09 December 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 November 2021.

Main outcomes from PRAC's latest safety assessment

The overall frequency of the side effects myocarditis and pericarditis has been determined to be very rare.

The risk has been confirmed to be highest in younger males; estimates of the risk will be included in the product information for Spikevax.

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 01 December 2021, more than 61.6 million doses of Spikevax have been administered in the EU/EEA[1].

More than 61.6 million
doses administered in EEA

1. Updates on safety assessments for Spikevax

During its meeting held 29 November to 02 December 2021, PRAC assessed new safety data for Spikevax (see section 2 'How safety is monitored').

Myocarditis and pericarditis

Update to the Spikevax product information

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.

EMA's safety committee (PRAC) has assessed recent data on the known risk of myocarditis and pericarditis following vaccination with mRNA vaccines, including Spikevax. This review included two large European epidemiological studies. One study was conducted using data from the French national health system (Epi-phare) and the other one was based on Nordic registry data.

Overall, the outcome of the review confirms the risk of myocarditis and pericarditis, which is already reflected in the product information for Spikevax, and provides further details on these two conditions.

Based on the reviewed data, PRAC has determined that the overall risk for both conditions is very rare', meaning that up to 1 in 10,000 vaccinated people may be affected. Additionally, the data show that the increased risk of myocarditis after vaccination is highest in younger males.
PRAC has recommended updating the product information accordingly.

Myocarditis and pericarditis can develop within just a few days after vaccination and occur primarily within 14 days. They have more often been observed after the second vaccination.

[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.

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. Viral infections, including infection with the virus that causes COVID-19, are a common cause of myocarditis.[2]

For Spikevax, the French study showed that in a period of 7 days after the second dose there were about 1.3 extra cases of myocarditis in 12- to 29-year-old males per 10,000 compared with unexposed persons. The Nordic study shows that in a period of 28 days after the second dose of Spikevax there were around 1.9 extra cases of myocarditis in 16- to 24-year-old males per 10,000 compared with unexposed persons. EMA will continue to closely monitor this issue and will communicate further when new information becomes available.

EMA confirms that the benefits of Spikevax continue to outweigh its risks, given the risk of COVID-19 illness and related complications, including hospitalisation and death.

Information for people receiving the vaccine:

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

Autoimmune hepatitis

Signal assessment started

PRAC started an assessment of autoimmune hepatitis (a condition in which the immune system attacks and damages the liver) to establish whether it may be a side effect of Spikevax.

With early diagnosis, autoimmune hepatitis generally responds well to treatment with medicines to suppress the immune system. Signs and symptoms of autoimmune hepatitis vary from person to person and may include yellowing of the skin (jaundice), build-up of fluid in the legs (oedema) or belly (ascites) and gastrointestinal symptoms.

The assessment follows a very small number of cases reported after vaccination with Spikevax in the medical literature and EudraVigilance. Further data and analyses have been requested from the marketing authorisation holder to support the ongoing assessment by PRAC.

PRAC encourages all healthcare professionals and patients to report any cases of autoimmune hepatitis and other adverse events in people after vaccination.

[2] Association Between COVID-19 and Myocarditis Using Hospital-Based Administrative Data — United States, March 2020–January 2021 | MMWR (cdc.gov)

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).

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 (afterwards, pandemic summary safety reports may cover time periods longer than a month). These 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. Search for "COVID-19 MRNA VACCINE MODERNA (CX-024414)" to see all suspected side effect cases reported for Spikevax.

As of 01 December 2021, a total of 108,583 cases of suspected side effects with Spikevax were spontaneously reported to EudraVigilance from EU/EEA countries; 588 of these reported a fatal outcome[3,4]. By the same

[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.

date, more than 61.6 million doses of Spikevax had been given to people in the EU/EEA[5].

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 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

[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.

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.

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