EMA advises against use of COVID-19 Vaccine Janssen in people with history of capillary leak syndrome

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Information on COVID-19 Vaccine Janssen

- COVID-19 Vaccine Janssen is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 18 years and older. COVID-19 is caused by SARS-CoV-2 virus. The vaccine is made up of another virus (of the adenovirus family) that has been modified to contain the gene for making the S protein from SARS-CoV-2. COVID-19 Vaccine Janssen does not contain the virus itself and cannot cause COVID-19.

- The most common side effects are usually mild or moderate and improve within a few days after vaccination.

The following products are authorised via centralised procedure.

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
COVID-19 vaccine (Ad26.COV2-S [recombinant])	COVID-19 Vaccine Janssen	Concentrate for dispersion for injection (sterile concentrate)	POM	EU/1/20/1525	Janssen-Cilag International NV

Information from the EMA about the safety concern

- A review was carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, in the context of a procedure known as a 'type II variation'. The PRAC's recommendations have been submitted to EMA's human medicine committee, and CHMP, has endorsed them.

- EMA's safety committee (PRAC) has recommended that people who have previously had capillary leak syndrome must not be vaccinated with COVID-19 Vaccine Janssen. The Committee also recommended that capillary leak syndrome should be added to the product information as a new side effect of the vaccine, together with a warning to raise awareness among healthcare professionals and patients of this risk.

- The Committee reviewed 3 cases of capillary leak syndrome in people who had received COVID-19 Vaccine Janssen, which occurred within 2 days of vaccination. One of those affected had a history of capillary leak syndrome and two of them subsequently died. As of 21 June 2021, more than 18 million doses of COVID-19 Vaccine Janssen had been administered worldwide.

- Capillary leak syndrome is a very rare, serious condition that causes fluid leakage from small blood vessels (capillaries), resulting in swelling mainly in the arms and legs, low blood pressure, thickening of the blood and low blood levels of albumin (an important blood protein).

- Healthcare professionals should be aware of the signs and symptoms of capillary leak syndrome and of its risk of recurrence in people who have previously been diagnosed with the condition.

- People who have been vaccinated with COVID-19 Vaccine Janssen should seek immediate medical assistance if they experience rapid swelling of the arms and legs or sudden weight gain in the days following vaccination. These symptoms are often associated with feeling faint (due to low blood pressure).

- PRAC will continue to monitor for cases of the condition and will take any further actions necessary. The Committee has also asked Janssen, the company marketing the vaccine, for further information about a possible mechanism for the development of capillary leak syndrome following vaccination.

- As for all vaccines, EMA will continue to monitor the vaccine's safety and effectiveness and provide the public with the latest information.

- A similar review was recently finalised for another COVID-19 vaccine, Vaxzevria (previously COVID-19 Vaccine AstraZeneca).

In Malta

For Healthcare Professionals

- EMA has reviewed cases of capillary leak syndrome in people who received COVID-19 Vaccine Janssen.

- Healthcare professionals must not give this vaccine to anyone who has a history of capillary leak syndrome.

- Capillary leak syndrome is a very rare, serious condition, which can be fatal if untreated. It causes fluid leakage from the capillaries, resulting in oedema mainly affecting the limbs, hypotension, haemoconcentration and hypoalbuminaemia.

- Healthcare professionals should be aware of the risk of recurrence of capillary leak syndrome in people who have previously experienced the condition.

- Healthcare professionals should be aware of the signs and symptoms of capillary leak syndrome. Patients with an acute episode of capillary leak syndrome following vaccination require prompt treatment and may require continuous specialist monitoring and intensive supportive therapy.

- Healthcare professionals should tell people receiving the vaccine that they must seek medical attention if they have the following symptoms in the days after vaccination, which may be associated with feeling faint (due to low blood pressure):
  - oedema in the extremities
  - sudden weight gain
- The product information will be updated to include a contraindication in people with a history of capillary leak syndrome. The condition will also be listed as a side effect with an unknown frequency.

A direct healthcare professional communication (DHPC) will be sent in due course to healthcare professionals prescribing, dispensing or administering the vaccine. The DHPC will also be published on a dedicated page on the ADM website.

Advice for Patients

- A very small number of cases of capillary leak syndrome have occurred in people who received COVID-19 Vaccine Janssen.
- You must not have this vaccine if you have previously experienced capillary leak syndrome.
- Capillary leak syndrome is a serious condition. The chance of the condition occurring is very low, but you should still be aware of the symptoms so that you can get prompt medical treatment to help recovery and avoid complications.
- You must seek medical attention immediately if you have the following symptoms in the days after vaccination, which may occur together with feeling faint (due to low blood pressure):
  - rapid swelling of the arms and legs
  - sudden weight gain

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance with COVID-19 Vaccine Janssen. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 **or** online to http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate

Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

Feedback:

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Pharmacovigilance Section

Post-Licensing Directorate

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