IMPORTANT MEDICINE SAFETY INFORMATION

25 February 2025

Dear Healthcare Professional,

RE: THE RISK OF MENINGIOMA ASSOCIATED WITH THE USE OF MEDROXYPROGESTERONE ACETATE.

Pfizer and Viatris Healthcare South Africa (Pty) Ltd, in collaboration with the South African Health Products Regulatory Authority (SAHPRA), would like to inform you of the increased risk of meningioma associated with prolonged use:

Summary:

- There is an increased risk of developing meningioma with high doses of medroxyprogesterone acetate (all injectable and ≥ 100 mg oral formulations), primarily after prolonged use (≥3 years).
- For contraception or non-oncological indications:
    - Medicines containing high doses medroxyprogesterone acetate are contraindicated in patients with meningioma or a history of meningioma.
    - If meningioma is diagnosed in a patient treated with medroxyprogesterone acetate, treatment must be stopped, as a precautionary measure.
- For oncological indications:
    - If a meningioma is diagnosed in a patient treated with medroxyprogesterone acetate, the need to continue the treatment should be carefully reconsidered, on a case-by-case basis taking into account individual benefits and risks.
- Patients treated with high doses medroxyprogesterone acetate or taking medroxyprogesterone acetate for a prolonged period should be monitored for signs and symptoms of meningioma in accordance with clinical practice.

Background on the Safety Concern:

Medroxyprogesterone acetate is available in both injectable and oral formulations for gynaecological (including contraception and endometriosis) and oncological indications.

Meningioma is a rare, usually benign tumour that forms from the meninges. Clinical signs and symptoms of meningioma may be non-specific and include changes in vision, hearing loss or ringing in the ears, loss of smell, headaches that worsen with time, memory loss, seizures or weakness in the extremities. While meningiomas are usually benign, their location may lead to serious consequences and may require surgery.

Based on results from a French epidemiological case-control study[1], an association between medroxyprogesterone acetate and meningioma has been observed. This study was based on data from the French National health data system (SNDS – Système National des Données de Santé) and included a population of 18, 061 women who had intracranial surgery for meningioma. Each case was matched to five controls per year of birth and area of residence (90, 305 controls).

[1] Roland N, Neumann A, Hoisnard L, Duranteau L, Froelich S, Zureik M et al. Use of progestogens and the risk of intracranial meningioma: national case-control study BMJ 2024; 384 :e078078 doi:10.1136/bmj-2023-078078

The exposure to medroxyprogesterone acetate 150 mg/3ml injectable was compared between women who had intracranial surgery for meningioma and women without meningioma. Analyses showed an excess risk of meningioma with the use of medroxyprogesterone acetate 150 mg/3 ml (9/18,061 cases (0.05%) vs. 11/90,305 controls (0.01%), odds ratio (OR) 5.55 (95% CI 2.27 to 13.56)). This excess risk seems to be driven by prolonged use (≥3 years) of medroxyprogesterone acetate 150 mg/3 ml. Although the relative risk of meningioma is significantly increased with the use of high dose medroxyprogesterone acetate, the absolute risks are very small.

No new safety concern regarding a risk of meningioma associated with the use of low dose (<100 mg) medroxyprogesterone and combination products containing medroxyprogesterone has been identified at this moment and therefore the recommendations do not apply for lower doses of oral formulations of MPA.

The product information for all relevant medroxyprogesterone acetate containing medicines will be updated accordingly and meningioma will be added as an adverse reaction with a frequency 'not known'.

Advice for healthcare professionals

Healthcare professionals are encouraged to provide counselling to patients about the side effects of medroxyprogesterone acetate detailed in the product information. SAHPRA recommends that patients treated with medroxyprogesterone acetate should be monitored for signs and symptoms of meningioma in accordance with clinical practice. If a meningioma is diagnosed in any patient treated with medroxyprogesterone acetate for a non-oncological indication, the use of medroxyprogesterone acetate must be stopped, as a precautionary measure. If a meningioma is diagnosed in any patient treated with medroxyprogesterone acetate for an oncological indication, the need for further use of medroxyprogesterone acetate should be carefully considered on a case-by-case basis, considering individual benefits and risks.

Advice for healthcare professionals to provide to patients

Understanding the potential side effects of any medicine is important for making informed choices about contraception and the management of endometriosis-associated pain. Patients should talk to a healthcare professional before taking or continuing medroxyprogesterone acetate. It is important to use medroxyprogesterone acetate for its approved indications and to follow the directions for use provided by healthcare professionals.

Call for reporting:

- Healthcare professionals are urged to report any adverse drug reactions (ADRs), or product quality issues associated with the use of the listed products to the companies below, or to SAHPRA via the e-Reporting link available on the SAHPRA website (www.sahpra.org.za).

- Alternatively, please complete the ADR reporting form accessible via the SAHPRA website and email it to adr@sahpa.org.za,or reporting can be done via the Med Safety App, downloadable through the Google Play or Apple App Store.

- For more information on ADR reporting of the products listed below, please use the contact details indicated.

[1] Roland N, Neumann A, Hoisnard L, Duranteau L, Froelich S, Zureik M et al. Use of progestogens and the risk of intracranial meningioma: national case-control study BMJ 2024; 384 :e078078 doi:10.1136/bmj-2023-078078

Company Point of Contact

For further information, please find the contact details below:

Company	Product	Active ingredient	Registration Number	Contact details
Pfizer Laboratories (PTY) Ltd	DEPO-PROVERA 150 injection	medroxyprogesterone acetate	E/21.8.2/114	Tel: 0860 PFIZER (0860734937) e-mail: ZAF.AEReporting@pfizer.com Medical information: Med.Info2@Pfizer.com
	PROVERA 100 mg tablets PROVERA 500 mg tablets		S/21.8.2/1 W/21.8.2/462	
Viatris Healthcare (Pty) Ltd	Mytricon 150 mg/mL, suspension for injection	medroxyprogesterone acetate	52/21.8.2/0991	Tel: 0114511300 e-mail: pv.southafrica@viatris.com Medical information: ZAmedinfo@viatris.com
	Medroxyprogesterone Mylan 150 mg/mL, suspension for injection	medroxyprogesterone acetate	52/21.8.2/0992.991	

Yours sincerely,

Lawrene Makamu Country Safety Lead Pfizer Laboratories (PTY) Ltd Signature Signed by: Lawrene Makamu Signer Name: Lawrene Makamu Signing Reason: I approve this document Signing Time: 25-Feb-2025 | 12:20:43 AM EST 2FE17577AA8F42E98422A7A3C4A53225	Sohana Sukhnandan Responsible Pharmacist Viatris Healthcare (Pty) Ltd Signature Digitally signed by Sohana Sukhnandan-M670600 Date: 2025.02.25 08:38:22 +02'00'

[1] Roland N, Neumann A, Hoisnard L, Duranteau L, Froelich S, Zureik M et al. Use of progestogens and the risk of intracranial meningioma: national case-control study BMJ 2024; 384 :e078078 doi:10.1136/bmj-2023-078078