Comirnaty and Spikevax: possible link to very rare cases of myocarditis and pericarditis

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Information on Comirnaty and Spikevax (COVID-19 mRNA Vaccine (nucleoside modified))

- Comirnaty and Spikevax (previously known as COVID-19 Vaccine Moderna) contain a molecule called mRNA which has instructions for making the spike protein. This is a protein on the surface of the SARS-CoV-2 virus which the virus needs to enter the body's cells.

- When a person is given one of these vaccines, some of their cells will read the mRNA instructions and temporarily produce the spike protein. The person's immune system will then recognise this protein as foreign and produce antibodies and activate T cells (white blood cells) to attack it. If, later on, the person comes into contact with SARS-CoV-2 virus, their immune system will recognise it and be ready to defend the body against it.

The following products are authorised via centralised procedure.

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
COVID-19 mRNA Vaccine (nucleoside modified)	Comirnaty	Concentrate for dispersion for injection (sterile concentrate)	POM	EU/1/20/1528/001	BioNTech Manufacturing GmbH
COVID-19 mRNA Vaccine (nucleoside modified)	Spikevax	Dispersion for injection	POM	EU/1/20/1507/001	Moderna Biotech Spain, S.L.

Information from the EMA about the safety concern

- EMA's safety committee (PRAC) has concluded that myocarditis and pericarditis can occur in very rare cases following vaccination with the COVID-19 vaccines Comirnaty and Spikevax (previously known as COVID-19 Vaccine Moderna).

- The Committee is therefore recommending listing myocarditis and pericarditis as new side effects in the product information for these vaccines, 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.

- In reaching its conclusion, the Committee took into consideration all currently available evidence which included an in-depth review of 145 cases of myocarditis in the European Economic Area (EEA) among people who received Comirnaty and 19 cases among people who received Spikevax. PRAC also reviewed reports of 138 cases of pericarditis following the use of Comirnaty and 19 cases following the use of Spikevax. As of 31 May 2021, around 177 million doses of Comirnaty and 20 million doses of Spikevax had been given in the EEA.

- In addition, the PRAC also looked into cases received worldwide. The Committee concluded that 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 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. They should tell people receiving these vaccines to seek immediate medical attention if symptoms indicative of myocarditis or pericarditis occur. These include breathlessness, a forceful heartbeat that may be irregular and chest pain. Healthcare professionals should consult applicable guidance and/or consult specialists (e.g. cardiologists) to diagnose and treat these conditions.

EMA's safety committee (PRAC) has concluded that:

- At this point in time, no causal relationship with myocarditis or pericarditis could be established with two other COVID-19 vaccines authorised in the EEA, COVID-19 Vaccine Janssen and Vaxzevria[1], and the Committee has requested additional data from the companies marketing these vaccines.

- EMA confirms that the benefits of all authorised COVID-19 vaccines continue to outweigh their risks, given the risk of COVID-19 illness and related complications and as scientific evidence shows that they reduce deaths and hospitalisations due to COVID-19.

- As for all vaccines, EMA will continue to monitor the vaccines' safety and effectiveness and provide the public with the latest information, particularly as more adolescents and young adults are vaccinated and more second doses are given. The agency will take necessary action if any new safety issues are identified.

In Malta

For Healthcare Professionals

Following a review of very rare cases of myocarditis and pericarditis in people who received Comirnaty and Spikevax (formerly COVID-19 Vaccine Moderna), healthcare professionals should:

[1] As of end of May 2021, cases of myocarditis reported in the EEA from the EudraVigilance database were: 38 for Vaxzevria and 0 for COVID-19 Vaccine Janssen. Cases of pericarditis were: 47 for Vaxzevria and 1 for COVID-19 Vaccine Janssen. The exposure in the EEA for each vaccine was around 40 million for Vaxzevria and 2 million for COVID-19 Vaccine Janssen.

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

- Tell people receiving the vaccine that they must seek immediate medical attention if they have the following symptoms suggestive of myocarditis and pericarditis after vaccination: (acute and persisting) chest pain, palpitations or shortness of breath. People with myocarditis or pericarditis may require specialist treatment;

- Consult applicable guidance and/or consult specialists (e.g. cardiologists) to diagnose and treat these conditions.

The product information will be updated to include myocarditis and pericarditis as side effects with unknown frequency.

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 page on the EMA website.

Advice for Patients

- Very rare cases of myocarditis and pericarditis (inflammatory conditions of the heart) have occurred in people who received Comirnaty and Spikevax (formerly COVID-19 Vaccine Moderna).

- The chance of these conditions occurring is very low, but you should be aware of the symptoms so that you can get prompt medical treatment to help recovery and avoid complications.

- You must seek medical attention immediately if you have the following symptoms after vaccination:
    - breathlessness
    - a forceful heartbeat that may be irregular
    - chest pain

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance with Comirnaty and Spikevax (previously known as COVID-19 Vaccine Moderna) medicinal product. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 **or** online to http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate

Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

Feedback:

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Malta Life Sciences Park

San Ġwann SĠN 3000