

Hypersensitivity (allergic reactions in general) is already included in the product information.

About 158 million doses of Spikevax, including about 3.1 million doses in children and adolescents (below 18 years of age), were administered in the EU/EEA from authorisation to 28 August 2022.[4]

The initial conditional marketing authorisation for Spikevax (previously COVID-19 Vaccine Moderna) in the EU was issued on 06 January 2021; following an assessment process, it was converted into a standard marketing authorisation on 3 October 2022. 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).

[4] 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.

Vaxzevria (AstraZeneca AB)

There are no safety updates for Vaxzevria.

About 69 million doses of Vaxzevria in adults were administered in the EU/EEA from authorisation to 28 August 2022.[5]

The initial conditional marketing authorisation for Vaxzevria (previously COVID-19 Vaccine AstraZeneca) 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).

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 all 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

[5] 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.

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 11 September 2022, EudraVigilance contained the following:

- Comirnaty: a total of 919,242 cases of suspected side effects spontaneously reported from EU/EEA countries; 8,237 of these reported a fatal outcome[6,7] (by 28 August 2022, about 665 million doses of Comirnaty had been given to people in the EU/EEA[8]);
- COVID-19 Vaccine (inactivated, adjuvanted) Valneva: 1 case of suspected side effects spontaneously reported from EU/EEA countries; there was no fatal outcome[6,7] (by 28 August 2022, the vaccine had not yet been used in the EU/EEA[8]; however, use may have started after this date);
- Jcovden: a total of 57,567 cases of suspected side effects spontaneously reported from EU/EEA countries; 333 of these reported a fatal outcome[6,7] (by 28 August 2022, about 19.4 million doses of Jcovden had been administered to people in the EU/EEA[8]);
- Nuvaxovid: a total of 1,319 cases of suspected side effects spontaneously reported from EU/EEA countries; none of these reported

[6] 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).

[7] 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.

[8] 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.

a fatal outcome[9,10] (by 28 August 2022, about 271,000 doses of Nuvaxovid had been administered to people in the EU/EEA[11]);

- Spikevax: a total of 252,725 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,129 of these reported a fatal outcome[9,10] (by 28 August 2022, about 158 million doses of Spikevax had been given to people in the EU/EEA[11]);
- Vaxzevria: a total of 315,312 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,566 of these reported a fatal outcome[9,10] (by 28 August 2022, about 69 million doses of Vaxzevria had been given to people in the EU/EEA[11]).

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 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 (RMP): Comirnaty, COVID-19 Vaccine (inactivated, adjuvanted) Valneva, Jcovden, Nuvaxovid, Spikevax and Vaxzevria.

A paediatric investigation plan (PIP) is in place for each authorised COVID-19 vaccine: Comirnaty, COVID-19 Vaccine (inactivated, adjuvanted) Valneva, Jcovden, 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 and adolescents (below 18 years of age). Three

[9] 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).

[10] 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.

[11] 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.

vaccines are authorised in the EU for use in children and adolescents: Comirnaty (as of 5 years), Nuvaxovid (as of 12 years) and Spikevax (as of 6 years).

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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