



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 January 2022 Rev.2¹

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Vaxzevria and Jcovden (previously COVID-19 Vaccine Janssen) were withdrawn from the EU market at the request of the marketing authorisation holders for commercial reasons.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 updates of 9 December 2021 and reflects the main assessment outcomes of the PRAC meeting held 10 to 13 January 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 (previously COVID-19 Vaccine Janssen), respectively.

Key messages from the latest safety assessments

COVID-19 Vaccine Janssen and Vaxzevria

- The product information will be updated to add transverse myelitis (inflammation in the spinal cord) as a side effect.
- Information on the known side effect of thrombosis with thrombocytopenia syndrome (TTS; blood clots with low blood platelets) will be updated in the product information.

Spikevax

- The product information will be updated to include paraesthesia (unusual feeling in the skin) as a rare side effect.

Comirnaty and Spikevax

- An assessment of whether vaccination can cause capillary leak syndrome (leakage of fluid from blood vessels) is ongoing.

1. Latest safety assessments

Comirnaty (BioNTech Manufacturing GmbH)



About 545 million doses of Comirnaty were administered in the EU/EEA between EU marketing authorisation on 21 December 2020 and 2 January 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.

Capillary leak syndrome

Ongoing assessment

In January 2022, PRAC started an assessment of reports of capillary leak syndrome (CLS) in people vaccinated with Comirnaty. CLS is a disorder characterised by leakage of fluid from blood vessels causing tissue swelling and a fall in blood pressure. The investigations of whether Comirnaty can cause CLS will include an assessment of the most recent scientific literature.

Use of the vaccine in pregnancy

No sign of adverse outcomes

A review of several studies involving around 65,000 pregnancies at different stages did not find any sign of an increased risk of pregnancy complications, miscarriages, preterm births or adverse effects in the unborn babies following vaccination with the mRNA vaccines Comirnaty and Spikevax. The review was conducted by EMA's [COVID-19 pandemic task force \(ETF\)](#) and further information can be found in this [EMA communication](#).

Information on how Comirnaty works is presented 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 Janssen (Janssen-Cilag International NV)



About 18,7 million doses of COVID-19 Vaccine Janssen were administered in the EU/EEA between EU marketing authorisation on 11 March 2021 and 2 January 2022.²

Transverse myelitis

Update to the product information

Following a previous assessment (see [safety update for COVID-19 Vaccine Janssen of 6 October 2021](#)), in January 2022 PRAC finalised the update of the product information on transverse myelitis (TM) as a side effect of COVID-19 Vaccine Janssen. TM is a neurological condition characterised by an inflammation in the spinal cord. The frequency category of this side effect will be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported by healthcare professionals or patients

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



People are advised to seek immediate medical attention if they develop weakness in the arms or legs, sensory symptoms (such as tingling, numbness, pain or loss of pain sensation) or problems with bladder or bowel function after vaccination.

Thrombosis with thrombocytopenia syndrome

Update to the product information

Following the last update to the product information regarding the very rare side effect of thrombosis (formation of blood clots in the blood vessels) with thrombocytopenia (low blood platelets) syndrome (TTS) ([see safety update for COVID-19 Vaccine Janssen of 11 May 2021](#)), in January 2022 PRAC concluded that the product information should be updated further. This update will remove the current statement that reported TTS cases occurred mostly in women, since the sex imbalance seems smaller than previously observed. The observed cases occurred within the first three weeks following vaccination, mostly in individuals under 60 years of age.



Reminder: People are advised to seek immediate medical attention if they experience severe or persistent headaches, seizures (fits), mental status changes or blurred vision, unexpected bleeding, unexpected skin bruising beyond the site of vaccination which appears days after vaccination, or pinpoint round spots beyond the site of vaccination, or develop shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain (see [product information](#)).

Information on how COVID-19 Vaccine Janssen works is presented 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). The product information will be updated in accordance with the latest safety assessment outcomes.

Nuvaxovid (Novavax CZ, a.s.)

Since its marketing authorisation in the European Union (EU) on 20 December 2021, Nuvaxovid has not yet been used in the EU/EEA.²

All relevant new information that may emerge worldwide will be collected, promptly reviewed and communicated as needed.

Information on how Nuvaxovid works is presented 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.)



About 103 million doses of Spikevax were administered in the EU/EEA between EU marketing authorisation on 6 January 2021 and 2 January 2022.²

Paraesthesia

Update to the product information

In January 2022, PRAC concluded that paraesthesia (unusual feeling in the skin, such as tingling or a crawling feeling) should be added to the product information as a side effect of Spikevax. The frequency of this side effect was estimated as rare (i.e. occurring in less than 1 in 1,000 vaccinated persons). Hypoesthesia (decreased feeling or sensitivity in the skin) is already included as a side effect in the current product information.

