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

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in December 2008 on request of the Sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of amiloride hydrochloride dihydrate for the treatment of cystic fibrosis

On 30 June 2003, orphan designation (EU/3/03/147) was granted by the European Commission to PulmoTec GmbH, Germany, for amiloride hydrochloride dihydrate for the treatment of cystic fibrosis.

What is cystic fibrosis?
Cystic fibrosis is a genetic disease. The genetic information that determines the characteristics of each individual is carried by genes located on structures called chromosomes. In humans, each cell has 23 pairs of chromosomes. For each pair one chromosome is inherited from the mother, and the other from the father. Cystic fibrosis is caused by abnormalities of a specific gene, called CFTR, carried by the seventh pair of chromosomes. The CFTR gene is responsible for the production of a protein that regulates the outflow of water and salts (like chloride) from cells that cover internal and external surfaces of the body, the so-called epithelial cells. Cystic fibrosis appears only when the CFTR is abnormal on both chromosomes of the seventh pair. The defective transport of water and salts, due to the lack of the regulatory protein, results in the thickening of the secretions in several organs (e.g. lungs, pancreas). This leads to chronic infection of the lungs and chronic inflammation (a response to the injury caused to the tissue). It can induce damage to the lung tissue and respiratory insufficiency, which is life threatening.

What is the estimated number of patients affected by the condition?
At the time of designation, cystic fibrosis affected approximately 1.1 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 42,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What are treatments are available?
Lung infection and inflammation in cystic fibrosis are treated mainly with antibiotics. These can be taken in a number of ways such as through the mouth, through a vein or they can be inhaled as a fine mist of particles. Associated treatments include daily exercise and physical therapies and several other types of medications such as pancreatic enzymes and food supplements. Bronchodilators are medications that can enlarge the lumen of the airways. Mucolytics help to dissolve the secretions. Still other medications are used to fight the inflammation. Amiloride hydrochloride dihydrate might be of potential significant benefit in the treatment of cystic fibrosis, because it is expected to act differently

[*] 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.

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from existing treatments, and because it can be inhaled. This assumption remains to be proven. This will be necessary to maintain the orphan status.

How is this medicine expected to work?
The cells that cover the surface of air passages of the lungs have channels that allow the transport of water and salts in and out of the cells. In cystic fibrosis, outflow of water and salts is not sufficient and this results in thick secretions inside the air passages. Amiloride blocks the channel used by a salt called sodium. Blocking the sodium channel is expected to increase the amount of salt outside the cells and, as a consequence, to increase also the amount of water on the surface of the air passages. The water would make the secretions more fluid so that they can be eliminated more easily. This is expected to decrease the risk of airway infections.

What is the stage of development of this medicine?
At the time of submission of the application for orphan designation, clinical trials in patients with cystic fibrosis were ongoing.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 8 May 2003 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal product designations are based on the following three criteria:
- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the Community) or insufficient returns on investment.

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

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