14 July 2021

COVID-19 vaccine safety update

COMIRNATY

BioNTech Manufacturing GmbH

The safety of Comirnaty 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 Comirnaty.

The product information will be updated.

Comirnaty is effective in preventing COVID-19.

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for Comirnaty are available at Comirnaty: safety updates.

Since its marketing authorisation in the European Union (EU) on 21 December 2020 until 4 July 2021, more than 276 million doses of Comirnaty have been administered in the EU/EEA[1].

1. Updates on safety assessments for Comirnaty

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

In reaching its conclusion, PRAC took into consideration all currently available evidence on both mRNA COVID-19 vaccines, i.e. Comirnaty and Spikevax. This included an in-depth review of 145 cases of myocarditis in

[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).

the EU/EEA among people who received Comirnaty. PRAC also reviewed reports of 138 cases of pericarditis following the use of Comirnaty. As of 31 May 2021, around 197 million doses of mRNA COVID-19 vaccines had been given in the EU/EEA (approximately 177 million doses of Comirnaty and 20 million doses of Spikevax). 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 Comirnaty 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].

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

Other events - Asthenia, lethargy, decreased appetite and (nocturnal) hyperhidrosis

Based on data from the ongoing clinical trials (see section 2), the following events are currently under consideration by the Committee for Medicinal Products for Human Use (CHMP) to be newly added as side effects to the product information of Comirnaty: asthenia (lack of energy or strength), lethargy (state of indifference and inactivity), decreased appetite and (nocturnal [nighttime]) hyperhidrosis (excessive sweating). The frequency category which is under consideration for all these events is 'uncommon' (i.e. occurring in less than 1 in 100 individuals).

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on Comirnaty 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).

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 PFIZER-BIONTECH (Tozinameran)" to see all suspected side effect cases reported for Comirnaty.

As of 4 July 2021, a total of 206,668 cases of suspected side effects with Comirnaty were spontaneously reported to EudraVigilance from EU/EEA countries; 3,848 of these reported a fatal outcome[4,5]. Around that time

[4] 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).
[5] 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.

about 276 million doses of Comirnaty had been given to people in the EU/EEA[6].

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 Comirnaty 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 Comirnaty, see the risk management plan.

A paediatric investigation plan (PIP) for Comirnaty 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 Comirnaty

Comirnaty is a vaccine that was authorised in the EU on 21 December 2020 to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. The initial marketing authorisation was for use in people aged 16 years and older; on 31 May 2021, the marketing authorisation was extended to

Similarly, this public database does not provide the total number of cases reported with a fatal outcome.

[6] 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.

use in individuals aged 12 years and older. COVID-19 is a potentially severe disease that may result in death.

Comirnaty 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 Comirnaty 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 18,000 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 Comirnaty are usually mild or moderate and get better within a few days after vaccination.

More information on how Comirnaty 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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