European Medicines Agency
Pre-Authorisation Evaluation of Medicines for Human Use

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SUMMARY OF POSITIVE OPINION*
for
CEPLENE

International Nonproprietary Name (INN): ***histamine dihydrochloride***

On 24 July 2008 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending to grant a marketing authorisation for the medicinal product Ceplene, 0.5 mg/0.5 ml, solution for injection, intended for the maintenance therapy of acute myeloid leukaemia. Ceplene was designated as an orphan medicinal product on 11 April 2005. The applicant for this medicinal product is EpiCept GmbH.

The active substance of Ceplene is histamine dihydrochloride a cytokine immunomodulator medicinal product (ATC Code L03AX14) which aims to induce immune-mediated destruction of residual myeloid leukaemic cells and thereby to prevent relapse of leukaemia in patients concomitantly treated with interleukin-2.

The benefits with Ceplene maintenance therapy used concomitantly with IL-2 in patients with acute myeloid leukaemia in first remission compared to no maintenance therapy are its effect in terms of leukaemia-free survival as observed in a randomised controlled trial. The most common side effects observed with maintenance therapy with Ceplene concomitantly with interleukin-2 were flushing, headache, fatigue, injection site granuloma, pyrexia and injection site erythema**.**

A pharmacovigilance plan for Ceplene, as for all medicinal products, will be implemented as part of the marketing authorisation.

The approved indication is: "Ceplene maintenance therapy is indicated for adult patients with acute myeloid leukaemia in first remission concomitantly treated with IL-2. The efficacy of Ceplene has not been fully demonstrated in patients older than age 60".
It is proposed that Ceplene be administered under the supervision of a physician experienced in the management of acute myeloid leukaemia.

Detailed recommendations for the use of this product will be described in the Summary of Product Characteristics (SPC) which will be published in the European Public Assessment Report (EPAR) and will be available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers that there is a favourable benefit to risk balance for Ceplene and therefore recommends the granting of the marketing authorisation under exceptional circumstances. **

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* Summaries of positive opinion are published without prejudice to the Commission Decision, which will normally be issued within 67 days from adoption of the Opinion.

** Marketing Authorisation under exceptional circumstances refers to the fact that in exceptional circumstances an authorisation may be granted subject to certain specific obligations, to be reviewed annually.

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