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3 August 2022 Rev.1¹

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)

Update as of 3 August 2022

Possible link to myocarditis and pericarditis with Nuvaxovid

The PRAC has concluded that myocarditis and pericarditis can occur following vaccination with Nuvaxovid. This conclusion is based on a small number of reported cases.

The Committee is therefore recommending listing myocarditis and pericarditis as new side effects in the product information for Nuvaxovid, together with a warning to raise awareness among healthcare professionals and people receiving this vaccine. The Committee has also requested that the marketing authorisation holder provides additional data on the risk of these side effects occurring.

Myocarditis and pericarditis are inflammatory conditions of the heart. Symptoms can vary but often include breathlessness, a forceful heartbeat that may be irregular (palpitations), and chest pain.

¹ This document was first published on 14 July 2022; it has been updated on 3 August to add information about myocarditis and pericarditis with Nuvaxovid.

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 June 2022 and reflects the main assessment outcomes of the PRAC meeting held 04 to 07 July 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.

Key messages from the latest safety assessments

The product information of Nuvaxovid will be updated with severe allergic reaction and unusual or decreased feeling in the skin as new side effects.

The product information of Spikevax will be updated with extensive swelling of the vaccinated limb as a new side effect.

The product information of Vaxzevria will be updated with tinnitus and unusual or decreased feeling in the skin as new side effects.

1. Latest safety assessments

Comirnaty (BioNTech Manufacturing GmbH)

There are no safety updates for Comirnaty.



About 649 million doses of Comirnaty, including about 55 million doses in children and adolescents (below 18 years of age) were administered in the EU/EEA from authorisation to 26 June 2022.²

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).

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

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

By 26 June 2022, COVID-19 Vaccine (inactivated, adjuvanted) Valneva had not yet been used in the EU/EEA².

The initial 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)

There are no safety updates for Jcovden.

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. As of May 2022, exposure figures are calculated using a new method. Figures should therefore not be compared with those in the safety updates of previous months.



About 19.4 million doses of Jcovden in adults were administered in the EU/EEA from authorisation to 26 June 2022.³

The initial 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.)

Anaphylaxis

Update to the product information

Following PRAC's assessment, anaphylaxis (severe allergic reaction) will be included in the EU product information as a side effect of Nuvaxovid, together with an update of the existing advice for managing risk of anaphylaxis (see box below). The frequency category will be 'not known', as it is generally difficult to robustly estimate side effect frequencies from spontaneously reported cases of suspected side effects.

A few cases of anaphylaxis have been reported spontaneously with use of Nuvaxovid. Generally, cases reported spontaneously by a patient or healthcare professional 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.



Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination.

A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of 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. As of May 2022, exposure figures are calculated using a new method. Figures should therefore not be compared with those in the safety updates of previous months.

Paraesthesia and hypoaesthesia

Update to the product information

Following PRAC's assessment, paraesthesia (unusual feeling in the skin, such as tingling or a crawling sensation) and hypoaesthesia (decreased feeling or sensitivity, especially in the skin) will be included in the EU product information as side effects of Nuvaxovid. The frequency category will be 'not known', as it is generally difficult to robustly estimate side effect frequencies from spontaneously reported cases of suspected side effects.

Cases of paraesthesia and hypoaesthesia have been reported spontaneously with use of Nuvaxovid (189 paraesthesia and 67 hypoaesthesia cases reported worldwide from more than 1.5 million vaccine doses distributed worldwide by 31 May 2022). Generally, cases reported spontaneously by a patient or healthcare professional 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.

Myocarditis and pericarditis⁴

Assessment ongoing

In June 2022, PRAC started an assessment of myocarditis and pericarditis (inflammatory conditions of the heart) to establish whether these may be side effects of Nuvaxovid (see [safety update of June 2022](#)).

In July 2022, PRAC assessed these cases and noted that the Australian Therapeutic Goods Administration (TGA) recently added pericarditis (inflammation of lining around the heart) to the product information as a side effect of unknown frequency (see [TGA COVID-19 vaccine safety report 30-06-2022](#)).

PRAC considered that only a small number of myocarditis and/or pericarditis cases have been reported spontaneously with use of Nuvaxovid in the EU (5 EU/EEA cases reported by 31 May 2022 from about 210,000 vaccine doses administered in the EU/EEA by 15 May 2022³). Generally, cases reported spontaneously by a patient or healthcare professional 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 has requested additional information and further data from the marketing authorisation holder to finalise their assessment of myocarditis and pericarditis.

Symptoms of myocarditis and pericarditis can vary but often include breathlessness, a forceful heartbeat that may be irregular (palpitations), and chest pain. These conditions can have various causes, including viral infection as a common cause and, less commonly, autoimmune disorders. Persons experiencing the above symptoms should seek immediate medical attention to obtain treatment.

