30 September 2015
EMA/COMP/500571/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human acid ceramidase for the treatment of cystic fibrosis

On 10 August 2015, orphan designation (EU/3/15/1536) was granted by the European Commission to Plexcera Therapeutics EU Limited, Ireland, for recombinant human acid ceramidase 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 long-term infection and inflammation of the lungs because of excess mucus not being cleared away, and to problems with the digestion and absorption of food, resulting in poor growth.

Cystic fibrosis is caused by defects ('mutations') in a gene that makes a protein called 'cystic-fibrosis transmembrane conductance regulator' (CFTR), which is involved in regulating the production of mucus and digestive juices.

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

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

At the time of designation, cystic fibrosis affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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. Kalydeco (ivacaftor) was authorised to treat a subgroup of patients with cystic fibrosis who have certain

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

mutations in the gene for the CFTR protein. 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 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 recombinant human acid ceramidase might be of significant benefit for patients with cystic fibrosis because studies in experimental models suggest that it can reduce the number of infections in patients with the 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?

In patients with cystic fibrosis, the lack of normal CFTR protein, in addition to its effects on mucus and digestive juices, also leads to build up of a fatty substance called ceramide in organs such as the lung. This build up of ceramide increases inflammation and promotes the lung infections that are symptoms of cystic fibrosis.

This medicine contains a copy of an enzyme naturally found in the body, acid ceramidase. This enzyme can break down the excess ceramide, converting it to sphingosine, a substance that helps to fight infection and reduce the growth of bacteria. This is expected to reduce the risk of dangerous chest infections in patients with the condition.

What is the stage of development of this medicine?

The effects of recombinant human acid ceramidase have been evaluated in experimental models.

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

At the time of submission, recombinant human acid ceramidase was not authorised anywhere in the EU for cystic fibrosis or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 July 2015 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:

Plexcera Therapeutics EU Limited
77 Sir John Rogerson's Quay
Dublin 2
Ireland
Tel. +353 1 649 9008
Fax +353 1 640 1899
E-mail: galanin@plexcera.com
http://www.plexcera.com/contact-3/

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 acid ceramidase	Treatment of cystic fibrosis
Bulgarian	Рекомбинантна, човешка кисела церамидаза	Лечение на кистозна фиброза
Croatian	Rekombinantna ljudska kisela ceramidaza	Liječenje cistične fibroze
Czech	Rekombinantní lidská ceramidasová kyselina	Léčba cystické fibrózy
Danish	Rekombinant human ceramidase	Behandling af cystisk fibrose
Dutch	Recombinant humaan ceramidasezuur	Behandeling van cystische fibrose
Estonian	Rekombinantne inimese happeline keramidaas	Tsüstilise fibroosi ravi
Finnish	Rekombinanttitekniikalla tehty ihmisen hapan seramidaasi	Kystisen fibroosin hoito
French	Céramidase acide humaine recombinante	Traitement de la mucoviscidose
German	Rekombinante menschliche saure Ceramidase	Behandlung zystischer Fibrose
Greek	Ανασυνδυασμένη ανθρώπινη όξινη κεραμιδάση	Θεραπεία της κυστικής ίνωσης
Hungarian	Rekombináns human savanyú ceramidase	Cisztikus fibrózis kezelése
Italian	Ceramidasi acida ricombinante umana	Trattamento della fibrosi cistica
Latvian	Rekombinanta cilvēka skābā keramidāze	Cistiskās fibrozes ārstēšana
Lithuanian	Rekombinantinė žmogaus rūgštinė ceramidazė	Cistinės fibrozės gydymas
Maltese	Aċidu ceramidase uman rikombinanti	Kura tal-fibroži ċistiku
Polish	Rekombinowana ludzka kwaśna ceramidaza	Leczenie zwłóknienia torbielowatego
Portuguese	Ceramidase ácida humana recombinante	Tratamento da fibrose quística
Romanian	Ceramidază acidă umană recombinantă	Tratamentul fibrozei chistice
Slovak	Rekombinantná ľudská kyslá ceramidáza	Terapia cystickej fibrózy
Slovenian	Rekombinantna humana kisla ceramidaza	Zdravljenje cistične fibroze
Spanish	Ceramidase ácido humano recombinante	Tratamiento de la fibrosis quística
Swedish	Rekombinant mänskligt surt ceramidas	Behandling av cystisk fibros
Norwegian	Rekombinant human sur ceramidase	Behandling av cystisk fibrose
Icelandic	Raðbrigða manna súr ceremídasi	Meðferð við slímseigjusjúkdómi

[1] At the time of designation