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

London, 20 November 2008
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SUMMARY OF POSITIVE OPINION*
for
ZARZIO

International Nonproprietary Name (INN): ***filgrastim***

On 20 November 2008 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion,** recommending to grant a marketing authorisation for the medicinal product Zarzio, 30 MU/0.5 ml, 48 MU/0.5 ml, solution for injection or infusion, intended for the treatment of neutropenia. The Applicant for this medicinal product is Sandoz GmbH.

The active substance of Zarzio is filgrastim, an immunostimulating medicinal product (ATC Code: L03AA02) which regulates the production and release of functional neutrophils from the bone marrow.

Zarzio is a biological medicinal product similar to the reference product Neupogen authorised in the EU. Studies have shown Zarzio to have a comparable quality, safety and efficacy profile to Neupogen (filgrastim). The most common side effects are bone, joint and muscle pain, elevations in blood levels of uric acid and certain enzymes, decreases in blood glucose, leucocytosis, thrombocytopenia, anaemia, headache, nose bleed and enlarged spleen.

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

- The approved indication is:

- Reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients treated with established cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes) and reduction in the duration of neutropenia in patients undergoing myeloablative therapy followed by bone marrow transplantation considered to be at increased risk of prolonged severe neutropenia. The safety and efficacy of filgrastim are similar in adults and children receiving cytotoxic chemotherapy.

- Mobilisation of peripheral blood progenitor cells.

- In patients (children or adults) with severe congenital, cyclic, or idiopathic neutropenia with an absolute neutrophil count (ANC) of $\leq 0.5 \times 10^9$/L, and a history of severe or recurrent infections, long term administration is indicated to increase neutrophil counts and to reduce the incidence and duration of infection-related events.

- Treatment of persistent neutropenia (ANC $\leq 1.0 \times 10^9$/L) in patients with advanced HIV infection, in order to reduce the risk of bacterial infections when other therapeutic options are inappropriate".

* 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.

** Applicants may request a re-examination of any CHMP opinion, provided they notify the EMEA in writing of their intention to request a re-examination within 15 days of receipt of the opinion.

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It is proposed that Zarzio therapy should only be given in collaboration with an oncology centre which has experience in granulocyte-colony stimulating factor (G-CSF) treatment and haematology and has the necessary diagnostic facilities. The mobilisation and apheresis procedures should be performed in collaboration with an oncology-haematology centre with acceptable experience in this field and where the monitoring of haematopoietic progenitor cells can be correctly performed.

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 Zarzio and therefore recommends the granting of the marketing authorisation.