European Medicines Agency

London, 16 August 2007
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**COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)**

**SUMMARY INFORMATION ON REFERRAL OPINION PURSUANT TO ARTICLE 31 OF COUNCIL DIRECTIVE 2001/83/EC, AS AMENDED, FOR**

**Bicalutamide 150 mg-containing medicinal products (See Annex 1)**

International Non-Proprietary Name (INN): bicalutamide

## BACKGROUND INFORMATION

Bicalutamide is an oral anti-androgen used in the management of prostate cancer. Bicalutamide 150 mg is marketed in the EU following national and Mutual Recognition application procedures. It is also approved in Norway and Iceland. Its authorised indications include the treatment of patients with locally advanced prostate cancer, as an immediate therapy either alone or as adjuvant to treatment by radical prostatectomy or radiotherapy. Locally advanced prostate cancer refers to larger tumours or tumours with spread to lymph nodes, but not involving spread to other organs.

On 27 July 2006, Belgium presented a referral to the EMEA under Article 31 of Directive 2001/83, as amended. The reasons for referral concerned a review of the benefit/risk profile of medicinal products containing bicalutamide 150 mg. The 4 issues raised in the referral concerned the analyses of the Early Prostate Cancer Programme (EPC):

- the lack of an overall survival benefit versus adverse events in 'locally advanced prostate cancer';
- statistical concerns regarding multiplicity;
- the standard of care for the placebo group in the relevant studies;
- the number of deaths due to cardiac failure.

The referral procedure started on 27 July 2006. The Rapporteur and Co-Rapporteur appointed were Dr Julia Dunne and Dr Ingemar Persson, respectively. Written explanations were provided by the Marketing Authorisation Holders on 20 October 2006, 22 March 2007 and on 15 May 2007. Oral explanations were given on 22 May 2007.

Based on evaluation of the available data and the Rapporteurs' assessment reports, the CHMP considered that the benefit/risk profile of bicalutamide 150 mg-containing medicinal products remains favourable, and therefore adopted an opinion on 24 May 2007 recommending the maintenance or the granting, as appropriate, of the Marketing Authorisations with amendments to the relevant sections of the Summary of Product Characteristics, for bicalutamide 150 mg-containing medicinal products.

The CHMP considered that bicalutamide 150 mg is effective in the treatment of locally advanced prostate cancer; however the CHMP considered that the therapeutic indication should be restricted to treatment of patients at high risk of disease progression.

In view of the available data, the CHMP concluded that a potential association between the use of bicalutamide 150 mg and heart failure cannot be ruled out and therefore considered that the need to further study cardiovascular morbidity and mortality remains. To address this concern, a new epidemiological study will be performed, as part of an agreed Risk Management Plan.

The list of product names concerned is given in the Annex I. The scientific conclusions are provided in the Annex II, together with the amended relevant sections of the Summary of Product Characteristics in the Annex III, and the conditions of the marketing authorisations in the Annex IV.

The final opinion was converted into a Decision by the European Commission on 03.09.2007.

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* **Note**: The information given in this document and Annexes reflect only the CHMP Opinion dated 24 May 2007. The Member States' competent authorities will continue to keep the product under regular review.