14 July 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 18 June 2021.

Main outcomes from PRAC's latest safety assessment

Inflammation of the heart muscle (myocarditis) or membrane (pericarditis) may occur in a small number of people after vaccination with Spikevax.

The product information will be updated.

Spikevax is effective in preventing COVID-19.

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 4 July 2021, more than 35 million doses of Spikevax have been administered in the EU/EEA[1].

More than 35 million
doses administered in EEA

1. Updates on safety assessments for Spikevax

Based on 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), PRAC assessed the following at its meeting held 5 to 8 July 2021:

Myocarditis and pericarditis

PRAC concluded that myocarditis and pericarditis can occur in very rare cases following vaccination with Spikevax and should be added in the product information as new side effects, together with a warning to raise awareness among healthcare professionals and people taking these vaccines.

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.

The product information will be updated to include these side effects with a frequency category of 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of

[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 known 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).

suspected side effects that have been reported by healthcare professionals or patients spontaneously.

In reaching its conclusion, PRAC took into consideration all currently available evidence on both mRNA COVID-19 vaccines, i.e. Spikevax and Comirnaty. This included an in-depth review of 19 cases of myocarditis in the EU/EEA among people who received Spikevax. PRAC also reviewed reports of 19 cases of pericarditis following the use of Spikevax. As of 31 May 2021, around 197 million doses of mRNA COVID-19 vaccines had been given in the EU/EEA (approximately 20 million doses of Spikevax and 177 million doses of Comirnaty). In addition PRAC also looked into cases received worldwide.

The cases primarily occurred within 14 days after vaccination, more often after the second dose and in younger adult men. In five cases that occurred in the EU/EEA, people died. They were either of advanced age or had concomitant diseases. Available data suggest that the course of myocarditis and pericarditis following vaccination is similar to the typical course of these conditions, usually improving with rest or treatment.

Healthcare professionals should:

- be alert to the signs and symptoms of myocarditis and pericarditis in people who have had these vaccines;

- tell people receiving these vaccines to seek immediate medical attention if symptoms indicative of myocarditis or pericarditis occur; and

- consult applicable guidance and/or consult specialists (e.g. cardiologists) to diagnose and treat these conditions, as people with myocarditis or pericarditis may require specialist treatment.

Although the risk of these conditions occurring is very low, people who have received this vaccine must seek immediate medical attention and treatment to help recovery and avoid complications if they have the following symptoms suggestive of myocarditis and pericarditis:

- breathlessness;

- a forceful heartbeat that may be irregular (palpitations); or

- (acute and persisting) chest pain.

Questions about the rollout of COVID-19 vaccines in EU Member States can be addressed to healthcare professionals or the national health authority.

EMA confirms that the benefits of Spikevax continue to outweigh the risks, given the risks of COVID-19 illness and related complications; scientific evidence shows that the vaccine reduces deaths and hospitalisations due to COVID-19.

A direct healthcare professional communication (DHPC) will be sent in due course to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC will also be published on a dedicated webpage.

The PRAC recommendations will be submitted to EMA's human medicine committee, CHMP, for endorsement[3].

Anaphylaxis and other hypersensitivity reactions

Anaphylaxis is a known side effect of Spikevax and listed in its product information. PRAC keeps anaphylaxis under close monitoring; an assessment is ongoing to consider providing more details of anaphylaxis and other hypersensitivity (allergic) reactions in the product information. Information on the clinical management of anaphylaxis is already available in the product information.

Delayed injection site reaction

In May 2021, based on cases reported in clinical trials and from vaccination campaigns, PRAC concluded that information on delayed injection site reaction should be added to the product information of Spikevax[4]. An assessment to describe the characteristics of this side effect and its frequency is ongoing.

Immune thrombocytopenia

PRAC concluded its assessment of immune thrombocytopenia (ITP, an auto-immune condition of low blood platelet levels that can lead to bruising and bleeding) reported with Spikevax. Although nine cases were considered possibly related to the vaccine, no clear causal relationship could be established in any of these cases. The patients also had other, non-vaccine-related, factors that could be linked to ITP. Nonetheless, PRAC concluded that, based on the current evidence, a causal relationship between ITP and Spikevax could not be excluded either and this topic will therefore remain under close monitoring in the context of the Periodic Safety Update Reports.

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).

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[3] See EMA public health communication on myocarditis and pericarditis with Comirnaty and Spikevax of 9 July 2021

[4] See safety update for COVID-19 vaccine Moderna 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 4 July 2021, a total of 36,294 cases of suspected side effects with Spikevax were spontaneously reported to EudraVigilance from EU/EEA countries; 347 of these reported a fatal outcome[5,6]. Around that time, about 35 million doses of Spikevax had been given to people in the EU/EEA[7].

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

[5] 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).
[6] 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.
[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.

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 will collect data on the vaccine's efficacy and safety for its potential 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) was authorised in the EU on 6 January 2021 for use in people aged 18 years and older to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death.

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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