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Direct Healthcare Professional Communication

# COVID-19 Vaccine Janssen: Contraindication in individuals with previous capillary leak syndrome and update on thrombosis with thrombocytopenia syndrome

Dear Healthcare Professional,

Janssen-Cilag International NV in agreement with the European Medicines Agency and the Medicines Authority would like to inform you of the following:


***Summary***

**Capillary leak syndrome (CLS):**

- **Very rare cases of capillary leak syndrome (CLS) have been reported in the first days after vaccination with COVID-19 Vaccine Janssen, in some cases with a fatal outcome. A history of CLS has been reported in at least one case.**
- **COVID-19 Vaccine Janssen is now contraindicated in individuals who have previously experienced episodes of CLS.**
- **CLS is characterised by acute episodes of oedema mainly affecting the limbs, hypotension, haemoconcentration and hypoalbuminaemia. Patients with an acute episode of CLS following vaccination require prompt recognition and treatment. Intensive supportive therapy is usually warranted.**

**Thrombosis with thrombocytopenia syndrome (TTS)**

- **Individuals diagnosed with thrombocytopenia within 3 weeks after vaccination with COVID-19 Vaccine Janssen should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within 3 weeks of vaccination should be evaluated for thrombocytopenia.**
- **TTS requires specialised clinical management. Healthcare professionals should consult applicable guidance and/or consult specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat this condition.**

***Background on the safety concerns***

COVID-19 Vaccine Janssen suspension for injection is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 18 years of age and older.

**Capillary leak syndrome (CLS)**

Very rare cases of capillary leak syndrome (CLS) have been reported following vaccination with COVID-19 Vaccine Janssen, with an estimated reporting rate of one case per approximately 6 million doses. A history of CLS has been reported in at least one of the cases.

CLS is a rare disorder characterised by dysfunctional inflammatory response, endothelial dysfunction, and extravasation of fluid from the vascular space to the interstitial space leading to shock, haemoconcentration, hypoalbuminaemia and potentially consequent organ failure. Patients may present with a rapid swelling of the arms and legs, sudden weight gain and feel faint due to low blood pressure.

Some cases of systemic CLS reported in the literature have been triggered by COVID-19 infection.

CLS occurs rarely in the general population with fewer than 500 cases described worldwide in the literature (National Organisation for Rare Disorders), however, it is likely that estimates are lower than the true event rates.

The European Medicines Agency has recommended an update to the product information of the COVID-19 Vaccine Janssen suspension for injection to reflect the current knowledge of the safety topic.

**Thrombosis with thrombocytopenia syndrome (TTS)**

A combination of thrombosis and thrombocytopenia (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with COVID-19 Vaccine Janssen. This includes severe cases of venous thrombosis at unusual sites such as cerebral venous sinus thrombosis, splanchnic vein thrombosis as well as arterial thrombosis concomitant with thrombocytopenia. Fatal outcome has been reported. These cases occurred within the first 3 weeks following vaccination and mostly in women under 60 years of age.

In several of the TTS cases, testing for anti-platelet factor (PF) 4-antibodies was positive or strongly positive. However, the exact pathophysiological mechanism for the occurrence of these thrombotic events is not defined yet, and no specific risk factors have been identified at this stage.

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia. Those vaccinated should be instructed to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms including severe or persistent headaches, seizures, mental status changes or blurred vision after vaccination, or who experiences skin bruising (petechia) beyond the site of vaccination after a few days, should seek prompt medical attention.

Thrombosis in combination with thrombocytopenia requires specialised clinical management. Healthcare professionals should consult applicable guidance and/or consult specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat this condition.

Individuals diagnosed with thrombocytopenia within 3 weeks after vaccination with COVID-19 Vaccine Janssen should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within 3 weeks of vaccination should be evaluated for thrombocytopenia.

**Call for reporting**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are reminded to continue to report suspected adverse reactions associated with COVID-19 Vaccine Janssen in accordance with the national spontaneous reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Post-licensing directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to postlicensing.medicinesauthority@gov.mt

▼ This product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

**Company contact point**

Should you have any questions or require additional information, please contact Janssen-Cilag International B.V. at:

| Company | Product Name | Website or Email | Phone |
|---|---|---|---|
| Janssen-Cilag International B.V. | COVID-19 Vaccine Janssen | JGCC_emea@its.jnj.com | Toll-free number: 80065007<br>Local number: +35 6 27 78 00 04 |

Yours faithfully,

**Post-Licensing Directorate**

**Medicines Authority**

***Disclaimer***

*This Direct Healthcare Professional Communication has been submitted to you on behalf of Janssen-Cilag Internatiional B.V. and their local representative A.M. Mangion Limited.*