Medroxyprogesterone acetate: Risk of meningioma and measures to minimise this risk

<Date>

Dear Healthcare Professional,

Pfizer in agreement with the European Medicines Agency and the <National Competent Authority> would like to inform you of the following:

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 (several 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 high doses medroxyprogesterone acetate, treatment must be stopped.**
- **For oncological indications:**
    - **If a meningioma is diagnosed in a patient treated with high doses 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 should be monitored for signs and symptoms of meningioma in accordance with clinical practice.**

Background on the safety concern

<The wording of the indication varies between EU countries. Indication details to be amended on national level as needed:>

Medroxyprogesterone acetate is available in both injectable and oral formulations for gynaecological (including contraception and endometriosis) and oncological indications. A table attached to this letter shows the formulations and indications available in the European Union/EEA.

Meningioma is a rare, most frequently 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). The exposure to medroxyprogesterone acetate 150 mg/3ml injectable was compared between women

[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.

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'.

Call for reporting

Healthcare professionals should report adverse events in patients taking medicines containing medroxyprogesterone acetate to [NCA] to < insert local details: names, postal address, fax number, website number.

Company contact point

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>

A table of presentations and pharmaceutical forms of MPA licensed in EEA is attached to this Annex 1.

Formulation	Route of Administration and Strengths	Indication
DMPA injectable suspension	IM 50mg/ml; Injection, suspension (150mg/3ml; Injection, suspension) 150mg/ml; Injection, suspension 500mg/3.3ml; Injection, suspension	Contraception Endometriosis Menopausal vasomotor symptoms Recurrent and/or metastatic (breast/endometrial/renal) cancer
	SC 104mg/0.65ml; Injection, suspension	Contraception
MPA tablets	Oral 2.5mg; tablet 5mg; tablet 10mg; tablet 20mg; tablet 100mg; tablet 200mg; tablet 250mg; tablet 400mg; tablet 500mg; tablet	Endometriosis Menopausal vasomotor symptoms Diagnosis of primary amenorrhea Diagnosis and treatment of secondary amenorrhea Dysfunctional (anovulatory) uterine bleeding Opposition of endometrial effects of estrogen in menopausal women being treated with estrogen (HT) Recurrent and/or metastatic (breast/endometrial/renal) cancer Metastatic prostate cancer Anorexia and cachexia syndrome

COMMUNICATION PLAN FOR DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Medroxyprogesterone acetate
Marketing authorisation holder(s)	Pfizer
Safety concern and purpose of the communication	Medroxyprogesterone acetate: new information on the occurrence of meningioma
DHPC recipients	General practitioners / family physicians, gynaecologists, oncologists, community pharmacists, hospital pharmacists, relevant professional societies (oncology, gynaecology), relevant national associations. 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 MSs where there the medicinal products are approved.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	05 September 2024
Submission of translated DHPCs to the national competent authorities for review	19 September 2024
Agreement of translations by national competent authorities	26 September 2024
Dissemination of DHPC	03 October 2024