3 May 2017
EMA/143975/2017
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Phosphoinositide 3-kinase gamma peptide for the treatment of cystic fibrosis

On 20 March 2017, orphan designation (EU/3/17/1859) was granted by the European Commission to Kither Biotech s.r.l., Italy, for phosphoinositide 3-kinase gamma peptide (also known as KIT2014) for the treatment of cystic fibrosis.

What is cystic fibrosis?

Cystic fibrosis is a hereditary disease that affects the secretion of fluids from cells in the lungs and from the glands in the gut and pancreas. In cystic fibrosis, these fluids become thick, blocking the airways in the lungs and the flow of digestive juices in the gut and pancreas. This leads to inflammation and long-term infection of the lungs because of the build-up of thick mucus, and to poor growth and nutrition because of problems with the digestion and absorption of food.

Cystic fibrosis is caused by changes (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 52,000 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, Kalydeco (ivacaftor) and Orcambi (ivacaftor and lumacaftor) were authorised to treat patients with cystic fibrosis who have certain mutations in the gene for CFTR. Lung

*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 515,700,000 (Eurostat 2017).

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infection in cystic fibrosis was mainly treated with antibiotics. Other medicines used to treat the lung disease included anti-inflammatory medicines, bronchodilators (medicines that help to open up the airways in the lungs) and mucolytics (medicines that break down 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 have physiotherapy.

The sponsor has provided sufficient information to show that phosphoinositide 3-kinase gamma peptide might be of significant benefit for patients with cystic fibrosis because laboratory studies suggest that it can produce long-term increase in CFTR activity. 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?

Mutations of *CFTR* gene in cystic fibrosis cause defects in the CFTR protein, which forms channels involved in the production of fluids such as mucus and digestive juices. These channels are involved in transporting ions (charged atoms and molecules) in and out of the fluid-producing cells. When the channels are defective, transport of ions is reduced and fluid secretions become abnormally thick. The channels are activated by a substance called cyclic AMP (cAMP).

Giving the medicine by inhalation is expected to increase cAMP in the airways, thereby increasing the activity of CFTR protein channels. In this way, the medicine is expected to prevent fluid secretions in the lungs from becoming abnormally thick and so reduce the respiratory symptoms of cystic fibrosis.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

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

At the time of submission, the medicine 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 February 2017 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Phosphoinositide 3-kinase gamma peptide	Treatment of cystic fibrosis
Bulgarian	Фосфоинозитид 3-киназа гама пептид	Лечение на кистозна фиброза
Croatian	Fosfoinozitid 3-kinaza gama peptid	Liječenje cistične fibroze
Czech	Fosfoinositid 3-kináza gamma-peptid	Léčba cystické fibrózy
Danish	Phosphatidylinositol 3-kinase gamma peptid	Behandling af cystisk fibrose
Dutch	Fosfoinositide 3-kinase gamma peptide	Behandeling van cystische fibrose
Estonian	Fosfoinositiid-3-kinaasi gamma-peptiid	Tsüstilise fibroosi ravi
Finnish	Fosfoinositidi-3-kinaasi gamma-peptidi	Kystisen fibroosin hoito
French	Peptide phosphoinositide 3-kinase gamma	Traitement de la mucoviscidose
German	Phosphoinositid 3-Kinase Gamma Peptid	Behandlung zystischer Fibrose
Greek	Πεπτίδιο γάμμα της φωσφοϊνοσιτίδιο 3-κινάσης	Θεραπεία της κυστικής ίνωσης
Hungarian	Foszfo-ionozitid-3-kináz-gamma-peptid	Cisztikus fibrózis kezelése
Italian	Peptide gamma della fosfoinositide 3-chinasi	Trattamento della fibrosi cistica
Latvian	Fosfoinozitīda-3-kināzes gamma peptīds	Cistiskās fibrozes ārstēšana
Lithuanian	Fosfoinozitido 3-kinazės gama peptidas	Cistinės fibrozės gydymas
Maltese	Fosfoinositid 3-kinaži gamma peptide	Kura tal-fibroži ċistiku
Polish	Peptyd kinazy 3 fosfatydyloinozytolu gamma	Leczenie zwłóknienia torbielowatego
Portuguese	Peptído gama fosfoinositído 3-quinase	Tratamento da fibrose quística
Romanian	Peptid gama al fosfatidilinozitol 3-kinazei	Tratamentul fibrozei chistice
Slovak	Fosfoinozitid 3-kináza gama-peptid	Terapia cystickej fibrózy
Slovenian	Fosfoinozitid 3-kinaza gama-peptid	Zdravljenje cistične fibroze
Spanish	Peptido gama Fosfoinositol 3-quinasa	Tratamiento de la fibrosis quística
Swedish	Fosfoinositid-3-kinas gamma-peptid	Behandling av cystisk fibros
Norwegian	Fosfoinositid 3-kinase gamma-peptid	Behandling av cystisk fibrose
Icelandic	Fosfóinósitíð 3-kínasa gamma peptíð	Meðferð við slímseigjusjúkdómi

[1] At the time of designation