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HPRA DRUG SAFETY
NEWSLETTER
103RD EDITION

COVID-19 Vaccine Janssen® – EMA review of very rare cases of thrombosis in combination with thrombocytopenia following vaccination

The European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) completed its initial investigation* of a signal of thrombotic events in combination with thrombocytopenia in people vaccinated with COVID-19 Vaccine Janssen® on 20 April 2021.

The EMA review considered that the benefits of the vaccine in combating the continuing widespread threat of COVID-19 (which itself results in clotting problems and may be fatal) outweigh the risks. However, the vaccine may be associated with very rare cases of blood clots, mostly occurring in unusual sites, associated with thrombocytopenia, including rare cases of Cerebral Venous Sinus Thrombosis (CVST), splanchnic vein thrombosis and arterial thrombosis, in some cases accompanied by bleeding. Eight cases of these rare types of events from the US, one of which resulted in a fatal outcome, were assessed as part of the EU review. Approximately 7 million people in the US had received the vaccine as of 13 April 2021.

A causal link with the vaccine is considered possible and the product information for COVID-19 Vaccine Janssen® will be updated to include a warning about thrombosis combined with thrombocytopenia, and will list these events as very rare side effects of the vaccine.

The PRAC reviewed all currently available evidence, including the eight reports from the US. All cases occurred in people under 60 years of age within 3 weeks of vaccination and the majority were women. At this time, investigations into a pathophysiological mechanism are ongoing, and it is currently not possible to identify specific risk factors. However, it is thought that the vaccine may trigger an immune response leading to a heparin-induced-thrombocytopenia (HIT)-like disorder. The cases reviewed were very similar to the cases that occurred with the COVID-19 vaccine developed by AstraZeneca, Vaxzevria® (previously called COVID-19 Vaccine AstraZeneca®), which were recently highlighted in HPRA Drug Safety Newsletter Edition 102.

Given the findings, healthcare professionals and vaccine recipients should be aware of the remote possibility of developing such syndromes and recipients should be advised to seek immediate medical attention if they develop symptoms and signs of bleeding or clotting and inform healthcare professionals of their recent vaccination.

While further analysis is ongoing, the product information for the vaccine will be updated to include more information on these risks. A direct healthcare professional communication (DHPC) is being sent to healthcare professionals and is published on the HPRA website.

Advice to healthcare professionals

Healthcare professionals should be vigilant to the signs and symptoms of thrombosis and/or thrombocytopenia in individuals vaccinated with COVID-19 Vaccine Janssen® and Vaxzevria®.

Those vaccinated should be advised of the signs and symptoms they need to be aware of, and 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 and 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. Guidance on the diagnosis and management of thrombocytopenia and thrombosis associated with adenoviral vector COVID-19 vaccination has been devised by the Irish Haematology Society Coagulation Special Interest Group and is available from the HSE website here. Healthcare professionals may also consult a specialist in haematology for advice on the investigation and management of patients presenting with thrombocytopenia and/or thrombosis following vaccination with either COVID-19 Vaccine Janssen® or Vaxzevria®.

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Key messages

Rare cases of thrombosis and thrombocytopenia, some presenting as cerebral venous sinus thrombosis or splanchnic vein thrombosis have been reported in persons who had recently received COVID-19 Vaccine Janssen®, mostly occurring within three weeks after vaccination.

The benefit-risk balance of the vaccine remains positive, however, healthcare professionals should be vigilant and alert to possible cases of thrombosis combined with thrombocytopenia, occurring in vaccinated individuals and advise recipients as to the symptoms and signs that require immediate medical attention.

Prompt recognition and immediate referral for specialist medical management is important to aid recovery and avoid complications.

Suspected adverse reactions** should be reported to the HPRA via the available methods (www.hpra.ie/report).

* Further information on the review is available on the EMA website and the HPRA website as well as updated advice for patients and healthcare professionals in the product information.

** Adverse reactions may be reported to the HPRA by members of the public, carers or healthcare professionals via www.hpra.ie/report.

Reporting adverse reactions to the HPRA supports continuous monitoring of safe and effective use of COVID-19 vaccines. When reporting, as much information as is known should be provided, and where possible, the vaccine batch number should be included.

The HPRA cannot provide clinical advice on individual cases. Members of the public should contact their health care professional (their doctor or pharmacist) with any medical concerns they may have.

Current product information and updates to those documents, as well as safety communications and information on regulatory actions in relation to medicines are published on www.hpra.ie.

Registering with the HPRA for safety alerts and updates

The HPRA website provides users with the option of registering their contact information with the HPRA to enable them to receive direct and immediate notification of alerts/updates by email. Users will be alerted to (depending on their recorded preferences) publications such as the HPRA Drug Safety Newsletter, Direct Healthcare Professional Communications (DHPCs) and alerts regarding new/updated safety/quality information on medicines/vaccines/medical devices etc.

To facilitate prompt access to these updates, users are encouraged to avail of this option by registering on the website:

- Go to the HPRA webpage www.hpra.ie
- Click on 'Register' in the 'My HPRA' box on the top right hand corner of the homepage
- Enter your details and click 'Register'
- You will be emailed a link to confirm registration to the email address nominated
- Once registration is confirmed, log in using your email address and password
- You will be brought to the 'My HPRA' page to manage your preferences
- Under 'My preferences', tick the stakeholder group (e.g. Healthcare Professionals), topics of interest that you wish to receive updates about (e.g. safety and quality) and products of interest (Medicines). Please note that at any time you, can log into 'My HPRA' to update your preferences.

Correspondence/comments should be sent **by email only** to the Pharmacovigilance Section, Health Products Regulatory Authority, medsafety@hpra.ie.

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