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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of alpha-1 proteinase inhibitor for the treatment of emphysema secondary to congenital alpha-1 antitrypsin deficiency

On 16 February 2006, orphan designation (EU/3/06/350) was granted by the European Commission to Octapharma (IP) Limited, United Kingdom, for alpha-1 proteinase inhibitor for the treatment of emphysema secondary to congenital alpha-1 antitrypsin deficiency.

What is emphysema secondary to congenital alpha-1 antitrypsin deficiency?

Congenital alpha-1 antitrypsin deficiency is an inherited disease characterised by reduced levels in the blood of the substance alpha-1 antitrypsin (AAT). This substance is a protein that is normally made by the liver and reaches other organs (such as the lungs) after being released into the blood circulation. Alpha-1 antitrypsin has the role of inactivating some substances, such as elastase, normally produced by the body. The action of elastase is to destroy certain molecules that form the lung tissue. AAT controls this action of elastase. If AAT is missing then the action of elastase is no longer opposed. In the long term, this may damage the lungs and cause a lung disease where air is abnormally accumulated in the tissue around the alveoli (the small cells containing the air in the lungs). Lung disease due to this deficiency is also called "hereditary emphysema" or emphysema secondary to congenital alpha-1 antitrypsin deficiency. The condition is chronically debilitating and life-threatening.

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

At the time of designation, emphysema secondary to congenital alpha-1 antitrypsin deficiency affected approximately 2.5 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 115,000 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 treatments are available?

Therapy for lung disease due to AAT deficiency includes the use of medicines to help breathing, or to help to clear mucus. Lung infections require treatment with antibiotics. Human AAT to be administered intravenously is authorised for replacement therapy of this condition. Oxygen may also be given in the more advanced stages and lung transplantation is used as a last resource. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that alpha-1 proteinase inhibitor might be of potential significant benefit for the treatment of emphysema secondary to congenital alpha-1 antitrypsin deficiency because it might represent a contribution to

*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 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

patient care. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Alpha-1 proteinase inhibitor (also known as alpha-1 antitrypsin) is derived from collected human blood. The administration of the alpha-1 proteinase inhibitor would reach the lungs where it would restore the level of AAT. In this way the alpha-1 proteinase inhibitor could oppose the effects of elastase. This action is expected to slow down the worsening of the lung disease.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, no clinical trials in patients with emphysema secondary to congenital alpha-1 antitrypsin deficiency were initiated.

Alpha-1 proteinase inhibitor was not authorised anywhere worldwide for emphysema secondary to congenital alpha-1 antitrypsin deficiency 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 11 January 2006 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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**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Alpha-1 proteinase inhibitor	Treatment of emphysema secondary to congenital alpha-1 antitrypsin deficiency
Czech	Inhibitor alfa-1 proteinázy	Léčba sekundárního emfyzemu při vrozeném deficitu alfa-1 antitrypsinu
Danish	Alfa-1 Proteinase hæmmer	Behandling af emfysem som følge af medfødt alfa-1 antitrypsinmangel
Dutch	Alpha-1 proteïnase-inhibitor	Behandeling van emfyseem ten gevolge van aangeboren alfa-1 antitrypsine deficiëntie
Estonian	Alfa-1 proteinaasi inhibiitor	Kaasasündinud alfa-1 antitrüpsiini puudulikkusest tingitud sekundaarse emfüseemi ravi
Finnish	Alfa-1 proteinaasi-estäjä	Synnynnäisestä alfa-1 antitrypsiinin puutteesta johtuvan emfyseeman hoito
French	Inhibiteur de l'alpha-1 protéinase	Traitement de l'emphysème secondaire à un déficit congénital en alpha-1 antitrypsine
German	Alpha-1 Proteinase-Inhibitor	Behandlung des durch erblichen Alpha-1 Antitrypsinmangel bedingten Emphysems
Greek	Αναστολέας άλφα-1 Πρωτεΐνάσης	Θεραπεία εμφυσήματος δευτερεύοντος σε συγγενή ανεπάρκεια άλφα-1 αντιθρυψίνης
Hungarian	Alfa-1 proteináz inhibitor	Kongenitális alfa-1 antitripszin hiány okozta emphysema kezelése
Italian	Inibitore dell'alfa-1 proteinasi	Trattamento dell'enfisema secondario a deficienza congenita di alfa-1 antitripsina
Latvian	Alfa-1 proteināzes inhibitors	Sekundāras emfizēmas ārstēšanai, ko izraisījusi iedzimta alfa-1 antitripsīna nepietiekamība
Lithuanian	Alfa-1 proteinazės inhibitorius	Antrinės emfizemos gydymas dėl įgimtos alfa-1 antitripsino stokos
Polish	Inhibitor proteiny Alpha-1	Leczenie wtórnej rozedmy spowodowanej wrodzonym niedoborem alfa-1 antytrypsyny
Portuguese	Inibidor da Proteinase –Alfa-1	Tratamento do enfisema secundário à deficiência congénita em antitripsina alfa-1
Slovak	Inhibitor alfa-1 proteinázy	Liečba sekundárneho emfyzému pri vrodenom deficite alfa-1 antitrypsínu
Slovenian	Inhibitor alfa-1 proteinaze	Zdravljenje sekundarnega emfizema zaradi kongenitalnega pomanjkanja alfa-1 antitripsina
Spanish	Inhibidor de la proteinasa alfa-1	Tratamiento del enfisema secundario a déficit congénito de alfa-1 antitripsina
Swedish	Alfa-1 proteinase- hämmare	Behandling av emfysem sekundär till kongenital alpha-1 antitrypsin brist
Norwegian	Alfa-1 proteinaseinhibitor	Behandling av emfysem som følge av medfødt mangel av alfa-1 antitrypsin
Icelandic	Alfa-1 proteinasa-hemill	Meðferð á lungnaþembu sem fylgikvilla meðfædds alfa-1 andtrýpsínsskorts