EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 September 2021

COVID-19 vaccine safety update

COVID-19 VACCINE JANSSEN

Janssen-Cilag International NV

The safety of COVID-19 Vaccine Janssen 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

PRAC finalised updates to the product information to include swollen lymph nodes, unusual or decreased feeling in the skin, tinnitus, diarrhoea and vomiting as side effects.

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

Since its marketing authorisation in the European Union (EU) on 11 March 2021 until 2 September 2021, more than 13.8 million doses of COVID-19 Vaccine Janssen have been administered in the EU/EEA[1].

More than 13.8 million
doses administered in EEA

1. Updates on safety assessments for COVID-19 Vaccine Janssen

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.

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)][3].

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

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 COVID-19 Vaccine Janssen 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[4].

Venous thromboembolism (VTE)

Assessment ongoing

As part of the ongoing close safety monitoring, PRAC is reviewing data on cases of venous thromboembolism (VTE, blood clots in the veins) with COVID-19 Vaccine Janssen.

This safety issue is distinct from the very rare side effect of thrombosis with thrombocytopenia syndrome (TTS) (i.e. blood clots with low blood platelets)[5].

VTE was included in the risk management plan for COVID-19 Vaccine Janssen as a safety issue to be investigated, based on a higher proportion of cases of VTE observed within the vaccinated group versus the placebo group in the first clinical studies used to authorise this vaccine.

PRAC will assess additional data from two large clinical trials of the vaccine, in order to further assess whether VTE may be causally related to the vaccine[6].

Other events: Lymphadenopathy, paraesthesia, hypoesthesia, tinnitus, diarrhoea and vomiting

Update to the COVID-19 Vaccine Janssen product information

PRAC finalised its assessment for updating the product information, concluding the following:

[4] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 30 August - 2 September 2021
[5] See safety update for COVID-19 Vaccine Janssen of 11 May 2021
[6] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 30 August - 2 September 2021

- Lymphadenopathy (swollen lymph nodes) should be added as a side effect of COVID-19 Vaccine Janssen; the frequency has been estimated as rare (i.e. occurring in less than 1 in 1,000 vaccinated persons).

- Paraesthesia (unusual feeling in the skin, such as tingling or a crawling feeling) and hypoesthesia (decreased feeling or sensitivity, especially in the skin) should be added as side effects of COVID-19 Vaccine Janssen; the frequency of paraesthesia has been estimated as uncommon (i.e. occurring in less than 1 in 100 vaccinated persons) and of hypoesthesia as rare (i.e. occurring in less than 1 in 1,000 vaccinated persons).

- Tinnitus[7] (persistent ringing in the ear) should be added as a side effect of COVID-19 Vaccine Janssen; the frequency has been estimated as rare (i.e. occurring in less than 1 in 1,000 vaccinated persons). Further data and analyses have been requested from the marketing authorisation holder to possibly further characterise the nature of tinnitus cases with a focus on course and duration of symptoms.

- Diarrhoea and vomiting after vaccination should be added as side effects of COVID-19 Vaccine Janssen; the frequency of diarrhoea has been estimated as uncommon (i.e. occurring in less than 1 in 100 vaccinated persons) and of vomiting as rare (i.e. occurring in less than 1 in 1,000 vaccinated persons).

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on COVID-19 Vaccine Janssen 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

[7] See safety update for COVID-19 Vaccine Janssen of 11 August 2021

languages. Search for "COVID-19 VACCINE JANSSEN (AD26.COV2.S)" to see all suspected side effect cases reported for COVID-19 Vaccine Janssen.

As of 2 September 2021, a total of 20,206 cases of suspected side effects with COVID-19 Vaccine Janssen were spontaneously reported to EudraVigilance from EU/EEA countries; 138 of these reported a fatal outcome[8,9]. By the same date, more than 13.8 million doses of COVID-19 Vaccine Janssen 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 monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Planned and ongoing studies

The company that markets COVID-19 Vaccine Janssen will continue to provide results from ongoing clinical trials. 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 COVID-19 Vaccine Janssen, see the risk management plan.

A paediatric investigation plan (PIP) for COVID-19 Vaccine Janssen is in place. This describes how the company will collect data on the vaccine's efficacy and safety for its potential use in children.

[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.

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 COVID-19 Vaccine Janssen

COVID-19 Vaccine Janssen is a vaccine that was authorised in the EU on 11 March 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.

COVID-19 Vaccine Janssen contains an adenovirus that has been modified to carry molecules of DNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The spike protein does not cause COVID-19. The adenovirus cannot reproduce and does not cause viral disease.

Before COVID-19 Vaccine Janssen 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 27,000 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 COVID-19 Vaccine Janssen are usually mild or moderate and get better within a few days after vaccination.

More information on how COVID-19 Vaccine Janssen 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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