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SCIENCE MEDICINES HEALTH

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Public summary of opinion on orphan designation

Gallium citrate for the treatment of cystic fibrosis

On 21 August 2019, orphan designation EU/3/19/2189 was granted by the European Commission to Clinical Network Services (NL) B.V, the Netherlands, for gallium citrate 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 approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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), Orkambi (ivacaftor and lumacaftor) and Symkevi (tezacaftor and ivacaftor) 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

*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 518,400,000 (Eurostat 2019).

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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 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 data showed that adding the medicine to colistin, an authorised antibiotic for treating cystic fibrosis, can increase effectiveness against bacteria called *Pseudomonas aeruginosa*, which cause long-term infection in patients with this 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?

Patients with cystic fibrosis often suffer from *P. aeruginosa* infections. Bacteria such as *P. aeruginosa* need iron to grow and multiply, to produce copies of their DNA (genetic material) and to protect themselves against damage known as 'oxidative stress'. This medicine contains gallium, which attaches to iron-binding proteins on bacterial cells instead of iron. This means the bacteria do not get enough iron and cannot function and grow properly. This restriction in bacterial growth is expected to reduce the symptoms of bacterial infection in patients with cystic fibrosis.

What is the stage of development of this medicine?

The effects of gallium citrate have been evaluated in experimental models.

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

At the time of submission, gallium citrate was not authorised anywhere in the EU for the treatment of cystic fibrosis. Orphan designation of gallium citrate had been granted in the United States for the treatment of lung infections in patients with cystic fibrosis.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 18 July 2019, 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.

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	Gallium citrate	Treatment of cystic fibrosis
Bulgarian	Галиев цитрат	Лечение на кистозна фиброза
Croatian	Galijum citrat	Liječenje cistične fibroze
Czech	Galium citrát	Léčba cystické fibrózy
Danish	Galliumcitrat	Behandling af cystisk fibrose
Dutch	Galliumcitraat	Behandeling van cystische fibrose
Estonian	Galliumtsitraat	Tsüstilise fibroosi ravi
Finnish	Galliumsitraatti	Kystisen fibroosin hoito
French	Citrate de gallium	Traitement de la mucoviscidose
German	Gallium citrat	Behandlung zystischer Fibrose
Greek	Κιτρικό Γάλλιο	Θεραπεία της κυστικής ίνωσης
Hungarian	Gallium citrát	Cisztikus fibrózis kezelése
Italian	Citrato di gallium	Trattamento della fibrosi cistica
Latvian	Gallija citrāts	Cistiskās fibrozes ārstēšana
Lithuanian	Galio citratas	Cistinės fibrozės gydymas
Maltese	Ċitrat tal-gallju	Kura tal-fibrożi ċistiku
Polish	Cytrynian galu	Leczenie zwłóknienia torbielowatego
Portuguese	Citrato de gálio	Tratamento da fibrose quística
Romanian	Citrat de galiu	Tratamentul fibrozei chistice
Slovak	Gálium citrát	Terapia cystickej fibrózy
Slovenian	Galijev citrat	Zdravljenje cistične fibroze
Spanish	Citrato de Galio	Tratamiento de la fibrosis quística
Swedish	Galliumcitrat	Behandling av cystisk fibros
Norwegian	Galliumsitrat	Behandling av cystisk fibrose
Icelandic	Gallíumsítrat	Meðferð við slímseigjusjúkdómi

[1] At the time of designation