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Direct Healthcare Professional Communication

COVID-19 Vaccine Janssen: link between the vaccine and the occurrence of thrombosis in combination with thrombocytopenia

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

- **A combination of thrombosis and thrombocytopenia, in some cases accompanied by bleeding, has been observed very rarely following vaccination with COVID-19 Vaccine Janssen. A causal relationship with the vaccine is considered plausible.**
- **These cases occurred within the first three weeks following vaccination, and mostly in women under 60 years of age.**
- **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 being vaccinated should be instructed to seek immediate medical attention if they develop symptoms of thromboembolism and, or thrombocytopenia following vaccination.**
- **Thrombosis in combination with thrombocytopenia requires specialised clinical management. Consult applicable guidance and/or specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat this condition.**

Background on the safety concern

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.

A combination of thrombosis and thrombocytopenia, 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 three weeks following vaccination, and mostly in women under 60 years of age.

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 swelling, or persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms including severe or persistent headaches 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.

In several of the cases with concomitant thrombosis and thrombocytopenia, testing for anti-platelet factor (PF) 4-antibodies was positive or strongly positive. Extensive work-up for other potential mechanisms that could cause thrombosis and/or thrombocytopenia has been provided for a minority of these cases; however, no other abnormalities have been found that are considered to explain the observed events. However, the exact pathophysiological mechanism for the occurrence of these thrombotic events is not defined yet. No specific risk factors have been identified at this stage.

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.

The Pharmacovigilance Risk Assessment Committee, PRAC, one of EMA's scientific committees, has performed a thorough investigation including a review of case reports of blood clots and thrombocytopenia in individuals who received the vaccine and has also evaluated an observed to expected analysis.

Based on the current evidence, the PRAC has recommended an update to the product information to reflect the current knowledge of this safety issue. This comprises an update of the warning section, as well as inclusion of thrombosis in combination with thrombocytopenia as an adverse reaction with a frequency of very rare.

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	Email	Phone
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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.