EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 February 2011
EMA/CHMP/110226/2011
Committee for medicinal products for human use (CHMP)

Summary of opinion[1] (initial authorisation)

Hizentra

human normal immunoglobulin

On 17 February 2011 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Hizentra, 200 mg/ml, solution for subcutaneous injection intended for replacement therapy in adults and children in primary immunodeficiency syndromes such as:

- congenital agammaglobulinaemia and hypogammaglobulinaemia
- common variable immunodeficiency
- severe combined immunodeficiency
- IgG subclass deficiencies with recurrent infections.

Replacement therapy in myeloma or chronic lymphatic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections.

The applicant for this medicinal product is CSL Behring GmbH. They may request a re-examination of any CHMP opinion, provided they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

The active substance of Hizentra is human normal immunoglobulin, an immune sera and immunoglobulins: immunoglobulins, normal human, for extravascular administration (ATC Code J06BA01).

Human normal immunoglobulin contains mainly immunoglobulin G (IgG) with a broad spectrum of antibodies against infectious agents. Human normal immunoglobulin contains the IgG antibodies present in the normal population. It is usually prepared from pooled plasma from not fewer than 1,000 donors. It has a distribution of immunoglobulin G subclasses closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low immunoglobulin G levels to the normal range.

[1] Summaries of positive opinion are published without prejudice to the commission decision, which will normally be issued 67 days from adoption of the opinion.

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In a study conducted in Europe, a total of 51 subjects with primary immunodeficiency syndromes aged between 3 and 60 years old were treated with Hizentra for up to 41 weeks. The mean dose administered each week was 0.12 g/kg body weight. Sustained IgG trough levels with mean concentrations of 7.99 – 8.25 g/l were thereby achieved throughout the treatment period. Subjects received in total 1,831 weekly Hizentra infusions.

In a study conducted in the US, a total of 49 subjects with primary immunodeficiency syndromes aged between 5 and 72 years old were treated with Hizentra for up to 15 months. The mean dose administered each week was 0.23 g/kg body weight. Sustained IgG trough levels with a mean concentration of 12.53 g/l were thereby achieved throughout the treatment period. Subjects received in total 2,264 weekly Hizentra infusions.

No serious bacterial infections were reported during the efficacy period in subjects receiving Hizentra during clinical studies.

Immunoglobulins are a normal constituent of the human body. L-proline is a physiological, non-essential amino acid. The safety of Hizentra has been assessed in several preclinical studies, with particular reference to the excipient L-proline. Non-clinical data reveal no special risk for humans based on safety pharmacology and toxicity studies.

A pharmacovigilance plan for Hizentra will be implemented as part of the marketing authorisation.

The approved indication is:

Replacement therapy in adults and children in primary immunodeficiency syndromes such as:

- congenital agammaglobulinaemia and hypogammaglobulinaemia

- common variable immunodeficiency

- severe combined immunodeficiency

- IgG subclass deficiencies with recurrent infections.

Replacement therapy in myeloma or chronic lymphatic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections.

It is proposed that Hizentra is prescribed by physicians experienced in the treatment of immunodeficiency.

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), 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 there to be a favourable benefit to risk balance for Hizentra and therefore recommends the granting of the marketing authorisation.