



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 June 2022 Rev.2¹

COVID-19 vaccines safety update

Comirnaty (BioNTech Manufacturing GmbH)

Jcovden (Janssen-Cilag International NV)

Nuvaxovid (Novavax CZ, a.s.)

Spikevax (Moderna Biotech Spain, S.L.)

Vaxzevria (AstraZeneca AB)

Marketing authorisation withdrawal

Vaxzevria and Jcovden were withdrawn from the EU market at the request of the marketing authorisation holders for commercial reasons.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 12 May 2022 and reflects the main assessment outcomes of the PRAC meeting held 7 to 10 June 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 and 9 August 2024 following the withdrawals of Vaxzevria and Jcovden, respectively.

Key messages from the latest safety assessments

The product information remains unchanged for all EU-authorised COVID-19 vaccines.

1. Latest safety assessments

Comirnaty (BioNTech Manufacturing GmbH)

Amenorrhoea and heavy menstrual bleeding

Available evidence does not support a causal relationship of amenorrhoea with Comirnaty; the assessment of heavy menstrual bleeding is ongoing

Having started its assessment of specific menstrual disorders in early 2022 ([see safety update February 2022](#)), PRAC has concluded that the currently available evidence does not support a causal relationship between Comirnaty and amenorrhoea (absence of menstruation); the assessment of heavy menstrual bleeding is ongoing.

Further information can be found in the [PRAC highlights of June 2022](#).



About 640 million doses of Comirnaty, including 55 million doses of Comirnaty in children and adolescents (below 18 years of age) were administered in the EU/EEA from authorisation to 15 May 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).

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.

Jcovden (Janssen-Cilag International NV)

Myocardial infarction

Available evidence does not support a causal relationship of myocardial infarction with Jcovden

Earlier in 2022 ([see safety update March 2022](#)), PRAC started a review of this topic following the publication of an epidemiological study based on French national databases and posted on the EPI-PHARE website. The study suggested a slightly increased risk for myocardial infarction (heart attack) with Jcovden within 3 weeks of the first dose.

PRAC considered that the design of the study had some limitations and noted that the observation of a slight increase in myocardial infarction was based on a few observed cases.

The spontaneously reported cases lacked sufficient information for assessment and/or reported underlying risk factors for myocardial infarction in the concerned patients. Generally, 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.

Furthermore, evidence from other data sources, such as large clinical trials, did not indicate an increased risk for myocardial infarction with Jcovden.

PRAC has therefore concluded that the available evidence does not support a causal relationship of myocardial infarction with Jcovden.



About 19.5 million doses of Jcovden in adults were administered in the EU/EEA from authorisation to 15 May 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).

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.

Nuvaxovid (Novavax CZ, a.s.)

Myocarditis and pericarditis

Assessment started

PRAC has started an assessment of myocarditis and pericarditis (inflammatory conditions of the heart), to establish whether these may be side effects of Nuvaxovid.

This is based on new safety data, including the latest monthly summary safety report (MSSR) from the marketing authorisation holder. A small number of spontaneous reports of suspected myocarditis and/or pericarditis have been received, mainly from [Australia](#). Generally, 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. Further information has been requested from the marketing authorisation holder, including a detailed analysis by age groups.

Symptoms of these conditions can vary but often include breathlessness, a forceful heartbeat that may be irregular (palpitations), and chest pain.



About 210,000 doses of Nuvaxovid in adults were administered in the EU/EEA from authorisation to 15 May 2022.⁴

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.)

Amenorrhoea and heavy menstrual bleeding

Available evidence does not support a causal relationship of amenorrhoea with Spikevax; the assessment of heavy menstrual bleeding is ongoing

Having started its assessment of specific menstrual disorders in early 2022 ([see safety update February 2022](#)), PRAC has concluded that the currently

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. 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.

available evidence does not support a causal relationship between Spikevax and amenorrhoea (absence of menstruation); the assessment of heavy menstrual bleeding is ongoing.

Further information can be found in the [PRAC highlights of June 2022](#).



About 152 million doses of Spikevax, including 3.2 million doses of Spikevax in children and adolescents (below 18 years of age) were administered in the EU/EEA from authorisation to 15 May 2022.⁵

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)

Myocardial infarction, pulmonary embolism and thrombosis

Available evidence does not support a causal relationships with Vaxzevria

Earlier in 2022 ([see safety update March 2022](#)), PRAC started a review of these topics following the publication of an epidemiological study based on French national databases and posted on the EPI-PHARE website. The study suggested a slightly increased risk of myocardial infarction (heart attack) and pulmonary embolism (a blocked blood vessel in the lungs) with Vaxzevria. In addition, a slightly increased risk of general venous and/or arterial thrombosis (blood clots) had been noted in other published studies.

PRAC considered that the designs of the studies had some limitations and that the results from other studies, including large clinical trials, did not indicate increased risks of myocardial infarction, pulmonary embolism or general thrombosis with Vaxzevria

PRAC has therefore concluded that the available evidence does not support a causal relationship of these events with Vaxzevria.

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. 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.

No updates to the product information are warranted. [The product information](#) already includes information on the specific risks of thrombosis with thrombocytopenia syndrome (TTS; blood clots combined with low platelets) and cerebrovascular venous and sinus thrombosis (blood clot in the brain's venous sinuses).



About 69 million doses of Vaxzevria in adults were administered in the EU/EEA from authorisation to 15 May 2022.⁶

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

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.

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 29 May 2022, EudraVigilance contained the following:

- Comirnaty: a total of 786,983 cases of suspected side effects spontaneously reported from EU/EEA countries; 7,935 of these reported a fatal outcome^{7,8} (by 15 May 2022, about 640 million doses of Comirnaty had been given to people in the EU/EEA⁹);
- Jcovden: a total of 50,410 cases of suspected side effects spontaneously reported from EU/EEA countries; 319 of these reported a fatal outcome^{7,8} (by 15 May 2022, about 19.5 million doses of COVID-19 Vaccine Janssen had been administered to people in the EU/EEA⁹);
- Nuvaxovid: a total of 964 cases of suspected side effects spontaneously reported from EU/EEA countries; none of these reported a fatal

⁷ 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).

⁸ 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.

⁹ 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.

outcome^{10,11} (by 15 May 2022, about 210,000 doses of Nuvaxovid had been administered to people in the EU/EEA¹²);

- Spikevax: a total of 219,135 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,059 of these reported a fatal outcome^{10,11} (by 15 May 2022, about 152 million doses of Spikevax had been given to people in the EU/EEA¹²);
- Vaxzevria: a total of 276,697 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,529 of these reported a fatal outcome^{10,11} (by 15 May 2022, about 69 million doses of Vaxzevria had been given to people in the EU/EEA¹²).

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](#), [Jcovden](#), [Nuvaxovid](#), [Spikevax](#) and [Vaxzevria](#).

A [paediatric investigation plan](#) (PIP) is in place for each authorised COVID-19 vaccine: [Comirnaty](#), [Jcovden](#), [Nuvaxovid](#), [Spikevax](#) and [Vaxzevria](#). The PIP describes how the company will collect data on the vaccine's efficacy

¹⁰ 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).

¹¹ 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.

¹² 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.

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.

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

