IMPORTANT MEDICINE SAFETY INFORMATION:
COVID-19 VACCINE JANSSEN

20 July 2021

Dear Healthcare Professional

COVID-19 VACCINE JANSSEN:

1. **CONTRAINDICATION IN INDIVIDUALS WITH PREVIOUS CAPILLARY LEAK SYNDROME (CLS) – (new safety information)**
2. **RISK OF THROMBOSIS IN COMBINATION WITH THROMBOCYTOPENIA (updated information)**

Janssen Pharmaceutica (Pty) Ltd, as directed by the South African Health Products Regulatory Authority (SAHPRA) would like to inform you about new safety information that has resulted in contraindication of the COVID-19 Vaccine Janssen in individuals with a history of Capillary Leak Syndrome (CLS).

CLS has been reported following vaccination with COVID-19 Vaccine Janssen.

The Professional Information (PI) of the COVID-19 Vaccine Janssen will be updated to appropriately reflect the above safety information.

1. CONTRAINDICATION IN INDIVIDUALS WITH PREVIOUS CAPILLARY LEAK SYNDROME (CLS)

Summary

- **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.**

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.

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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.

Advice to healthcare professionals

- Healthcare professionals should be alert to the signs and symptoms of Capillary Leak Syndrome (CLS) which are tiredness, nausea, abdominal pain, dyspnoea, extreme thirst and sudden increase in body weight, few days following vaccination. Complications can include general swelling, compartment syndrome, kidney failure and stroke.
- Individuals with an acute episode of CLS require prompt treatment and may require continuous specialist monitoring and intensive supportive therapy.
- Healthcare professionals should advise those vaccinated to consult a healthcare professional if they develop any of the above-mentioned signs and symptoms.

2. RISK OF THROMBOSIS IN COMBINATION WITH THROMBOCYTOPENIA

Summary

- 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.

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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 (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 three 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.

Advice to healthcare professionals

- Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia which are shortness of breath, chest pain, leg pain, leg swelling, or persistent headaches and abdominal pain, following vaccination.
- Healthcare professionals should advise those vaccinated to consult a healthcare professional if they develop any of the above-mentioned signs and symptoms.
- Additionally, those who receive the vaccine should be advised to consult a healthcare professional promptly when experiencing neurological symptoms including severe or persistent headaches, seizures, mental status changes or blurred vision after vaccination, or if experiencing skin bruising (petechia) beyond the site of vaccination after a few days.
- Healthcare professionals should actively investigate individuals diagnosed with thrombocytopenia within 3 weeks after vaccination with COVID-19 Vaccine Janssen for signs of thrombosis.
- Similarly, individuals who present with thrombosis within 3 weeks of vaccination should be evaluated for thrombocytopenia.
- Thrombosis in combination with thrombocytopenia requires specialised clinical management. Healthcare professionals are advised to consult applicable guidance and/or consult specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat this condition.

Healthcare professionals are urged to report all suspected adverse events following immunisation or product quality issues associated with the use of COVID-19 Vaccine Janssen to SAHPRA via Med Safety App. The App can be downloaded into a smart mobile phone through google Play or App store. For more information on Med Safety App, please visit SAHPRA website.

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Alternatively, the ADR reporting form accessible via the SAHPRA website at https://www.sahpra.org.za/wp-content/uploads/2021/04/6.04 ARF1 v5.3 April2021-addition of Med Safety App.pdf can be completed and emailed to adr@sahpra.org.za.

Additionally, reporting can be done via the eReporting link available on the SAHPRA website (www.sahpra.org.za). For more information on ADR reporting, please contact the SAHPRA vigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details below:

PRODUCT	ACTIVE INGREDIENT	REGISTRATION NUMBER	CONTACT DETAILS Pharmacovigilance Unit	CONTACT DETAILS Medical Information
COVID-19 VACCINE JANSSEN	COVID-19 vaccine (Ad26.COV2-S [recombinant])	55/30.5/0849	**Tel:** +2711 518 7100 **Fax:** +2786 687 8942 or +2711 518 7108 **Email:** AdverseEventZA@its.jnj.com	**Janssen COVID-19 Vaccine Dedicated Line** **Tel:** +27 21 672 2331 **Email:** JGCC EMEA@its.jnj.com

Yours sincerely

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