4 February 2014
EMA/COMP/109837/2004 Rev.6
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

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

First publication	4 October 2005
Rev.1: transfer of sponsorship	18 August 2008
Rev.2: transfer of sponsorship	28 August 2009
Rev.3: transfer of sponsorship	7 March 2011
Rev.4: sponsor's name and address change	5 April 2013
Rev.5: transfer of sponsorship	12 September 2013
Rev.6: sponsor's change of address	4 February 2014
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 16 November 2004, orphan designation (EU/3/04/243) was granted by the European Commission to BCG (Europe) Ltd, United Kingdom, for alpha-1antitrypsin (inhalation use) for the treatment of cystic fibrosis.

The sponsorship was transferred to The Weinberg Group LLC, United Kingdom, in July 2007, then to The Weinberg Group Limited, United Kingdom, in April 2009 and subsequently to Innovative Drug European Associates Limited, United Kingdom, in December 2010.

In December 2012, Innovative Drug European Associates Limited changed name to IDEA Innovative Drug European Associates Limited.

The sponsorship was then transferred to Triskel EU Services Ltd., United Kingdom, in July 2013.

What is cystic fibrosis?

Cystic fibrosis is an inherited 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 cystic CFTR, carried by the seventh pair of chromosomes. Cystic fibrosis appears only when the CFTR is abnormal on both

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chromosomes of the seventh pair. The CFTR gene is responsible for the production of a protein that regulates outflow of water and salts (like chloride) from cells that cover internal and external surfaces of the body, the so-called epithelial cells. The defective transport of water and salts due to the lack of the regulatory protein, results in the thickening of the secretions (mucous) in several organs (e.g. lungs, pancreas). This leads to reduced functioning and chronic infection of the lungs and chronic inflammation (a body response to the injury caused to the tissue). In the long run, these events can induce damage to the lung tissue and the disease can become life-threatening.

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

At the time of designation, cystic fibrosis affected approximately 1.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 60,000 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 the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of submission of the application for the orphan drug designation lung infection and inflammation in cystic fibrosis were 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 lumen of the airways. Mucolytics help to dissolve the secretions. Still other medications were used to fight the inflammation.

Alpha-1antitrypsin (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 the orphan status.

How is this medicine expected to work?

Alpha-1antitrypsin is a protein that is naturally/normally made by the liver and reaches other organs (such as the lungs) after being released into the blood circulation. This protein has the role of inactivating some harmful substances produced by the body itself called neutrophil elastases that are usually involved in the inflammation. In cystic fibrosis, due to the chronic inflammation, there is an excess of this elastase in the lung contributing to the damage of the lung tissue. By local administration of additional alpha-1antitrypsin (inhalation use) it is expected that it might help to reduce the accumulation of this harmful elastases and thereby it might contribute in the reduction of the inflammation in the lungs.

What is the stage of development of this medicine?

The effects of alpha-1 antitrypsin (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 were initiated.

[*]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.
At the time of designation, this represented a population of 464,200,000 (Eurostat 2004).

Alpha-1 antitrypsin (inhalation use) was not marketed anywhere worldwide for cystic fibrosis or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 October 2004 recommending the granting of this designation.

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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

Sponsor's contact details:

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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 antitrypsin (inhalation use)	Treatment of cystic fibrosis
Bulgarian	Алфа-1 антитрипсин (за инхалаторно приложение)	Лечение на кистозна фиброза
Croatian	Alfa-1 antitripsin (u dišne puteve)	Liječenje cistične fibroze
Czech	Alfa-1 antitrypsin (k inhalaci)	Léčba cystické fibrózy
Danish	Alpha-1 antitrypsin (til inhalation)	Behandling af cystisk fibrose
Dutch	Alfa-1 antitrypsine (inhalatie)	Behandeling van cystische fibrose
Estonian	Alfa-1 antitrüpsiin (inhalatsiooniks)	Tsüstilise fibroosi ravi
Finnish	Alfa-1 antitrypsiini (inhalaatioon)	Kystisen fibroosin hoito
French	Alpha-1 antitrypsine (voie inhalée)	Traitement de la mucoviscidose
German	Alpha-1 Antitrypsin (zur Inhalation)	Behandlung von zystischer Fibrose
Greek	Άλφα-1 αντιθρυψίνη (Χρήση δια ειδπνοής)	Θεραπεία της κυστικής ίνωσης
Hungarian	Alfa-1 antitripszin (inhalációs alkalmazásra)	Cisztikus fibrózis kezelése
Italian	Alfa-1 antitripsina (per inalazione)	Trattamento della fibrosi cistica
Latvian	Alfa-1 antitripsīns (inhalācijām)	Cistiskās fibrozes ārstēšana
Lithuanian	Alfa-1 antitripsinas (inhaliacijoms)	Cistinės fibrozės gydymas
Maltese	Alpha-1 antitrypsin (għal biex jingibed man-nifs)	Kura tal-fibrożi ċistiku
Polish	Alfa-1-antytrypsyna (inhalacja)	Leczenie zwłóknienia torbielowatego
Portugese	Alfa-1 anti-tripsina (via inalatoria)	Tratamento da fibrose quística
Romanian	Alfa-1 antitripsină (administrare inhalatorie)	Tratamentul fibrozei chistice
Slovak	Alfa-1 antitrypsín (inhalácia)	Terapia cystickej fibrózy
Slovenian	Alfa-1 antitripsin (za inhalacijo)	Zdravljenje cistične fibroze
Spanish	Alfa-1-antitripsina (vía inhalatoria)	Tratamiento de la fibrosis quística
Swedish	Alpha-1 antitrypsin (användning för inhalation)	Behandling av cystisk fibros
Norwegian	Alpha-1 antitrypsin (til inhalasjon)	Behandling av cystisk fibrose
Icelandic	Alfa-1 andtrypsín (til innöndunar)	Meðferðar slímseigjuvanþrifa

[1] At the time of transfer of sponsorship