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Public summary of opinion on orphan designation

Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-glutamyl-L-threonyl]acetate for the treatment of cystic fibrosis

On 19 November 2018, orphan designation (EU/3/18/2086) was granted by the European Commission to Santhera Pharmaceuticals (Deutschland) GmbH, Germany, for cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-glutamyl-L-threonyl]acetate (also known as POL6014) 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).

^{*}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).

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 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 show that it may improve inflammation in the lung and could be used in combination with other authorised medicines.

These assumptions 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 to be inhaled directly into the lungs, where it is expected to block the action of neutrophil elastase, an enzyme involved in inflammation. By reducing elastase activity, the medicine is expected to reduce the inflammation of the lung tissue, thereby improving the symptoms of the disease.

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, clinical trials with the medicine in patients with cystic fibrosis were ongoing.

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 11 October 2018 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:

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl]acetate	Treatment of cystic fibrosis
Bulgarian	Цикло[L-аланил-L-серил-L-изолеуцил-L-пролил-L-пролил-L-глутаминил-L-лизил-L-тирозил-D-пролил-L-пролил-(2S)-2-аминодеканойл-L-алфа-глутамил-L-треонил]ацетат	Лечение на кистозна фиброза
Croatian	Ciklo[L-alanil-L-seril-L-izoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodekanoil-L-alfa-glutamil-L-treonil]acetat	Liječenje cistične fibroze
Czech	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl] acetát	Léčba cystické fibrózy
Danish	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alfa-glutamyl-L-threonyl]acetat	Behandling af cystisk fibrose
Dutch	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl]acetaat	Behandeling van cystische fibrose
Estonian	Tsüklo[L-alanüül-L-serüül-L-isoleutsüül-L-prolül-L-prolül-L-glutaminüül-L-lüsüül-L-türosüül-D-prolül-L-prolül-(2S)-2-aminodekanoüül-L-alfa-glutamüül-L-treonüül]atsetaat	Tsüstilise fibroosi ravi
Finnish	Syklo[L-alanyyli-L-seryyli-L-isoleussyli-L-prolyyli-L-prolyyli-L-glutaminyyli-L-lysyli-L-tyrosyyli-D-prolyyli-L-prolyyli-(2S)-2-aminodekanoyli-L-alfa-glutamyyli-L-treonyyli]asettaatti	Kystisen fibroosin hoito
French	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodécanoyl-L-alpha-glutamyl-L-thréonyl]acétate	Traitement de la mucoviscidose
German	Cyclo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminy-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodecanoyl-L-alpha-glutamyl-L-threonyl]Acetat	Behandlung zystischer Fibrose
Greek	Κύκλο [L-αλανυλο-L-σερυλο-L-ισολευκυλο-L-προλυλο-L-προλυλο-L-γλουταμινυλο-L-λυσυλο-L-τυρόσυλο-D-προλυλο-L-προλυλο-(2S)-2-αμινοδεκανοϋλο-L-α-γλουταμυλο-L-θρεονυλο]οξικό	Θεραπεία της κυστικής ίνωσης
Hungarian	Ciklo[L-alanil-L-szeril-L-izoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodekanoil-L-alfa-glutamil-treonil]acetát	Cisztikus fibrózis kezelése

¹ At the time of designation

Language	Active ingredient	Indication
Italian	Ciclo[L-alanil-L-seril-L-isoleucil-L-prolil-L-prolil-L-glutaminil-L-lisil-L-tyrosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-threonil] acetato	Trattamento della fibrosi cistica
Latvian	Ciklo[L-alanil-L-seril-L-izoleicil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-treonil]acetāts	Cistiskās fibrozes ārstēšana
Lithuanian	Ciklo[L-alanil-L-seril-L-izoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-treonil]acetatas	Cistinės fibrozės gydymas
Maltese	Ċiklo[L-alanil-L-seril-L-isolewċil-L-prolil-L-prolil-L-glutaminil-L-lisil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-treonil] aċetat	Kura tal-fibroži ċistiku
Polish	Cyklo[L-alanylo-L-serylo-L-izoleucylo-L-prolino-L-prolino-L-glutamylo-L-lizylo-L-tyrozynylo-D-prolino-L-prolino-(2S)-2-aminodekanoilo-L-alfa-glutamylo-L-treonylu]octan	Leczenie zwłóknienia torbielowatego
Portuguese	Acetato de ciclo[L-alanil-L-seril-L-isoleucil-L-prolil-L-prolil-L-glutaminil-L-lisil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alpha-glutamil-L-treonil]	Tratamento da fibrose quística
Romanian	Ciclo[L-alanil-L-seril-L-isoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirozil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-treonil]acetat	Tratamentul fibrozei chistice
Slovak	Cyklo[L-alanyl-L-seryl-L-izoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lyzyl-L-tyrozyl-D-prolyl-L-prolyl-(2S)-2-aminodekanoyl-L-alfa-glutamyl-L-treonyl]acetát	Terapia cystickej fibrózy
Slovenian	Ciclo[L-alanil-L-seril-L-izoleucil-L-prolil-L-prolil-L-glutaminil-L-lizil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodekanoil-L-alfa-glutamil-L-treonil]acetat	Zdravljenje cistične fibroze
Spanish	Acetato de ciclo[L-alanil-L-seril-L-isoleucil-L-proliil-L-prolil-L-glutaminil-L-lisil-L-tirosil-D-prolil-L-prolil-(2S)-2-aminodecanoil-L-alfa-glutamil-L-treonil]	Tratamiento de la fibrosis quística
Swedish	Cyklo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodekanoyl-L-alfa-glutamyl-L-threonyl]acetat	Behandling av cystisk fibros
Norwegian	Syklo[L-alanyl-L-seryl-L-isoleucyl-L-prolyl-L-prolyl-L-glutaminyl-L-lysyl-L-tyrosyl-D-prolyl-L-prolyl-(2S)-2-aminodekanoyl-L-alfa-glutamyl-L-treonyl]acetat	Behandling av cystisk fibrose
Icelandic	Cýcló[L-alanýl-L-serýl-L-ísóleucýl-L-prólýl-L-prólýl-L-glútamínýý-L-lýsýl-L-týrósfýl-D-prólýl-L-prólýl-(2S)-2-amínódecanóýl-L-alfa-glútamýl-L-threónýl]acetat	Meðferð við slímseigjusjúkdómi