8 September 2021

COVID-19 vaccine safety update

SPIKEVAX

Moderna Biotech Spain, S.L.

The safety of Spikevax is continuously monitored and safety updates are regularly provided to the public. This document outlines the outcomes from the assessment of emerging worldwide safety data carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (see section 1). It also contains high-level information from the reporting of suspected adverse reactions, which PRAC takes into account in its assessments (see section 2).

This safety update follows the update of 11 August 2021.

Main outcomes from PRAC's latest safety assessment

No new updates to the product information are currently recommended.

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for Spikevax (previously known as COVID-19 Vaccine Moderna) are available at Spikevax: safety updates.

Since its marketing authorisation in the European Union (EU) on 6 January 2021 until 2 September 2021, more than 54.2 million doses of Spikevax have been administered in the EU/EEA[1].

More than 54.2 million
doses administered in EEA

1. Updates on safety assessments for Spikevax

PRAC assessed new safety data, including the latest Monthly Summary Safety Report (MSSR)[2] from the marketing authorisation holder and data reported by patients and healthcare professionals to EudraVigilance (see section 2), during its meeting held 30 August to 2 September 2021.

No new updates to the product information are currently recommended.

Myocarditis and pericarditis

Assessment finalised - no further update to the Spikevax product information at present

Myocarditis and pericarditis were added to the product information of Spikevax in the side effects and warning sections, following the assessment by PRAC in July 2021[3].

Myocarditis and pericarditis are inflammatory conditions of the heart.

In September 2021, PRAC finalised a further assessment, concluding that there is no new information on which base to change the product information.

Reminder: To help recovery and avoid complications, people must seek immediate medical attention and treatment if they experience breathlessness, a forceful heartbeat that may be irregular or (acute and persisting) chest pain, as these could be signs of myocarditis and pericarditis.

[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.
[2] Monthly Summary Safety Reports, also referred to as pandemic summary safety reports, will be compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. These reports complement the submission of Periodic Safety Update Reports (PSURs).
[3] See safety update for Spikevax of 14 July 2021

Multisystem inflammatory syndrome (MIS)

Assessment ongoing

PRAC is assessing whether there is a risk of multisystem inflammatory syndrome (MIS) with COVID-19 vaccines following a report of MIS with Comirnaty, another COVID-19 vaccine, in Denmark. Some cases of MIS after administering Comirnaty or other COVID-19 vaccines were reported in adults and/or from outside EU/EEA. 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.

MIS is a serious inflammatory condition affecting many parts of the body and symptoms can include tiredness, persistent severe fever, diarrhoea, vomiting, stomach pain, headache, chest pain and difficulty breathing. MIS is rare and its incidence rate before the COVID-19 pandemic estimated from 5 European countries was around 2 to 6 cases per 100,000 per year in children and adolescents below 20 years of age and less than 2 cases per 100,000 per year in adults aged 20 years or above [data from observational studies coordinated by EMA (see section 2)][4]. MIS has also been reported following COVID-19 disease. The Danish patient, however, had no history of COVID-19.

As of 19 August 2021, no cases were reported as MIS in a child after vaccination with Spikevax in the EEA/EU to EudraVigilance (for information on EudraVigilance, see section 2).

PRAC will now assess the available data on MIS to determine whether the condition can be caused by COVID-19 vaccines and recommend whether any changes to the product information are needed.

PRAC encourages all healthcare professionals to report any cases of MIS and other adverse events in people who have had these vaccines (for advice on reporting, see section 2).

At this stage, there is no change to the current EU recommendations for the use of COVID-19 vaccines.

EMA and national authorities will provide further updates as necessary[5].

[4] See European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

[5] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 30 August - 2 September 2021

Anaphylaxis and other hypersensitivity reactions

No further update to the Spikevax product information at present

Anaphylaxis is a known side effect of Spikevax and listed in its product information, together with information on the clinical management of anaphylaxis. PRAC keeps anaphylaxis under close monitoring and in September 2021 assessed the latest data. PRAC concluded that no update to the product information is currently necessary.

Delayed injection site reaction

Assessment ongoing

Following PRAC's assessment in May and July 2021[6], the Spikevax product information was updated to include delayed injection site reaction (rash, redness or hives) as a side effect of the vaccine with a frequency of common (i.e. occurring in less than 1 in 10 persons). PRAC has requested the marketing authorisation holder to further specify characteristics of this side effect, such as typical time to onset, duration and severity of the reactions. The product information will then be updated accordingly. This assessment remains ongoing.

Diarrhoea

Assessment ongoing

PRAC continued their assessment of May 2021 regarding diarrhoea[7] and requested the marketing authorisation holder to add diarrhoea as a side effect of the vaccine, together with the frequency category based on the latest clinical trial data. This assessment remains ongoing.

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on Spikevax is collected and promptly reviewed. 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).

[6] See safety update for Spikevax of 14 July 2021
[7] See safety update for Spikevax of 11 May 2021

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, 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. Search for "COVID-19 MRNA VACCINE MODERNA (CX-024414)" to see all suspected side effect cases reported for Spikevax.

As of 2 September 2021, a total of 64,885 cases of suspected side effects with Spikevax were spontaneously reported to EudraVigilance from EU/EEA countries; 447 of these reported a fatal outcome[8,9]. By the same date, more than 54.2 million doses of Spikevax had been given to people in the EU/EEA[10].

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. EMA's detailed assessments take into account all available data from all sources to draw a robust conclusion on the safety of the vaccine. These data include clinical trial results, reports of suspected side effects in EudraVigilance, epidemiological studies

[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 effects. 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.

monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Planned and ongoing studies

The company that markets Spikevax will continue to provide results from the main clinical trial, which is ongoing for up to two years. It will also conduct additional studies to monitor the safety and effectiveness of the vaccine as it is used in vaccination campaigns and other clinical practice. For the list of planned and ongoing safety studies for Spikevax, see the risk management plan.

A paediatric investigation plan (PIP) for Spikevax is in place. This describes how the company collects data on the vaccine's efficacy and safety for its 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.

3. Other information for Spikevax

Spikevax (previously known as COVID-19 Vaccine Moderna) is a vaccine that was authorised in the EU on 6 January 2021 to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death. The initial marketing authorisation was for use in people aged 18 years and older; on 23 July 2021, the marketing authorisation was extended to use in individuals aged 12 years and older.

Spikevax contains a molecule called mRNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The mRNA is broken down shortly after vaccination. The spike protein does not cause COVID-19.

Before Spikevax was granted an EU marketing authorisation, the efficacy and safety of the vaccine were assessed through pre-clinical studies and large clinical trials. More than 14,000 participants had been given the vaccine in clinical trials.

Like all medicines, this vaccine can cause side effects, although not everybody will experience them. The most common side effects known for Spikevax are usually mild or moderate and get better within a few days after vaccination.

More information on how Spikevax works and its use is available in all EU/EEA languages in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

The full product information with the summary of product characteristics and the package leaflet is also available in all EU/EEA languages.

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

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