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Public summary of opinion on orphan designation

Poly(N-acetyl, N-arginyl)glucosamine for the treatment of cystic fibrosis

On 26 February 2019, orphan designation (EU/3/19/2144) was granted by the European Commission to Accelsiors Ltd, Hungary, for poly(N-acetyl, N-arginyl)glucosamine (also known as PAAG15A or SNSP113) 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 mutations (changes) 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) 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 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 the medicine is more effective than authorised mucolytics at disrupting bacterial 'biofilms' (when bacterial cells group together on a surface, such as the lining of the lung), and can also make antibiotics work better.

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?

In patients with cystic fibrosis, the lungs produce excessively thick mucus which allows bacteria to grow more easily and to form biofilms, which further protect bacteria from antibiotics. This medicine disrupts the structure of biofilms and makes the mucus less thick, thus helping to unblock the airways and relieve the symptoms of cystic fibrosis. By making the mucus less thick it also allows antibiotics to reach bacteria more easily.

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. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 24 January 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 the 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	Poly(N-acetyl, N-arginyl)glucosamine	Treatment of cystic fibrosis
Bulgarian	Поли (N-ацетил, N-аргинил) глукозамин	Лечение на кистозна фиброза
Croatian	Poli (N-acetil, N-arginil) glukozamin	Liječenje cistične fibroze
Czech	Poly (N-acetyl, N-arginyl) glukosamin	Léčba cystické fibrózy
Danish	Poly (N-acetyl, N-arginyl)glucosamin	Behandling af cystisk fibrose
Dutch	Poly (N-acetyl, N-arginyl) glucosamine	Behandeling van cystische fibrose
Estonian	Polü (N-atsetüül, N-arginüül) glükoosamiin	Tsüstilise fibroosi ravi
Finnish	Poly (N-asetyyli, N-arginyyli) glukosamiini	Kystisen fibroosin hoito
French	Poly (N-acétyl, N-arginyl) glucosamine	Traitement de la mucoviscidose
German	Poly (N-acetyl, N-arginyl) glucosamin	Behandlung zystischer Fibrose
Greek	Πολυ(N-ακέτυλο, N-αργίνυλο) γλυκοζαμίνη	Θεραπεία της κυστικής ίνωσης
Hungarian	Poli (N-acetil, N-arginil) glükózamin	Cisztikus fibrózis kezelése
Italian	Poli (N-acetile, N-arginil) glucosamina	Trattamento della fibrosi cistica
Latvian	Poli (N-acetil, N-arginil) glikozamīns	Cistiskās fibrozes ārstēšana
Lithuanian	Poli (N-acetil, N-arginil) gliukozaminas	Cistinės fibrozės gydymas
Maltese	Poli(N-aċetil, N-arginil)glukożammina	Kura tal-fibrożi ċistiku
Polish	Poli (N-acetyl, N-arginyl) glukozamina	Leczenie zwłóknienia torbielowatego
Portuguese	Poli (N-cetil, N-arginil) glucosamina	Tratamento da fibrose quística
Romanian	Poli (N-acetil, N-arginil) glucozamină	Tratamentul fibrozei chistice
Slovak	Poly (N-acetyl, N-arginyl) glukózamín	Terapia cystickej fibrózy
Slovenian	Poli (N-acetil, N-arginil) glukozamin	Zdravljenje cistične fibroze
Spanish	Poli (N-acetil, N-arginil) glucosamina	Tratamiento de la fibrosis quística
Swedish	Poly (N-acetyl, N-arginyl) glukosamin	Behandling av cystisk fibros
Norwegian	Poly(N-acetyl, N-arginyl)glukosamin	Behandling av cystisk fibrose
Icelandic	Fjöl (N-asetýl, N-arginýl) glúkósamín	Meðferð við slímseigjusjúkdómi

[1] At the time of designation