The European Agency for the Evaluation of Medicinal Products
Pre-authorisation Evaluation of Medicines for Human Use

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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF benzoic acid, sodium salt for the treatment of non-ketotic hyperglycinaemia

On 11 September 2002, orphan designation (EU/3/02/111) was granted by the European Commission to Ethicare GmbH, Germany, for benzoic acid, sodium salt for the treatment of non-ketotic hyperglycinaemia.

What is non-ketotic hyperglycinaemia?
Non-ketotic hyperglycinemia is a disease that is also called "glycine encephalopathy" or "idiopathic hyperglycinemia". It is due to a shortfall in enzymes that are involved in chemical activities of a substance called glycine. Glycine is an amino acid, one of the building blocks of proteins. If glycine accumulates in the tissues, it can cause problems to the nervous system. In the most severe cases, newborn children present with disease of the brain. The disease is passed on from one generation to the next through a recessive gene. For recessive genes, the disease only appears if the same gene is transmitted by both parents to the child.

What are the methods of treatment available?
There were no medicinal products specifically authorised for use in this disease in the Community. Medicinal products, such as those to treat epilepsy, are authorised for the treatment of complications to the nervous system.

What is the estimated number of patients affected by the condition?
According to the information provided by the sponsor, non-ketotic hyperglycinaemia was considered to affect about 750 patients in the European Union.

How is this medicinal product expected to act?
Sodium benzoate reacts with glycine producing a substance called hippuric acid. Hippuric acid can be eliminated by the kidney into the urines. Administration of sodium benzoate in non-ketotic hyperglycinaemia patients reduces the concentration of glycine in the blood and in the fluid which surrounds the central nervous system, and this may avoid or limit neurological complications.

What is the stage of development of this medicinal product?
Benzoic acid has an unpleasant taste. For this reason, some patients cannot follow the treatment as they should. The sponsor is developing ways to mask the taste of benzoic acid, using very small pills (microcapsule).

At the time of submission of the application for orphan designation, no clinical trials in patients with non-ketotic hyperglycinaemia had been initiated with this medicinal product.
Benzoic acid had not been marketed anywhere worldwide for non-ketotic hyperglycinaemia or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

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According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 18 July 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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*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.