



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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# 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 8 September 2021.

### **Main outcomes from PRAC's latest safety assessment**

Venous thromboembolism (VTE, blood clotting in the veins) and immune thrombocytopenia (ITP, an autoimmune condition with low blood platelet levels) will be added to the product information as side effects of COVID-19 Vaccine Janssen, together with warnings and advice.

Transverse myelitis (inflammation in parts of the spinal cord) was recommended by PRAC to be added to the product information as a side effect of COVID-19 Vaccine Janssen.

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 30 September 2021, more than 14.3 million doses of COVID-19 Vaccine Janssen have been administered in the EU/EEA<sup>1</sup>.



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

During its meeting held 27 to 30 September 2021, PRAC assessed new safety data (see section 2 'How safety is monitored').

### Venous thromboembolism (VTE)

*Update to the COVID-19 Vaccine Janssen product information*

Venous thromboembolism (VTE) has been kept under close monitoring by PRAC due to a higher proportion of cases of VTE observed in the vaccinated group compared with the placebo group in the large clinical trial used to authorise COVID-19 Vaccine Janssen (see section 3).

VTE is a condition in which a blood clot forms in a deep vein, usually in a leg, arm or groin, and may travel to the lungs causing a blockage of the blood supply, with possibly life-threatening consequences (this safety issue is distinct from thrombosis with thrombocytopenia syndrome [TTS], see below).

At its meeting held 27 to 30 September 2021, PRAC reviewed new data from the clinical trial used to authorise COVID-19 Vaccine Janssen (COV3001), as well as data from another large clinical study (COV3009).

During the double-blind period (median follow-up time of 123 days) of the first, still ongoing, phase 3 study (COV3001), venous thromboembolic events were observed in 26 out of 21,894 (0.1%) individuals who received COVID-19 Vaccine Janssen and in 9 out of 21,882 (0.04%) individuals who received placebo. Of these, venous thromboembolic events were observed within 28 days in 8 individuals who received COVID-19 Vaccine Janssen and in 4 individuals who received placebo. Most of the observed

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<sup>1</sup> 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.

events involved deep vein thrombosis and pulmonary embolism (21 individuals who received COVID-19 Vaccine Janssen and 8 individuals who received placebo during the entire double-blind phase). The majority of events were reported in individuals with at least one predisposing risk factor for VTE.

In the other ongoing phase 3 study (COV3009, 15,708 individuals receiving the vaccine and 15,592 receiving placebo), there was no increase in venous thromboembolic events among individuals who received COVID-19 Vaccine Janssen (median follow-up time of 70 days).

When taking all evidence into account, PRAC concluded that there is a reasonable possibility that VTE is linked to vaccination with COVID-19 Vaccine Janssen. PRAC therefore recommended adding VTE to the product information of COVID-19 Vaccine Janssen as a rare side effect (i.e. occurring in less than 1 in 1,000 individuals), together with warnings for healthcare professionals and people taking the vaccine, especially those who may have an increased risk of VTE.

PRAC also agreed on a direct healthcare professional communication (DHPC) to raise awareness among healthcare professionals. Following agreement of the [Committee for Medicinal Products for Human Use](#) (CHMP) on the product information update and the DHPC, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holder according to an agreed communication plan. The DHPC will be available on a [dedicated page](#) on the EMA website and in the [national DHPC registers](#) of EU Member States<sup>2</sup>.

Healthcare professionals should be aware that:

- VTE has been observed rarely following vaccination with COVID-19 Vaccine Janssen; and
- the risk of VTE should be considered for individuals with increased risk factors for thromboembolism (blood clots).

*Reminder:* Individuals diagnosed with thrombocytopenia within three weeks after vaccination with COVID-19 Vaccine Janssen should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within three weeks of vaccination should be evaluated for thrombocytopenia. This is important to assess a potential diagnosis of thrombosis with thrombocytopenia syndrome (TTS), which requires specialised clinical management.

Vaccinated individuals should seek immediate medical attention if they:

- develop shortness of breath, chest pain, leg swelling, leg pain or persistent abdominal pain following vaccination; or
- experience severe or persistent headaches, blurred vision, mental status changes or seizures (fits) a few days following vaccination.

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<sup>2</sup> See [Meeting Highlights from the Pharmacovigilance Risk Assessment Committee \(PRAC\) 27 - 30 September 2021](#)

## Immune thrombocytopenia (ITP)

### *Update to the COVID-19 Vaccine Janssen product information*

In August 2021, PRAC recommended updating the product information of COVID-19 Vaccine Janssen to include immune thrombocytopenia (ITP) as a side effect, together with a warning to alert healthcare professionals and people taking the vaccine<sup>3</sup>.

ITP is a condition in which the immune system mistakenly targets blood cells called platelets that are needed for normal blood clotting. Very low levels of blood platelets can be associated with bleeding and serious health problems.

