23 September 2014
EMA/COMP/440253/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lumacaftor/ivacaftor for the treatment of cystic fibrosis

On 22 August 2014, orphan designation (EU/3/14/1333) was granted by the European Commission to Vertex Pharmaceuticals (U.K.) Limited, United Kingdom, for lumacaftor/ivacaftor 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 abnormalities 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 approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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. Ivacaftor was authorised to treat a subgroup of patients with cystic fibrosis who have a specific mutation

*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 511,100,000 (Eurostat 2014).

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

(defect) called 'G551D' in the gene for CFTR. 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. Regular exercise and physiotherapy were also part of the treatment.

The sponsor has provided sufficient information to show that lumacaftor/ivacaftor might be of significant benefit for patients with cystic fibrosis because early studies showed an improvement in patients' lung function when used together with current treatments. 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?

This medicine is a fixed-dose combination of ivacaftor and lumacaftor. Both ivacaftor and lumacaftor are expected to act on the defective CFTR in cystic fibrosis patients.

Ivafactor works by increasing the activity of the defective CFTR while lumacaftor is thought to help produce some amount of functional CFTR protein. These actions are expected to normalise the transport of ions in and out of cells making the secretions less think and thereby relieving the symptoms of the disease.

What is the stage of development of this medicine?

The effects of lumacaftor/ivacaftor have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with lumacaftor/ivacaftor in patients with cystic fibrosis were ongoing.

At the time of submission, lumacaftor/ivacaftor was not authorised anywhere in the EU for cystic fibrosis or designated as an orphan medicinal product elsewhere for this condition. The single components lumacaftor and ivacaftor both have orphan designations in the EU for cystic fibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 July 2014 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:

Vertex Pharmaceuticals (U.K.) Limited
Cardinal Point
Park Road
Rickmansworth
Hertfordshire WD3 1RE
United Kingdom
Tel. +44 192 3432 655
Fax +44 192 3432 870
E-mail: vertexmedicalinfo@vrtx.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	Lumacaftor / ivacaftor	Treatment of cystic fibrosis
Bulgarian	Лумакафтор / ивакафтор	Лечение на кистозна фиброза
Croatian	Lumakaftor / ivakaftor	Liječenje cistične fibroze
Czech	Lumakaftor / ivakaftor	Léčba cystické fibrózy
Danish	Lumacaftor / ivacaftor	Behandling af cystisk fibrose
Dutch	Lumacaftor / ivacaftor	Behandeling van cystische fibrose
Estonian	Lumakaftoor / ivakaftoor	Tsüstilise fibroosi ravi
Finnish	Lumakaftori / ivakaftori	Kystisen fibroosin hoito
French	Lumacaftor / ivacaftor	Traitement de la mucoviscidose
German	Lumacaftor / Ivacaftor	Behandlung zystischer Fibrose
Greek	Lumacaftor / ivacaftor	Θεραπεία της κυστικής ίνωσης
Hungarian	Lumakaftor / ivakaftor	Cisztikus fibrózis kezelése
Italian	Lumacaftor / ivacaftor	Trattamento della fibrosi cistica
Latvian	Lumakaftors / ivakaftors	Cistiskās fibrozes ārstēšana
Lithuanian	Lumakaftoras / ivakaftoras	Cistinės fibrozės gydymas
Maltese	Lumacaftor / ivacaftor	Kura tal-fibrożi ċistiku
Polish	Lumakaftor / iwakaftor	Leczenie zwłóknienia torbielowatego
Portuguese	Lumacaftor / ivacaftor	Tratamento da fibrose quística
Romanian	Lumacaftor / ivacaftor	Tratamentul fibrozei chistice
Slovak	Lumakaftor / ivakaftor	Terapia cystickej fibrózy
Slovenian	Lumakaftor / ivakaftor"	Zdravljenje cistične fibroze
Spanish	Lumacaftor / ivacaftor	Tratamiento de la fibrosis quística
Swedish	Lumakaftor / ivakaftor	Behandling av cystisk fibros
Norwegian	Lumakaftor / ivakaftor	Behandling av cystisk fibrose
Icelandic	Lumacaftor / ívacaftor	Meðferð við slímseigjusjúkdómi

[1] At the time of designation