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 <National Competent 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

Healthcare professionals should report any suspected adverse reactions associated with the use of COVID-19 Vaccine Janssen in accordance with the national spontaneous reporting system <*include the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system*>.

▼ 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

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address (company contact point in the concerned EU MS should be included, respectively)>

Yours Faithfully

Medical Director of Janssen-Cilag International B.V.

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	COVID-19 Vaccine Janssen suspension for injection (Ad26.COV2-S [recombinant])
Marketing authorisation holder(s)	Janssen-Cilag International N.V.
Safety concern and purpose of the communication	Information on the risk of thrombosis in combination with thrombocytopenia.
DHPC recipients	General practitioners, specialists in internal medicine, haematology, emergency medicine and vaccination centres. The target group should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU member states where COVID-19 Vaccine Janssen is authorised.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	Tue 20/04/2021
DHPC and communication plan (in English) agreed by CHMP	Wed 21/04/2021
Submission of translated DHPCs to the national competent authorities for review	Thu 22/04/2021
Agreement of translations by national competent authorities	Fri 23/04/2021
Dissemination of DHPC	Mon 26/04/2021