EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 February 2022

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)

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 20 January 2022 and reflects the main assessment outcomes of the PRAC meetings held 26 January and 7 to 10 February 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

Comirnaty and Spikevax

- The product information of these mRNA vaccines will be updated to reflect the accumulating evidence that they can be used during pregnancy and breastfeeding.
- PRAC started a further assessment of menstrual disorders following use of mRNA vaccines with a focus on heavy menstrual bleeding and the absence of menstruation (amenorrhoea).

1. Latest safety assessments

Comirnaty (BioNTech Manufacturing GmbH)

and Spikevax (Moderna Biotech Spain, S.L.)

About 570 million doses of Comirnaty were administered in the EU/EEA between 21 December 2020 (EU marketing authorisation date) and 30 January 2022[1].

About 139 million doses of Spikevax were administered in the EU/EEA between 6 January 2021 (EU marketing authorisation date) and 30 January 2022[1].

Use of the vaccines in pregnancy

Update to the product information

Further to recent reviews by EMA's COVID-19 pandemic task force (ETF) and information provided in an EMA communication of 18 January 2022 (see also COVID-19 Vaccines Safety Update of January 2022), PRAC provided advice to the Committee for Medicinal Products for Human Use (CHMP) which recommended updating the product information of the mRNA vaccines Comirnaty and Spikevax regarding their use in pregnancy and breastfeeding.

A large amount of information from pregnant women vaccinated with these products during the second and third trimester has not shown negative

[1] 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.

effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no change to the risk for miscarriage has been seen.

Comirnaty or Spikevax can be used during pregnancy and breastfeeding.

Menstrual disorders

Further assessment started

In October 2021, PRAC concluded that there was insufficient evidence to suggest a causal relationship between vaccination with Comirnaty and menstrual disorders (Safety Update for Comirnaty of 6 October 2021).

A further assessment has started following published studies[2] suggesting there may be short-lived changes in menstrual patterns, including absence of menstrual bleeding (amenorrhoea) and heavier than usual menstrual bleeding following vaccination with Comirnaty or Spikevax. Further information can be found in the PRAC highlights of February 2022.

Information on how Comirnaty and Spikevax work is provided in their respective medicine overviews: Comirnaty and Spikevax (in all EU/EEA languages). Full information on the vaccines, including all identified side effects and advice on how to use them, is available in their respective product informations: Comirnaty and Spikevax (in all EU/EEA languages). The product information will be updated to reflect the latest safety assessment outcomes.

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

About 19 million doses of COVID-19 Vaccine Janssen were administered in the EU/EEA between 11 March 2021 (EU marketing authorisation date) and 30 January 2022[1].

There are no safety updates for COVID-19 Vaccine Janssen.

[2] Including: https://www.fhi.no/en/news/2022/menstrual-changes-following-covid-19-vaccination/ and Association Between Menstrual Cycle Length and Coronavirus Disease 2019 (COVID-19) Vaccination, Obstetrics & Gynecology (lww.com)

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).

Nuvaxovid (Novavax CZ, a.s.)

There are no safety updates for Nuvaxovid. The vaccine is not yet in use in the EU/EEA.

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).

Vaxzevria (AstraZeneca AB)

About 69 million doses of Vaxzevria were administered in the EU/EEA between 29 January 2021 (EU marketing authorisation date) and 30 January 2022[1].

There are no safety updates for Vaxzevria.

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 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 and 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 30 January 2022, EudraVigilance contained the following figures:

- Comirnaty: a total of 582,074 cases of suspected side effects spontaneously reported from EU/EEA countries; 7,023 of these reported a fatal outcome[3,4] (by the same date about 570 million doses of Comirnaty had been given to people in the EU/EEA[1])
- COVID-19 Vaccine Janssen: a total of 40,766 cases of suspected side effects spontaneously reported from EU/EEA countries; 279 of these

[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.

reported a fatal outcome[2,3] (by the same date, about 19 million doses of had been administered to people in the EU/EEA[1])

- Spikevax: a total of 150,807 cases of suspected side effects spontaneously reported from EU/EEA countries; 834 of these reported a fatal outcome[2,3] (by the same date, about 139 million doses of Spikevax had been given to people in the EU/EEA[1])
- Vaxzevria: a total of 244,603 cases of suspected side effects spontaneously reported from EU/EEA countries; 1,447 of these reported a fatal outcome[2,3] (by the same date, about 69 million doses of Vaxzevria had been given to people in the EU/EEA[1]).

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, 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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