14 November 2012
EMA/COMP/612138/2012
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Alpha-1 proteinase inhibitor (for inhalation use) for the treatment of cystic fibrosis

On 10 October 2012, orphan designation (EU/3/12/1045) was granted by the European Commission to Grifols Deutschland GmbH, Germany, for alpha-1 proteinase inhibitor (for inhalation use) for the treatment of cystic fibrosis.

What is Cystic fibrosis?

Cystic fibrosis is a hereditary disease that affects the cells in the lungs and the glands in the gut and pancreas that secrete fluids such as mucus and digestive juices. In cystic fibrosis these fluids become thick and viscous, blocking the airways and the flow of digestive juices. This leads to problems with the digestion and absorption of food, resulting in poor growth, and long-term infection and inflammation of the lungs because of excess mucus not being cleared away.

Cystic fibrosis is a long-lasting and life-threatening disease because it severely damages the lung tissue, which leads to problems with breathing and recurrent chest infections.

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

At the time of designation, cystic fibrosis affected approximately 0.7 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 35,000 people, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, lung infection in cystic fibrosis was mainly treated with antibiotics. Other medicines used to treat the lung disease included anti-inflammatory agents, bronchodilators (medicines that help to open up the airways in the lungs) and mucolytics (medicines that help dissolve the mucus in the lungs). In addition, patients with cystic fibrosis were often given other types of

[*]Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 506,300,000 (Eurostat 2011).

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medicines such as pancreatic enzymes (substances that help to digest and absorb food) and food supplements. They were also advised to exercise and to undergo physiotherapy.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with cystic fibrosis because it works in a different way to existing treatments and early studies in patients with cystic fibrosis suggest that may improve the outcome of patients with this condition. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Patients with cystic fibrosis have excessive amounts of the enzyme elastase in their lungs. Elastase is usually produced as part of the inflammatory response and is inactivated by a protein called alpha-1 proteinase inhibitor (also known as alpha-1 antitrypsin). In cystic fibrosis, not all elastases are inactivated as they should, and therefore remain active causing inflammation and lung damage.

This medicine is made of alpha-1 proteinase inhibitor derived from the blood of human donors. By giving additional alpha-1 proteinase inhibitor (via inhalation), it is expected that additional elastases can be inactivated, thereby reducing the amount of active elastases and in turn the damage to the lungs in patients with cystic fibrosis.

What is the stage of development of this medicine?

The effects of alpha-1 proteinase inhibitor have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with alpha-1 proteinase inhibitor in patients with cystic fibrosis were ongoing.

At the time of submission, alpha-1 proteinase inhibitor was not authorised anywhere in the EU for cystic fibrosis. Orphan designation had been granted in the United States of America for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 September recommending the granting of this 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 EU) 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.

For more information

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Alpha-1 proteinase inhibitor (for inhalation use)	Treatment of cystic fibrosis
Bulgarian	инхибитор на алфа-1 протеиназа (за инхалационна употреба)	Лечение на кистозна фиброза
Czech	Inhibitor alfa-1 proteinázy (určeno k inhalaci)	Léčba cystické fibrózy
Danish	Alfa1-proteinasehæmmer (til inhalation)	Behandling af cystisk fibrose
Dutch	Alfa-1 proteinaseremmer (voor inhalatie gebruik)	Behandeling van cystische fibrose
Estonian	Alfa-1 proteinaasi inhibiitor (inhalatsiooniks)	Tsüstilise fibroosi ravi
Finnish	Alfa-1-proteaasinestäjä (inhalaatiokäyttöön)	Kystisen fibroosin hoito
French	Inhibiteur de la protéinase alpha-1 (pour utilisation par inhalation)	Traitement de la mucoviscidose
German	Alpha-1-Proteinase-Inhibitor (zur inhalativen Behandlung)	Behandlung zystischer Fibrose
Greek	αναστολέας της α-1 πρωτεϊνάσης (για χορήγηση μέσω της αναπνευστικής οδού)	Θεραπεία της κυστικής ίνωσης
Hungarian	Alfa-1 proteáz inhibitor (inhalációs használatra)	Cisztikus fibrózis kezelése
Italian	Inibitore dell'alfa-1 proteasi (per uso inalatorio)	Trattamento della fibrosi cistica
Latvian	Alfa-1 proteināzes inhibitors (inhalāciju veikšanai)	Cistiskās fibrozes ārstēšana
Lithuanian	Alfa-1 proteinazės inhibitorius (įkvėpimui)	Cistinės fibrozės gydymas
Maltese	Inibitur tal-alpha-1 proteinase(għal biex jingibed man-nifs)	Kura tal-fibrożi ċistiku
Polish	Inhibitor alfa-1 proteinazy (do inhalacji)	Leczenie zwłóknienia torbielowatego
Portuguese	Inibidor da proteinase alfa-1 (para usopor via inalatória)	Tratamento da fibrose quística
Romanian	Inhibitor al alfa-1 proteinazei (pentru uz inhalator)	Tratamentul fibrozei chistice
Slovak	Inhibítor alfa-1 proteinázy (na inhalačné použitie)	Terapia cystickej fibrózy
Slovenian	Alfa-1 proteinazni inhibitor (za inhalacijsko uporabo)	Zdravljenje cistične fibroze
Spanish	Inhibidor de la alfa-1 proteinasa (parainhalacion)	Tratamiento de la fibrosis quística
Swedish	Alfa-1-proteinashämmare (användning för inhalation)	Behandling av cystisk fibros
Norwegian	Alfa-1-proteinasehemmer (bruk til inhalasjon)	Behandling av cystisk fibrose
Icelandic	Alfa-1 próteinasahemill (til innöndunar)	Meðferð við slímseigjusjúkdómi

[1] At the time of designation