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Public summary of opinion on orphan designation

6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate for the treatment of cystic fibrosis

On 26 October 2018, orphan designation (EU/3/18/2072) was granted by the European Commission to FGK Representative Service GmbH, Germany, for 6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate (also known as ELX-02) for the treatment of cystic fibrosis.

What is cystic fibrosis?

Cystic fibrosis is an inherited 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 Orkambi (ivacaftor and lumacaftor) were authorised in the EU to treat patients with cystic fibrosis who have certain mutations in the gene for

[*]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 517,400,000 (Eurostat 2018).

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CFTR. Lung 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 help 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 the medicine might be of significant benefit for patients with cystic fibrosis. Laboratory studies showed that it may improve the function of the CFTR protein in patients for whom no specific treatments are authorised. Laboratory data also showed that adding this medicine to some authorised treatments can increase their effects.

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 some patients with cystic fibrosis, mutations in the gene for CFTR result in the production of a shorter, non-functional protein. This medicine allows the cell components that produce the CFTR protein to read through these mutations, resulting in the production of a full-length and functional CFTR. By producing a functioning protein, the medicine is expected to slow down or stop further damage to the lungs and relieve the symptoms of cystic fibrosis.

What is the stage of development of this medicine?

The effects of the medicine 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, 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 13 September 2018 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	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate	Treatment of cystic fibrosis
Bulgarian	6'-(R)-метил-5-O-(5-амино-5,6-дидеокси-алфа-L-талофуранозил)-паромамин сулфат	Лечение на кистозна фиброза
Croatian	6'-(R)-metil-5-O-(5-amino-5,6-dideoksi-alfa-L-talofuranosil)-paromamin sulfat	Liječenje cistične fibroze
Czech	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alfa-L-talofuranosyl)-paromamine sulfát	Léčba cystické fibrózy
Danish	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alfa-L-talofuranosyl)-paromaminesulfat	Behandling af cystisk fibrose
Dutch	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alfa-L-talofuranosyl)-paromaminesulfaat	Behandeling van cystische fibrose
Estonian	6'-(R)-metüül-5-O-(5-amino-5,6-dideoksü-alfa-L-talofuranosüül)-paromamiinsulfaat	Tsüstilise fibroosi ravi
Finnish	6'-(R)-metyyli-5-O-(5-amino-5,6-dideoksi-alfa-L-talofuranosyyli)-paromamiini sulfaatti	Kystisen fibroosin hoito
French	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate	Traitement de la mucoviscidose
German	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alfa-L-talofuranosyl)-paromaminsulfat	Behandlung zystischer Fibrose
Greek	θειική 6'-(R)-μεθυλ-5-O-(5-αμινο-5,6-διδεοξυ-α-L-ταλοφουρανοσυλ-παρομαμίνη	Θεραπεία της κυστικής ίνωσης
Hungarian	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alfa-L-talofuranosyl)-paromamin szulfát	Cisztikus fibrózis kezelése
Italian	6'-(R)-metil-5-O-(5-amino-5,6-dideossi-alfa-L-talofuranosil)-paromamine solfato	Trattamento della fibrosi cistica
Latvian	6'-(R)-metil-5-O-(5-amino-5,6-dideoksi-alfa-L-talofuranozil)-paromamīna sulfāts	Cistiskās fibrozes ārstēšana
Lithuanian	6'-(R)-metil-5-O-(5-amino-5,6-dideoksi-alfa-L-talofuranosil)-paromamino sulfatase	Cistinės fibrozės gydymas
Maltese	6'-(R)-methyl-5-O-(5-amino-5,6-dideoxy-alpha-L-talofuranosyl)-paromamine sulfate	Kura tal-fibrożi ċistiku
Polish	Siarczan 6'-(R)-metylo-5-O-(5-amino-5,6-dideoksy-alfa-L-talofuranozylo)-paromaminy	Leczenie zwłóknienia torbielowatego
Portuguese	Sulfato de 6'-(R)-metil-5-O-(5-amino-5,6-didesoxi-alfa-L-talofuranosil)-paromamina	Tratamento da fibrose quística
Romanian	Sulfat de 6'-(R)-metil-5-O-(5-amino-5,6-dideoxi-alfa-L-talofuranozil)-paromamină	Tratamentul fibrozei chistice
Slovak	6'-(R)-metyl-5-O-(5-amino-5,6-dideoxy-alfa-L-talofuranozyl)-paromamín sulfát	Terapia cystickej fibrózy

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	6'-(R)-metil-5-O-(5-amino-5,6-dideoksi-alfa-L-talofuranozil)-paromamin sulfat	Zdravljenje cistične fibroze
Spanish	Sufato de 6'-(R)-metil-5-O-(5-amino-5,6-dideoxi-alfa-L-talofuranosil)-paromamine	Tratamiento de la fibrosis quística
Swedish	6'-(R)-metyl-5-O-(5-amino-5,6-dideoxy-alfa-L-talofuranosyl)-paromaminsulfat	Behandling av cystisk fibros
Norwegian	6'-(R)-metyl-5-O-(5-amino-5,6-dideoksy-alfa-L-talofuranosyl)-paromaminsulfat	Behandling av cystisk fibrose
Icelandic	6'-(R)-methýl-5-O-(5-amínó-5,6-dídeoxý-alfa-L-talófúranósýl)-parómamíne súlfat	Meðferð við slímseigjusjúkdómi