



COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

**PUBLIC SUMMARY OF
POSITIVE OPINION FOR ORPHAN DESIGNATION
OF
recombinant human porphobilinogen deaminase
for the treatment of acute intermittent porphyria**

On 12 June 2002, orphan designation (EU/3/02/103) was granted by the European Commission to HemeBiotech A/S, Denmark, for recombinant human porphobilinogen deaminase (rhPBGD) for the treatment of acute intermittent porphyria.

What is acute intermittent porphyria?

Acute intermittent porphyria is a clinical manifestation of a genetic disorder affecting the production of an enzyme involved in the synthesis of heme (component of molecules such as hemoglobin or myoglobin): the porphobilinogen deaminase enzyme (PBGD). The genetic disorder is caused by mutation in the PBGD gene, resulting in a 50% reduction of enzymatic activity. This may lead to an increase in blood and urinary concentrations of heme precursors (products leading to heme synthesis such as porphobilinogen or PBG, and delta-aminolevulinic acid or ALA) and a deficit in heme synthesis.

Lack of heme and/or accumulation of heme precursors (such as PBG and ALA) are the main hypotheses to explain development of symptoms of acute intermittent porphyria. Manifestations of the disease are usually linked to triggering factors such as hormonal changes.

What are the methods of treatment available?

The first treatment objective is to remove the precipitating factors. A high carbohydrate (sugars) intake produces a decrease in production of heme precursors and clinical improvement. Intravenous heme arginate, an inhibitor of ALA synthetase, is also available and authorised for the treatment of acute intermittent porphyria in the Community.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that rhPBGD might be of potential significant benefit for the treatment of acute intermittent porphyria, particularly in terms of its novel mechanism of action.

What is the estimated number of patients affected by acute intermittent porphyria?

According to the information provided by the sponsor, acute intermittent porphyria was considered to affect about 38,000 persons in the European Union.

How is this medicinal product expected to act?

Administration of rhPBGD is expected to act by decreasing plasma concentrations of heme precursors.

What is the stage of development of this medicinal product?

The effects of rhPBGD have been evaluated in experimental models. At the time of submission of the application for orphan designation, no clinical trials in patients with attacks of acute intermittent porphyria had been initiated.

rhPBGD had not been marketed anywhere worldwide for acute intermittent porphyria or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 30 April 2002 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which have been considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

For more information:

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