11 March 2013
EMA/COMP/7913/2005 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human bile salt-stimulated lipase for the treatment of cystic fibrosis

On 26 January 2005, orphan designation (EU/3/04/257) was granted by the European Commission to Arexis AB, Sweden, for recombinant human bile salt-stimulated lipase for the treatment of cystic fibrosis.

What is cystic fibrosis?

Cystic fibrosis is a genetic disease. Genes located on structures (the so-called chromosomes) carry the genetic information that determines the characteristics of each individual. 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. Cystic fibrosis appears only when the CFTR gene is abnormal on both chromosomes of the seventh pair. 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. 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 a reduced functioning, chronic infection of the lungs and chronic inflammation (a body response to the injury caused to the tissue). Damage to the pancreas may impair the ability to break down and take up fat from the diet, causing faulty nourishment (malnutrition). In the long run, these events can induce damage the organs 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 61,000 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).

[*]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 466,600,000 (Eurostat 2005).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What treatments are available?

Several medicinal products were authorised for the treatment of cystic fibrosis within the Community at the time of submission of the application for orphan drug designation. The lung infection and inflammation in cystic fibrosis is treated mostly with antibiotics. 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.

Recombinant human bile salt-stimulated lipase might be of potential significant benefit for the treatment of cystic fibrosis because it might influence the nutritional status of the patient. 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?

One of the most important causes of malnutrition in patients with cystic fibrosis is the inability to break down fat, a process that is essential for the body's further digestion of fats (absorption of fatty acids, cholesterol and fat-soluble vitamins). This can contribute to general malnutrition and indirectly also to increased frequency of infections. Recombinant bile salt-stimulated lipase is an enzyme that might break down fat and might thereby lead to an improved nutritional status, leading to an increased body weight and improve the general health status.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, two clinical trials in patients with cystic fibrosis were completed.

Recombinant bile salt-stimulate lipase 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 8 December 2004 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

Sponsor's contact details:

Arexis AB
Drottninggatan 98
112 76 Stockholm
Sweden
Telephone: +46 8 697 20 00
Telefax: +468 697 23 30
E-mail: info@arexis.com

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	Recombinant human bile salt-stimulated lipase	Treatment of cystic fibrosis
Czech	Rekombinantní lidská lipase stimulována žlučovými solemi	Léčba cystické fibrózy
Danish	Rekombinant humant galdesaltstimuleret lipase	Behandling af cystisk fibrose
Dutch	Recombinant humaan galzuur-gestimuleerd lipase	Behandeling van cystische fibrose
Estonian	Rekombinantne inimese sapisoola poolt stimuleeritud lipaas	Tsüstilise fibroosi ravi
Finnish	Humaani rekombinantti sappisuolastimuloitu lipaasi	Kystisen fibroosin hoito
French	Lipase recombinante humaine stimulée par du sel de bile	Traitement de la mucoviscidose
German	Rekombinante humane gallensalzstimulierte Lipase	Behandlung von zystischer Fibrose
Greek	Ανασυνδυασμένη ανθρώπινη λιπάση ενεργοποιούμενη από χολικό άλας	Θεραπεία της κυστικής ίνωσης
Hungarian	Rekombináns humán Eepesavas sóval stimulált lipáz	Cisztikus fibrózis kezelése
Italian	Lipasi ricombinante umana stimolata del sale di bile	Trattamento della fibrosi cistica
Latvian	Cilvēka rekombinētā žults sāļu stimulētā lipāze	Cistiskās fibrozes ārstēšana
Lithuanian	Rekombinantinė žmogaus tulžies druskos stimuliuota lipazė	Cistinės fibrozės gydymas
Polish	Rekombinowana ludzka lipaza stymulowana solami żółciowymi	Leczenie zwłóknienia torbielowatego
Portuguese	Lipase recombinante humana estimulante dos sais biliares	Tratamento da fibrose quística
Slovak	Rekombinantná ľudská lipáza stimulovaná žlčovými soľami	Terapia cystickej fibrózy
Slovenian	Rekombinantna humana lipaza, stimulirana z žočnimi solmi	Zdravljenje cistične fibroze
Spanish	Lipasa estimulada por la secreción de sales biliares (colesterol esterasa) recombinante humana	Tratamiento de la fibrosis quística
Swedish	Rekombinant human gallsaltstimulerat lipas	Behandling av cystisk fibros
Norwegian	Rekombinant human gallesaltstimulert lipase	Behandling av cystisk fibrose

[1] At the time of designation

Language	Active Ingredient	Indication
Icelandic	Raðbrigða manna gallsalta örvaður fitukljúfur.	Til meðferðar á slímseigjukvilla