



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 recombinant dog gastric lipase for the treatment of cystic fibrosis

On 9 July 2003, orphan designation (EU/3/03/157) was granted by the European Commission to Meristem Therapeutics S.A., France, for recombinant dog gastric lipase for the treatment of cystic fibrosis.

What is cystic fibrosis?

Cystic fibrosis is a genetic disease caused by mutations in a gene on chromosome 7. Each individual has a pair of these chromosomes, each derived from one parent. The disease appears only when the gene is mutated on both chromosomes. This type of genetic disease is called "autosomal recessive". Normally, the gene is used to make a protein, called cystic fibrosis transmembrane conductance regulator (CFTR), that regulates transport of water and salts in certain cells. These are the cells that cover internal and external surfaces of the body, the so-called epithelial cells. In cystic fibrosis the protein is defective due to the mutations. This results in defective water and salt transport and thick secretions in several organs (e.g. lungs, pancreas). For example, secretions in the airways show a decrease in water content. This leads to chronic infection of the lungs and chronic inflammation (a response to the injury caused to the tissue). This is a major burden for cystic fibrosis patients. In the long run, these events damage the lung (fibrosis) and the disease can become life-threatening. Damage to the pancreas may impair the ability to break down and take up fat from the diet, causing faulty nourishment (malnutrition).

What are the methods of treatment available?

Several medicinal products were authorised for the treatment of cystic fibrosis within the Community at the time of submission of the application for orphan drug designation. The lung infection and inflammation in cystic fibrosis is treated mostly with antibiotics. Associated treatments include daily exercise and physical therapies and several other types of medications such as pancreatic enzymes and food supplements.

Recombinant dog gastric lipase might be of potential significant benefit for the treatment of cystic fibrosis by increasing the breakdown of fat. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

What is the estimated number of patients affected by the condition?

According to the information provided by the sponsor, cystic fibrosis was considered to affect about 49,000 in the European Union.

How is this medicinal product expected to act?

One of the most important causes of malnutrition in patients with cystic fibrosis is the inability to break down and take up fat. This can contribute to general malnutrition and indirectly also to increased frequency of infections. Recombinant dog gastric lipase is an enzyme that breaks down fat. By giving recombinant dog gastric lipase to cystic fibrosis patients the sponsor hopes to improve breakdown and

uptake of fat thus the energy available to the body. This would ultimately increase the patients' weight and improve the general health status.

What is the stage of development of this medicinal product?

The effects of recombinant dog gastric lipase were evaluated in experimental models. At the time of submission of the application for orphan designation, one clinical trial in patients with cystic fibrosis was completed.

Recombinant dog gastric lipase was not marketed anywhere worldwide for cystic fibrosis 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 13 June 2003 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 were 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.

Translations of the active ingredient and indication in all EU languages

| Language | Active Ingredient | Indication |
|------------|---|-------------------------------------|
| English | Recombinant dog gastric lipase | Treatment of cystic fibrosis |
| Danish | Rekombinant gastrisk lipase fra hunde | Behandling af cystisk fibrose |
| Dutch | Recombinant gastric lipase (hond) | Behandeling van cystische fibrose |
| Finnish | Rekombinantti koiran gastrinen lipaasi | Kystisen fibroosin hoito |
| French | Lipase gastrique de chien recombinante | Traitement de la mucoviscidose |
| German | Rekombinante Magenlipase (Hund) | Behandlung der zystischen Fibrose |
| Greek | Ανασυνδυασμένη γαστρική λιπάση κυνός | Θεραπεία της κυστικής ίνωσης |
| Italian | Lipasi gastrica ricombinante del cane | Trattamento della fibrosi cistica |
| Portuguese | Lipase gástrica recombinante de origem canina | Tratamento da fibrose quística |
| Spanish | Lipasa gástrica recombinate de origen canino | Tratamiento de la fibrosis quística |
| Swedish | Rekombinant gastriskt lipas från hund | Behandling av cystisk fibros |