⁴ See [update](#) on page 1



About 216,000 doses of Nuvaxovid in adults were administered in the EU/EEA from authorisation to 26 June 2022.⁵

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).

Spikevax (Moderna Biotech Spain, S.L.)

Extensive swelling of the vaccinated limb

Update to the product information

Following PRAC's assessment, extensive swelling of the vaccinated limb will be included in the EU product information as a side effect of Spikevax. The frequency category will be 'not known', as it is generally difficult to robustly estimate side effect frequencies from spontaneously reported cases of suspected side effects.

Cases of extensive swelling of the vaccinated limb have been reported spontaneously with use of Spikevax (more than 3,200 EU/EEA cases reported to EudraVigilance (see section 2) by 2 May 2022). Generally, cases reported spontaneously by a patient or healthcare professional 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.

In general, extensive swelling of the vaccinated limb is a condition that does not require treatment and resolves after some days.

⁵ The [European Centre for Disease Prevention and Control](#) (ECDC) collects these exposure data from EU Member States as well as from the additional EU countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein. As of May 2022, exposure figures are calculated using a new method. Figures should therefore not be compared with those in the safety updates of previous months.



About 155 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 26 June 2022.⁶

The initial marketing authorisation for Spikevax (previously COVID-19 Vaccine Moderna) 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).

Vaxzevria (AstraZeneca AB)

Tinnitus

Update to the product information

Following PRAC's assessment, tinnitus (persistent ringing in the ears) will be included in the EU product information as a side effect of Vaxzevria. The frequency category will be 'uncommon', i.e. occurring in less than 1 in 100 vaccinated persons.

Cases of tinnitus have been reported spontaneously with use of Vaxzevria. Generally, cases reported spontaneously by a patient or healthcare professional 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. In addition, new data on tinnitus was provided from an ongoing clinical trial.

Paraesthesia and hypoaesthesia

Update to the product information

Following PRAC's assessment, paraesthesia (unusual feeling in the skin, such as tingling or a crawling sensation) and hypoaesthesia (decreased feeling or sensitivity, especially in the skin) will be included in the EU product information as side effects of Vaxzevria. The frequency category will be 'uncommon', i.e. occurring in less than 1 in 100 vaccinated persons.

Cases of paraesthesia and hypoaesthesia have been reported spontaneously with use of Vaxzevria. Generally, cases reported spontaneously by a patient or healthcare professional concern suspected side effects, i.e. medical

⁶ 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. As of May 2022, exposure figures are calculated using a new method. Figures should therefore not be compared with those in the safety updates of previous months.

events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine. In addition, new data on paraesthesia and hypoaesthesia were provided from ongoing clinical trials.



About 69 million doses of Vaxzevria in adults were administered in the EU/EEA from authorisation to 26 June 2022.⁷

The initial 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,

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. As of May 2022, exposure figures are calculated using a new method. Figures should therefore not be compared with those in the safety updates of previous months.

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 4 July 2022, EudraVigilance contained the following:

- Comirnaty: a total of 848,204 cases of suspected side effects spontaneously reported from EU/EEA countries; 8,032 of these reported a fatal outcome^{8,9} (by 26 June 2022, about 649 million doses of Comirnaty had been given to people in the EU/EEA¹⁰)
- COVID-19 Vaccine (inactivated, adjuvanted) Valneva: no cases of suspected side effects spontaneously reported from EU/EEA countries^{6,7} (by 26 June 2022, the vaccine had not yet been used in the EU/EEA⁸)
- Jcovden: a total of 54,475 cases of suspected side effects spontaneously reported from EU/EEA countries; 322 of these reported a fatal outcome^{6,7} (by 26 June 2022, about 19.4 million doses of Jcovden had been administered to people in the EU/EEA⁸)
- Nuvaxovid: a total of 1,094 cases of suspected side effects spontaneously reported from EU/EEA countries; none of these reported

⁸ 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).

⁹ 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.

¹⁰ 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. As of May 2022, exposure figures are calculated using a new method. Figures should therefore not be compared with those in the safety updates of previous months.

a fatal outcome^{6,7} (by 26 June 2022, about 216,000 doses of Nuvaxovid had been administered to people in the EU/EEA⁸)

- Spikevax: a total of 230,524 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,086 of these reported a fatal outcome^{6,7} (by 26 June 2022, about 155 million doses of Spikevax had been given to people in the EU/EEA⁸)
- Vaxzevria: a total of 297,917 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,552 of these reported a fatal outcome^{6,7} (by 26 June 2022, about 69 million doses of Vaxzevria had been given to people in the EU/EEA⁸).

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: [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 (PIP under publication), [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. Two vaccines, Comirnaty and Spikevax, are authorised in the EU 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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