European Medicines Agency
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 alpha-1proteinase inhibitor (inhalation use) for the treatment of cystic fibrosis

On 14 September 2007, orphan designation (EU/3/07/474) was granted by the European Commission to CSL Behring GmbH, Germany, for alpha-1 proteinase inhibitor (inhalation use) for the treatment of cystic fibrosis.

What is cystic fibrosis?

Cystic fibrosis is an inherited disease. Cystic fibrosis is caused by abnormalities of a specific gene called CFTR. Cystic fibrosis appears only when the CFTR gene is abnormal on both chromosomes of the seventh pair (one inherited from the father, the other from the mother). In cystic fibrosis, defects of the CFTR gene decrease production of a protein that regulates outflow of water and ions (like chloride) from the cells that line the internal and external surfaces of the body, the so-called epithelial cells. This defective transport of water and salts results in the thickening of the secretions (mucus) in several organs, including the lungs and the pancreas. In turn, this leads to chronic and acute infections of the lungs, chronic inflammation (a body response to the injury caused to the tissue), and digestive difficulties. In the long term, these events can induce damage to the lung tissue and the disease becomes life-threatening.

What are the methods of treatment available?

At the time of submission of the application for the orphan drug designation, lung infection and inflammation in cystic fibrosis was 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 included 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 airways. Mucolytics help to make the secretions thinner. Other medications were also used to fight the inflammation.

Alpha-1 proteinase inhibitor (inhalation use) might be of potential significant benefit for the treatment of cystic fibrosis because it can act in a different way than other available medicines. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain 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 65,000 persons in the European Union.

How is this medicinal product expected to act?

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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Alpha-1 proteinase inhibitor (also known as alpha-1 antitrypsin) is derived from the blood of human donors. This protein has the role of inactivating some harmful substances produced by the body itself, called neutrophil elastases, which are usually involved in the inflammation. In cystic fibrosis, due to the chronic inflammation, there is an excess of these elastases in the lung, contributing to the damage of the lung tissue. By local administration of additional alpha-1 proteinase inhibitor (via inhalation) it is expected that the accumulation of this harmful elastases wil be reduced, thereby slowing down the progression of the lung disease.

What is the stage of development of this medicinal product?
The effects of alpha-1 proteinase inhibitor (inhalation use) were evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with cystic fibrosis had been initiated.

Alpha-1 proteinase inhibitor (inhalation use) was not authorised anywhere in the world for treatment of 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 25 July 2007 a positive opinion recommending the grant of the above-mentioned designation.

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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.

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Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Alpha-1 proteinase inhibitor (inhalation use)	Treatment of cystic fibrosis
Bulgarian	Алфа-1 протеиназен инхибитор (за инхалаторно приложение)	Лечение на кистозна фиброза
Czech	Inhibitor alfa-1 proteinázy (inhalační podání)	Léčba cystické fibrózy
Danish	Alfa-1 Proteinase hæmmer (til inhalation)	Behandling af cystisk fibrose
Dutch	Alpha-1 proteïnase-inhibitor (inhalatie gebruik)	Behandeling van cystische fibrose
Estonian	Alfa-1 proteinaasi inhibiitor (inhalatsiooniks)	Tsüstilise fibroosi ravi
Finnish	Alfa-1-proteinaasin estäjä (inhalaatioon)	Kystisen fibroosin hoito
French	Inhibiteur de l'alpha-1 protéinase (voie inhalée)	Traitement de la mucoviscidose
German	Alpha-1 Proteinase-Inhibitor (zur Inhalation)	Behandlung der zystischen Fibrose
Greek	Αναστολέας άλφα-1 Πρωτεϊνάσης (εισπνεόμενη)	Θεραπεία της κυστικής ίνωσης
Hungarian	Alfa-1 proteináz inhibitor (inhalációs alkalmazás)	Cisztikus fibrózis kezelése
Italian	Inibitore dell'alfa-1 proteinasi (uso inalatorio)	Trattamento della fibrosi cistica
Latvian	Alfa-1 proteināzes inhibitors (inhalācijām)	Cistiskās fibrozes ārstēšana
Lithuanian	Alfa-1 proteinazės inhibitorius (inhaliuoti)	Cistinės fibrozės gydymas
Maltese	Inibitur ta' l-alpha-1 proteinase (għal biex jingħibed man-nifs)	Kura tal-fibroži ċistiku
Polish	Inhibitor proteinazy Alpha-1 (podanie wziewne)	Leczenie zwłóknienia torbielowatego
Portuguese	Inibidor da Proteinase –Alfa-1 (via inalatória)	Tratamento da fibrose quística
Romanian	Inhibitor de Alfa-1 proteinază (administrare inhalatorie)	Tratamentul fibrozei chistice
Slovak	Inhibítor alfa-1 proteinázy (inhalačné použitie)	Terapia cystickej fibrózy
Slovenian	Inhibitor alfa-1 proteinaze (za inhaliranje)	Zdravljenje cistične fibroze
Spanish	Inhibidor de la alfa-1 proteinasa (via inhalatoria)	Tratamiento de la fibrosis quística
Swedish	Alfa-1 proteinase- hämmare (användning för inhalation)	Behandling av cystisk fibros

Norwegian	Alfa-1 proteinaseinhibitor (til inhalasjon)	Behandling av cystisk fibrose
Icelandic	Alfa-1 proteinasa hemill (til innöndunar)	Meðferð við slímseigjusjúkdómi