This assessment was finalised within the review of the six-month cumulative periodic safety update report submitted on 26 August 2021. The conclusion was based on worldwide spontaneously reported cases of paraesthesia that were considered to be unrelated to anxiety possibly caused by vaccination. These cases included 1,425 cases with a time-to-onset after vaccination of at least 3 days and 56 cases that had a duration after vaccination of 7 days or longer (reported by 30 June 2021, by when more than 182,7 million doses of the vaccine had been administered worldwide). The conclusion was also based on clinical trial results, which reported a higher number of paraesthesia cases in people who received the vaccine (2 cases) than in those who received placebo (0 cases).

Capillary leak syndrome

Ongoing assessment

In November 2021, PRAC started an assessment of reports of capillary leak syndrome (CLS) in people vaccinated with Spikevax ([see safety update for Spikevax of 11 November 2021](#)). CLS is a disorder characterised by leakage of fluid from blood vessels causing tissue swelling and a fall in blood pressure. In January 2022, PRAC assessed the data further. The

investigation of whether Spikevax can cause CLS is still ongoing and will include an assessment of the most recent scientific literature.

Use of the vaccine in pregnancy

No sign of adverse outcomes

A review of several studies involving around 65,000 pregnancies at different stages did not find any sign of an increased risk of pregnancy complications, miscarriages, preterm births or adverse effects in the unborn babies following vaccination with the mRNA vaccines Comirnaty and Spikevax. The review was conducted by EMA's [COVID-19 pandemic task force \(ETF\)](#) and further information can be found in this [EMA communication](#).

Information on how Spikevax works is presented 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). The product information will be updated in accordance with the latest safety assessment outcomes.

Vaxzevria (AstraZeneca AB)



About 69 million doses of Vaxzevria were administered in the EU/EEA between EU marketing authorisation on 29 January 2021 and 2 January 2022.²

Thrombosis with thrombocytopenia syndrome

Update to the product information

Following the last update to the product information regarding the very rare side effect of thrombosis (formation of blood clots in the blood vessels) with thrombocytopenia (low blood platelets) syndrome (TTS) (see [safety update for Vaxzevria of 8 September 2021](#)), in January 2022 PRAC concluded that the product information should be updated further. This update will reflect that the majority of TTS cases were reported after the first, rather than the second, dose. Further information can be found in the [PRAC highlights of January 2022](#).



Reminders: The administration of Vaxzevria is contraindicated in individuals who have experienced TTS following vaccination with this vaccine.

People should seek immediate medical attention if they develop shortness of breath, chest pain, leg swelling, leg pain or persistent abdominal pain following vaccination, or experience after a few days following vaccination severe or persistent headaches, blurred vision, confusion or seizures (fits), or unexplained bleeding or skin bruising or pinpoint round spots beyond the site of vaccination which appears after a few days (see [product information](#)).

Transverse myelitis

Update to the product information

In January 2022, PRAC concluded that transverse myelitis (TM) should be added to the product information as a side effect of Vaxzevria. TM is a neurological condition characterised by an inflammation in the spinal cord. The frequency category of this side effect will be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported by healthcare professionals or patients spontaneously. Further information can be found in the [PRAC highlights of January 2022](#).



People are advised to seek immediate medical attention if they develop weakness in the arms or legs, sensory symptoms (such as tingling, numbness, pain or loss of pain sensation) or problems with bladder or bowel function after vaccination.

Information on how Vaxzevria works is presented 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). The product information will be updated in accordance with the latest safety assessment outcomes.

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 for at least the first six months of marketing. After the first six months, summary safety reports may cover time periods longer than a month or not be necessary anymore. MSSRs/ summary safety reports complement the submission of [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 2 January 2022, EudraVigilance contained:

- for Comirnaty: a total of 522,530 cases of suspected side effects spontaneously reported from EU/EEA countries; 6,490 of these reported a

fatal outcome^{3,4} (by the same date about 545 million doses of Comirnaty had been given to people in the EU/EEA²);

- for COVID-19 Vaccine Janssen: a total of 35,027 cases of suspected side effects spontaneously reported from EU/EEA countries; 254 of these reported a fatal outcome^{3,4} (by the same date, about 18.7 million doses of had been administered to people in the EU/EEA²);

- for Spikevax: a total of 124,410 cases of suspected side effects spontaneously reported from EU/EEA countries; 685 of these reported a fatal outcome^{3,4} (by the same date, about 103 million doses of Spikevax had been given to people in the EU/EEA²);

- for Vaxzevria: a total of 231,363 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,378 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/EEA²).

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 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](#),

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.

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.

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

