HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Cyproterone acetate – Restrictions in use due to risk of meningioma

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) recently completed a review of the available data on the risk of meningioma associated with cyproterone acetate* (CPA). The PRAC took into consideration data from epidemiological studies, post-marketing case reports and data submitted by the relevant marketing authorisation holders (MAHs, i.e. the companies that hold the licences for CPA-containing medicines).

The PRAC concluded from their review of the data that, while the absolute risk of meningioma in association with CPA use remains low, the risk increases with increasing cumulative doses. The PRAC noted that most cases occur after prolonged exposure to high doses of CPA, but cases of meningioma have also been identified after short-term exposure to high doses. The PRAC therefore recommended that in all indications except prostate carcinoma, treatment with daily doses of ≥10 mg of CPA should be restricted to situations where alternative treatments or interventions are unavailable or are considered inappropriate, and that the lowest possible effective dose should be used.

While the PRAC noted that the available data do not indicate an increased risk of meningioma in association with low-dose combination products containing 2 mg or less of CPA, the PRAC recommended that low-dose combination products should also be contraindicated in patients with meningioma or history of meningioma.

The product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) for CPA-containing medicines will be updated to reflect current knowledge on the risk of meningioma associated with treatment. A Direct Healthcare Professional Communication (DHPC) was prepared by the MAH in April 2020 advising healthcare professionals of the outcome of the PRAC review and is available from the HPRA website (www.hpra.ie).

Background to the PRAC review

CPA is a synthetic progesterone derivative with anti-androgenic properties. It is authorised at a strength of 100 mg for use in men for antiandrogen treatment in inoperable carcinoma of the prostate, and for reduction of drive in sexual deviations. CPA is also authorised at a strength of 2 mg in combination with ethinylestradiol for the treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhoea) and/or hirsutism, in women of reproductive age. For this indication, CPA in combination with ethinylestradiol should only be used after topical therapy or systemic antibiotic treatments have failed and should not be used in combination with other hormonal contraceptives.

The association of high-dose (50 mg/day) CPA with meningioma was first described in 2008[1] and the Summary of Product Characteristics (SmPC) of CPA-containing medicines with a strength of ≥ 10 mg was updated at that time. The update included a contraindication in patients with meningioma or a history of meningioma, in addition to a warning regarding the risk of meningioma associated with long-term use of CPA at doses of 25 mg/day and above. A recently conducted epidemiological cohort study based on data from the French National Health Data System (SNDS) included a population of 253,777 women using 50 or 100 mg CPA[2]. The incidence of meningioma requiring surgery or radiotherapy was compared between women who had received a cumulative dose of ≥ 3 g and women who had received a cumulative dose of < 3 g. The results of the study demonstrated that there is a cumulative dose-dependent association between CPA and meningioma.

Advice to Healthcare Professionals

- The occurrence of meningiomas (single and multiple) has been reported in association with the use of CPA, primarily at doses of 25 mg/day and above.
- The risk of meningioma increases with increasing cumulative dose.
- Use of CPA is contraindicated in patients with a meningioma or a history of meningioma.
- Patients should be monitored for meningiomas in accordance with clinical practice.
- If a patient treated with CPA is diagnosed with meningioma, treatment must be stopped permanently.
- For reduction of drive in sexual deviations in men, CPA 100 mg can be used when other interventions are considered inappropriate.
- The use of CPA for the treatment of inoperable prostate cancer remains unchanged.
- The product information for CPA-containing medicines will be updated to reflect current knowledge on the risk of meningioma associated with treatment.
- A Direct Healthcare Professional Communication (DHPC) advising healthcare professionals of the outcome of the PRAC review is available from the HPRA website (www.hpra.ie).

Key Message

- Use of CPA is contraindicated in patients with a meningioma or a history of meningioma.
- Patients should be monitored for meningioma in accordance with clinical practice and if a patient treated with CPA is diagnosed with meningioma, treatment must be stopped permanently.
- For reduction of drive in sexual deviations in men, CPA 100 mg can be used when other interventions are considered inappropriate.
- The use of CPA for the treatment of inoperable prostate cancer remains unchanged.
- All reports of suspected adverse reactions should be reported to the HPRA via the available methods (www.hpra.ie/report).

** Cyproterone acetate-containing products include Androcur and Dianette. Further details are available at www.hpra.ie.*

References

1. Froelich S, Dali-Youcef N, Boyer P, et al. Does cyproterone acetate promote multiple meningiomas? Endocrine Abstracts. 2008; 16: P158.
2. Weill A et al. (2019 Jun). Exposition prolongée à de fortes doses d'acétate de cyprotérone et risque de méningiome chez la femme. Paris: ANSM.

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