At its meeting held 27 to 30 September 2021, PRAC finalised the update of the product information, allocating ITP to the 'unknown frequency' category, 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. Spontaneously 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.

PRAC also agreed on a direct healthcare professional communication (DHPC) to raise awareness among healthcare professionals. Following agreement of the [Committee for Medicinal Products for Human Use](#) (CHMP) on the product information update and the DHPC, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holder according to an agreed communication plan. The DHPC will be available on a [dedicated page](#) on the EMA website and in the [national DHPC registers](#) of EU Member States<sup>4</sup>.

Healthcare professionals should be aware that:

- cases of ITP, some with very low platelet levels (<20,000 per  $\mu\text{L}$ ), have been reported very rarely, usually within the first four weeks after receiving COVID-19 Vaccine Janssen; this included cases with bleeding and cases with a fatal outcome; some of these occurred in individuals with a history of ITP;
- if an individual has a history of ITP, the risk of developing low platelet levels should be considered before vaccination, and platelet monitoring is recommended after vaccination.

*Reminder:* Individuals diagnosed with thrombocytopenia within three weeks after vaccination with COVID-19 Vaccine Janssen should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within three weeks of vaccination should be evaluated for thrombocytopenia. This is important to assess a potential diagnosis of thrombosis with thrombocytopenia syndrome (TTS), which requires specialised clinical management.

<sup>3</sup> See [safety update for COVID-19 Vaccine Janssen of 11 August 2021](#)

<sup>4</sup> See [Meeting Highlights from the Pharmacovigilance Risk Assessment Committee \(PRAC\) 27 - 30 September 2021](#)

Vaccinated individuals should:

- seek immediate medical attention if they experience unexplained bleeding or skin bruising or pinpoint round spots beyond the site of vaccination, appearing a few days after vaccination.

## Thrombosis with thrombocytopenia syndrome (TTS)

*Update to the COVID-19 Vaccine Janssen product information*

In May 2021, the product information of 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)<sup>5</sup>.

Data on TTS are kept under close monitoring for further characterisation of risk factors, and PRAC now concluded that the product information should be further updated by removing the current statement that reported TSS cases occurred mostly in women, since the previously observed sex imbalance between cases could no longer be observed.

Of the cases reported spontaneously as TTS worldwide by the end of August 2021, 73% of cases were reported in subjects below 60 years of age. In most cases sex was known, and around 44% were in women below the age of 60 years. Spontaneously 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.

*Reminder:* People should seek immediate medical attention if they experience severe or persistent headache, blurred vision, confusion, seizures, shortness of breath, chest pain, leg swelling, leg pain, persistent abdominal pain, unusual bleeding or skin bruising or pinpoint round spots beyond the site of vaccination within three weeks of vaccination, as these could be signs of TTS.

## Transverse myelitis

*Update to the COVID-19 Vaccine Janssen product information*

PRAC recommended that transverse myelitis (inflammation in parts of the spinal cord) should be added to the product information as a side effect of COVID-19 Vaccine Janssen.

This conclusion is based on worldwide transverse myelitis cases spontaneously reported by 31 August 2021, of which 10 have been assessed to have at least a possible causal relationship with the vaccine, and 1 a probable causal relationship (more than 33 million doses of COVID-19 Vaccine Janssen were estimated to have been administered worldwide by 31 August 2021). Spontaneously reported cases concern

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

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.

The frequency category is proposed to be '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.

## Dizziness

*Update to the COVID-19 Vaccine Janssen product information*

In August 2021, PRAC recommended adding dizziness to the product information as a side effect of COVID-19 Vaccine Janssen<sup>6</sup>.

PRAC has now finalised the product information and allocated this side effect to the frequency category 'uncommon' (i.e. occurring in less than 1 in 100 individuals), based on clinical trial data.

## 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).

### 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

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<sup>6</sup> See [safety update for COVID-19 Vaccine Janssen of 11 August 2021](#)

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

As of 30 September 2021, a total of 23,455 cases of suspected side effects with COVID-19 Vaccine Janssen were spontaneously reported to EudraVigilance from EU/EEA countries; 171 of these reported a fatal outcome<sup>7,8</sup>. By the same date, more than 14.3 million doses of COVID-19 Vaccine Janssen had been given to people in the EU/EEA<sup>9</sup>.

**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

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<sup>7</sup> 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).

<sup>8</sup> 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.

<sup>9</sup> 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.

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.



## European Medicines Agency

**Official address** Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

**Address for visits and deliveries** Refer to [www.ema.europa.eu/how-to-find-us](http://www.ema.europa.eu/how-to-find-us)

**Send us a question** Go to [www.ema.europa.eu/contact](http://www.ema.europa.eu/contact)

**Telephone** +31 (0)88 781 6000

