



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 July 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 18 June 2021.

Main outcomes from PRAC's latest safety assessment

People who have previously had capillary leak syndrome must not receive COVID-19 Vaccine Janssen.

Capillary leak syndrome may also occur as a side effect of COVID-19 Vaccine Janssen.

The product information will be updated.

COVID-19 Vaccine Janssen is effective in preventing COVID-19.

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 4 July 2021, around 8.5 million doses of COVID-19 Vaccine Janssen have been administered in the EU/EEA¹.



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

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:

Capillary leak syndrome

PRAC recommended that people who have previously had capillary leak syndrome must not be vaccinated with COVID-19 Vaccine Janssen (contraindication). The Committee also recommended that capillary leak syndrome should be added to the product information as a new side effect of the vaccine, together with a warning to raise awareness among healthcare professionals and patients of this risk.

Capillary leak syndrome is a very rare, serious condition that causes fluid leakage from small blood vessels (capillaries), resulting in swelling mainly in the arms and legs, low blood pressure, thickening of the blood and low blood levels of albumin (an important blood protein).

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

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).

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

PRAC reviewed 3 cases of capillary leak syndrome in people who had received COVID-19 Vaccine Janssen, which occurred within 2 days of vaccination. One of those affected had a history of capillary leak syndrome and two of them subsequently died. As of 21 June 2021, more than 18 million doses of COVID-19 Vaccine Janssen had been administered worldwide.

Healthcare professionals should be aware that:

- COVID-19 Vaccine Janssen must not be given to anyone who has a history of capillary leak syndrome;
- capillary leak syndrome is a very rare, serious condition, which can be fatal if untreated (it causes fluid leakage from the capillaries, resulting in oedema mainly affecting the limbs, hypotension, haemoconcentration and hypoalbuminaemia);
- there is a risk of recurrence of capillary leak syndrome in people who have previously experienced the condition;
- patients with an acute episode of capillary leak syndrome following vaccination require prompt treatment and may require continuous specialist monitoring and intensive supportive therapy; and
- people receiving the vaccine must be instructed to seek medical attention if they have signs and symptoms of capillary leak syndrome in the days after vaccination, i.e. oedema in the extremities and sudden weight gain, which may be associated with feeling faint (due to low blood pressure).

People should be aware that:

- they must not have this vaccine if they had previously experienced capillary leak syndrome.

People who have been vaccinated with COVID-19 Vaccine Janssen should be aware that:

- capillary leak syndrome is a serious condition; while the risk of the condition occurring is very low, they should still be aware of the symptoms so that they can get prompt medical treatment to help recovery and avoid complications;
- they must seek medical attention immediately if the following symptoms occur in the days after vaccination:
 - rapid swelling of the arms and legs; or
 - sudden weight gain,

which may occur together with feeling faint (due to low blood pressure).

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

PRAC will continue to monitor for cases of the condition and will take any further actions necessary. PRAC has also asked the company marketing the vaccine for further information about a possible mechanism for the development of capillary leak syndrome following vaccination. A similar review was recently finalised for another COVID-19 vaccine, Vaxzevria³.

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 endorsement⁴.

Thrombosis with thrombocytopenia syndrome (TTS)

In April and May 2021, the product information for COVID-19 Vaccine Janssen was updated with regard to the very rare risk of thrombosis (formation of blood clots in the blood vessels) with thrombocytopenia (low blood platelets) syndrome (TTS)⁵. In July 2021, PRAC updated the risk management plan (see section 2) accordingly. Further, PRAC agreed that awareness of how to manage TTS should be raised among healthcare professionals by means of a direct healthcare professional communication (DHPC), covering both TTS and capillary leak syndrome (see above). PRAC is keeping TTS under close monitoring

As of 27 June 2021, 21 cases of suspected TTS with COVID-19 Vaccine Janssen were spontaneously reported to EudraVigilance (see section 2) from EU/EEA countries; 4 of these reported a fatal outcome^{6,7} (these suspected TTS figures refer to cases where events of thrombosis and thrombocytopenia were reported in combination; further case ascertainment is required to confirm TTS in these reported cases). About 7 million of doses of COVID-19 Vaccine Janssen had been given to people in the EU/EEA by 20 June 2021⁸.

³ See [safety update for Vaxzevria of 18 June 2021](#)

⁴ See [EMA public health communication on capillary leak syndrome with COVID-19 Vaccine Janssen of 9 July 2021](#)

⁵ See [safety update for COVID-19 Vaccine Janssen of 11 May 2021](#)

⁶ 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).

⁷ 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.

⁸ 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.

Guillain-Barré syndrome (GBS)

As part of the review of the regular MSSRs, PRAC is analysing cases of Guillain-Barré syndrome (GBS) reported following vaccination with COVID-19 Vaccine Janssen. GBS is an adverse event of special interest for all COVID-19 vaccines requiring specific safety monitoring.

GBS is an immune system disorder that causes nerve inflammation and can result in pain, numbness, muscle weakness and difficulty walking.

A total of 15 cases of GBS had been reported from the EU/EEA to EudraVigilance with COVID-19 Vaccine Janssen by 27 June 2021, while around 7 million doses of COVID-19 Vaccine Janssen had been given to people in the EU/EEA by 20 June 2021. 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. At this stage the available data neither confirm nor rule out a causal relationship with the vaccine.

PRAC has requested the marketing authorisation holder to provide further detailed data, including an analysis of all the reported cases, for continued assessment by PRAC.

Myocarditis and pericarditis

PRAC continued its assessment of myocarditis and pericarditis (inflammatory conditions of the heart) reported in a small number of people after vaccination with COVID-19 vaccines. As of end of May 2021, one case of pericarditis was reported from the EU/EEA to EudraVigilance (see section 2) after vaccination with COVID-19 Vaccine Janssen and no case of myocarditis had been reported for COVID-19 Vaccine Janssen by that date; 2 million doses of the vaccine had been administered in the EU/EEA. Further information is needed to assess whether there is a causal relationship between myocarditis/pericarditis and COVID-19 Vaccine Janssen, and PRAC has therefore requested additional data from the marketing authorisation holder.

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 languages. Search for “COVID-19 VACCINE JANSSEN (AD26.COVS)” to see all suspected side effect cases reported for COVID-19 Vaccine Janssen.

As of 4 July 2021, a total of 12,036 cases of suspected side effects with COVID-19 Vaccine Janssen were spontaneously reported to EudraVigilance from EU/EEA countries; 68 of these reported a fatal outcome^{9,10}. Around that time, about 8.5 million of doses of COVID-19 Vaccine Janssen had been given to people in the EU/EEA¹¹.

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.

⁹ 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).

¹⁰ 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.

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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.

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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