

衛生署藥物辦公室
藥物資訊及警戒科
香港九龍觀塘巧明街 100 號
Landmark East 友邦九龍大樓
20 樓 2002-05 室



DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG INFORMATION AND
PHARMACOVIGILANCE DIVISION
Suites 2002-05, 20/F, AIA Kowloon Tower
Landmark East, 100 How Ming Street
Kwun Tong, Kowloon, Hong Kong

電話號碼 Tel. No.: (852) 3974 4175
詢問處 Enquiries (852) 3974 4175
傳真號碼 Faxline No.: (852) 2803 4962
本署檔號 OUR REF.: DH DO PRIE/7-30/15

17 Feb 2020

(來函請敘明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

Restrictions in use of cyproterone due to meningioma risk

Your attention is drawn to the European Medicines Agency's (EMA) announcement that EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended medicines with daily doses of 10 mg or more of cyproterone should only be used for androgen-dependent conditions such as hirsutism, alopecia, acne and seborrhoea once other treatment options, including treatment with lower doses, have failed. Once higher doses have started working, the dose should be gradually reduced to the lowest effective dose.

The medicines should only be used for reduction of sex drive in sexual deviations in men when other treatment options are not suitable.

There is no change in use of the medicines in men for prostate cancer.

The recommendations follow a review of the risk of the rare tumour meningioma with cyproterone. Overall, this side effect is rare: it may affect between 1 and 10 in 10,000 people, depending on the dose and duration of treatment. The risk increases with increasing cumulative doses (the total amount of medicine a patient has taken over time).

Available data do not indicate a risk for low-dose cyproterone medicines containing 1 or 2 milligrams cyproterone in combination with ethinylestradiol or estradiol valerate and used for acne, hirsutism, contraception, or hormone replacement therapy. However, as a precaution, they should not be used in people who have or have had a meningioma. This restriction is already in place for the higher dose medicines.

Doctors should monitor patients for symptoms of meningioma, which can include changes in vision, hearing loss or ringing in the ears, loss of smell, headaches, memory loss, seizures or weakness in arms and legs. If a patient is diagnosed with meningioma, treatment with cyproterone medicines must be stopped permanently.

As part of the ongoing surveillance of the safety of the medicines, companies marketing medicines containing 10 mg or more of cyproterone will be required to carry out a study to assess doctors' awareness of the risk of meningioma and how to avoid it.

Meningioma is a rare tumour of the membranes covering the brain and spinal cord. It is usually non-malignant and is not considered to be a cancer, but due to their location in and around the brain and spinal cord, meningiomas can cause serious problems.

Information for patients:

- There is a risk of meningioma (a non-cancerous brain tumour) from medicines containing cyproterone. The risk, which is very low, occurs especially when the medicines are taken at high doses (25 mg daily or more) .
- For some uses – excess hair growth, hair loss, acne and oily skin – medicines containing 10 mg or more cyproterone should only be given when other treatment options, including lower-dose cyproterone medicines, have not worked or cannot be used. Once they have started working, the dose should be gradually reduced to the lowest dose that works.
- Cyproterone medicines should only be used to reduce sex drive in sexual deviations in men when other options for treatment are not suitable.
- Although there is no evidence of a risk for low-dose products containing cyproterone in combination with ethinylestradiol or estradiol valerate, as a precaution, these medicines should not be used in people who have or have had a meningioma. Higher-dose cyproterone-containing medicines already have this restriction not to use with meningioma.
- There is no change in the use of cyproterone medicines for prostate cancer.
- If they are taking a cyproterone medicine and have any questions about their treatment, talk to their doctor or pharmacist.

Information for healthcare professionals:

- The occurrence of meningiomas (single and multiple) has been reported in association with the use of cyproterone acetate, primarily at doses of 25 mg/day and above.
- The risk increases with increasing cumulative doses of cyproterone acetate. Most cases have been reported after prolonged exposure (several years) to high doses of cyproterone (25 mg a day and above).
- Medicines containing 10 mg or more of cyproterone should only be used for hirsutism, androgenic alopecia, acne and seborrhoea once other treatment options, which could include low-dose cyproterone-containing medicines such as cyproterone acetate 2 mg/ethinylestradiol 35 micrograms, have not worked. After clinical improvement, the dose should be gradually reduced to the lowest effective dose.
- Cyproterone medicines should only be used in men for reduction of sex drive in sexual deviations when other treatments are not appropriate.
- Healthcare professionals should monitor patients for clinical signs and symptoms of meningioma in line with clinical practice. Symptoms may be unspecific 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 extremities.

- If a patient treated with cyproterone acetate is diagnosed with meningioma, treatment with all cyproterone-containing products must be permanently stopped.
- Cyproterone acetate (1 and 2 mg) in combination with ethinylestradiol or estradiol valerate will be contraindicated in patients with a meningioma or history of meningioma. Higher-dose cyproterone medicines already have this contraindication.
- There is no change in the use of cyproterone medicines for prostate cancer. These medicines are used as antiandrogen treatment in inoperable prostate cancer, including for prevention of the initial flare-up in treatment with luteinizing hormone-releasing hormone (LHRH) agonists.
- The association of cyproterone acetate with meningioma was first added to the product information for medicines with cyproterone daily doses of 10 mg or more in 2009, with a contraindication for people with a history of meningioma.
- This review included recent results from a French epidemiological study showing a cumulative dose-dependent association between cyproterone acetate and meningioma and an analysis by the French medicines agency ANSM of cases of meningioma with cyproterone use in France. Recent published literature and analysis of the EU database of adverse events, EudraVigilance, were also included.

Please refer to the following website in EMA for details:

<https://www.ema.europa.eu/en/news/restrictions-use-cyproterone-due-meningioma-risk>

In Hong Kong, there are three registered pharmaceutical products containing more than 10mg of cyproterone, namely, Androcur Tab 50mg (HK-46443), Procur Tab 50mg (HK-58614) and Apo-Cyproterone Tab 50mg (HK-55387); there are six registered pharmaceutical products containing 2mg cyproterone in combination with ethinyloestradiol. All products are prescription-only medicines. So far, the Department of Health (DH) has not received any case of adverse drug reaction related cyproterone.

In light of the EMA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Undesirable Medical Advertisements and Adverse Drug Reaction Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": <http://www.drugoffice.gov.hk/adr.html>. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,



(Joseph LEE)

for Assistant Director (Drug)