



30 September 2024<sup>1</sup>  
EMA/PRAC/373355/2024  
Pharmacovigilance Risk Assessment Committee (PRAC)

## New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 2-5 September 2024 PRAC

The product information wording in this document is extracted from the document entitled 'PRAC recommendations on signals' which contains the whole text of the PRAC recommendations for product information update, as well as some general guidance on the handling of signals. It can be found on the webpage for [PRAC recommendations on safety signals](#) (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

### 1. Medroxyprogesterone acetate (MPA) – Meningioma (EPITT no 20030)

*Taking into account the already existing wording in some nationally authorised products, the text may need to be adapted by marketing authorisation holders to individual products.*

#### Summary of product characteristics

##### 4.3 Contraindications

#### **MPA containing products with non-oncological indications (all injectable formulations and $\geq 100$ mg oral formulations):**

Meningioma or history of meningioma.

#### **MPA containing products with both non-oncological and oncological indications (all injectable formulations and $\geq 100$ mg oral formulations):**

Meningioma or history of meningioma (for non-oncological indications).

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<sup>1</sup> Expected publication date. The actual publication date can be checked on the webpage dedicated to [PRAC recommendations on safety signals](#).



#### 4.4 Special warnings and precautions for use

##### **MPA containing products with non-oncological indications (all injectable formulations and $\geq 100$ mg oral formulations):**

###### Meningioma

Cases of meningioma (single and multiple) have been reported in patients treated with medroxyprogesterone acetate for a prolonged time (several years). Patients treated with medroxyprogesterone acetate should be monitored for signs and symptoms of meningioma in accordance with clinical practice. If a patient is diagnosed with meningioma, medroxyprogesterone acetate must be stopped, as a precautionary measure.

In some cases, shrinkage of meningioma was observed after treatment discontinuation of depot medroxyprogesterone acetate.

##### **MPA containing products for oncological indications (all injectable formulations and $\geq 100$ mg oral formulations):**

###### Meningioma

Cases of meningioma (single and multiple) have been reported in patients treated with medroxyprogesterone acetate for a prolonged time (several years). Patients should be monitored for signs and symptoms of meningiomas in accordance with clinical practice. If a patient is diagnosed with meningioma, the need for further treatment with medroxyprogesterone acetate should be carefully considered on a case-by-case basis taking into account individual benefits and risks. In some cases, shrinkage of meningioma was observed after treatment discontinuation of depot medroxyprogesterone acetate.

##### **MPA containing products which have both non-oncological and oncological indications (all injectable formulations and $\geq 100$ mg oral formulations):**

###### Meningioma

Cases of meningioma (single and multiple) have been reported in patients treated with medroxyprogesterone acetate for a prolonged time (several years). Patients treated with medroxyprogesterone acetate should be monitored for signs and symptoms of meningioma in accordance with clinical practice.

In some cases, shrinkage of meningioma was observed after treatment discontinuation of depot medroxyprogesterone acetate. If a patient treated for a non-oncological indication is diagnosed with meningioma, medroxyprogesterone acetate must be stopped, as a precautionary measure.

If a patient treated for an oncological indication is diagnosed with meningioma, the need for further treatment with medroxyprogesterone acetate should be carefully considered on a case-by-case basis taking into account individual benefits and risks.

#### 4.8 Undesirable effects

##### **MPA containing products for all injectable formulations and $\geq 100$ mg oral formulations:**

SOC Neoplasms benign, malignant and unspecified: meningioma, frequency "not known".

## 5.1 Pharmacodynamic properties

### **MPA containing products for all injectable formulations and $\geq 100$ mg oral formulations:**

Based on results from a French epidemiological case-control study, 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 and 90,305 women without meningioma. 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 (0.05%) v 11/90 305 (0.01%), OR 5.55 (95%CI 2.27 to 13.56)). This excess risk seems to be driven primarily by prolonged use ( $\geq 3$  years) of medroxyprogesterone acetate.

### **Package leaflet**

2. What you need to know before you take <product name>

### **MPA containing products with non-oncological indications (all injectable formulations and $\geq 100$ mg oral formulations):**

Do not use <product name>

If you have meningioma or have ever been diagnosed with a meningioma (a usually benign tumour of the tissue layer surrounding the brain and spinal cord).

Tell your doctor if any of the following conditions apply to you.

Subsection "warnings and precautions"

#### Meningioma

Use of medroxyprogesterone acetate has been linked to the development of a usually benign tumour of the tissue surrounding the brain and spinal cord (meningioma). The risk increases especially when you use it for longer duration (several years). If you are diagnosed with meningioma, your doctor will stop your treatment with <product name> (see section 'Do not take...'). If you notice any symptoms such as changes in vision (e.g. seeing double or blurriness), hearing loss or ringing in the ears, loss of smell, headaches that worsen with time, memory loss, seizures, weakness in your arms or legs, you must tell your doctor straightaway.

### **MPA containing products with oncological indications (all injectable formulations and $\geq 100$ mg oral formulations):**

Subsection "warnings and precautions"

#### Meningioma

Use of medroxyprogesterone acetate has been linked to the development of a usually benign tumour of the tissue surrounding the brain and spinal cord (meningioma). The risk increases especially when you use it for longer duration (several years). If you are diagnosed with meningioma, your doctor will reconsider your treatment with <product name>. If you notice any symptoms such as changes in vision (e.g. seeing double or blurriness), hearing loss or ringing in the ears, loss of smell, headaches that worsen with time, memory loss, seizures, weakness in your arms or legs, you must tell your doctor straightaway.

**MPA containing products which have both non-oncological and oncological indications (all injectable formulations and  $\geq 100$  mg oral formulations):**

Do not use <product name>

If you have meningioma or have ever been diagnosed with a meningioma (usually benign tumour of the tissue surrounding the brain and spinal cord) unless you use <product name> for cancer.

Tell your doctor if any of the following conditions apply to you.

Subsection "Warnings and precautions"

**Meningioma**

Use of medroxyprogesterone acetate has been linked to the development of a usually benign tumour of the tissue surrounding the brain and spinal cord (meningioma). The risk increases especially when you use it for longer duration (several years). If you are diagnosed with meningioma, your doctor will reconsider your treatment with <product name>. If you notice any symptoms such as changes in vision (e.g. seeing double or blurriness), hearing loss or ringing in the ears, loss of smell, headaches that worsen with time, memory loss, seizures, weakness in your arms or legs, you must tell your doctor straightaway.

4. Possible side effects

**MPA containing products for all injectable formulations and  $\geq 100$  mg oral formulations**

Usually benign tumour of the tissue surrounding the brain and spinal cord (meningioma) with a frequency not known (see section 2 "Warnings and precautions").