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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sodium nitrite and ethylenediaminetetraacetic acid for the treatment of cystic fibrosis

On 30 May 2016, orphan designation (EU/3/16/1668) was granted by the European Commission to Arch Bio Ireland Ltd, Ireland, for sodium nitrite and ethylenediaminetetraacetic acid (EDTA, edetic acid) for the treatment of cystic fibrosis.

What is cystic fibrosis?

Cystic fibrosis is a hereditary disease that affects the cells in the lungs, and the glands in the gut and pancreas, that secrete fluids. 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 51,000 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 513,700,000 (Eurostat 2016).

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What treatments are available?

At the time of designation, lung infection in cystic fibrosis was mainly treated with antibiotics. Kalydeco (ivacaftor) and Orcambi (ivacaftor and lumacaftor) were authorised to treat patients with cystic fibrosis who have certain mutations in the gene for CFTR. Other medicines used to treat the lung disease included anti-inflammatory agents, bronchodilators (medicines that help to open up the airways in the lungs) and mucolytics (medicines that help dissolve the 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 undergo physiotherapy.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with cystic fibrosis because laboratory studies indicate that it increases the effect of currently authorised antibiotics against bacteria. 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?

This medicine contains 2 substances, sodium nitrite and ethylenediaminetetraacetic acid (EDTA, edetic acid), and is given by inhalation. Once in the lungs of cystic fibrosis patients, sodium nitrite is converted into nitric oxide. EDTA acts on the bacterial membrane, allowing more nitric oxide to enter the bacteria. Once inside bacteria, nitric oxide starts a series of reactions that lead to their death. By killing the bacteria, this medicine helps to clear the infection and improve lung function in cystic fibrosis patients.

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 of the application for orphan designation, no clinical trials with this 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 *Pseudomonas aeruginosa* pulmonary infections in patients with cystic fibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 April 2016 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	Sodium nitrite and ethylenediaminetetraacetic acid	Treatment of cystic fibrosis
Bulgarian	Натриев нитрит и етилендиаминтетраоцетна киселина	Лечение на кистозна фиброза
Croatian	Natrijev nitrit i etilendiamintetraoctena kiselina	Liječenje cistične fibroze
Czech	Dusitan sodný a kyselina ethylendiamintetraoctová	Léčba cystické fibrózy
Danish	Natriumnitrit og ethylendiamintetraeddikesyre	Behandling af cystisk fibrose
Dutch	Natriumnitriet en ethyleendiaminetetraazijnzuur	Behandeling van cystische fibrose
Estonian	Naatriumnitrit ja etüleendiamiintetraatseethape	Tsüstilise fibroosi ravi
Finnish	Natriumnitriitti ja etyleenidiamiinitetraetikkahappo	Kystisen fibroosin hoito
French	Nitrite de sodium et acide éthylène diamine tétra-acétique	Traitement de la mucoviscidose
German	Natriumnitrit und Ethylendiamintetraessigsäure	Behandlung zystischer Fibrose
Greek	Νιτρώδες νάτριο και αιθυλενοδιαμινοτετραοξικό οξύ	Θεραπεία της κυστικής ίνωσης
Hungarian	Nátrium-nitrit és etiléndiamintetraecetsav	Cisztikus fibrózis kezelése
Italian	Nitrito di sodio e acido etilendiamminotetraacetico	Trattamento della fibrosi cistica
Latvian	Nātrija nitrīts un etilēndiamīntetraetiķskābes acid	Cistiskās fibrozes ārstēšana
Lithuanian	Natrio nitritas ir etilendiaminotetraacto rūgštis	Cistinės fibrozės gydymas
Maltese	Sodium nitrite u aċidu ethylenediaminetetraacetic	Kura tal-fibrożi ċistiku
Polish	Azotyn sodu i kwas etylenodiaminotetraoctowy	Leczenie zwłóknienia torbielowatego
Portuguese	Nitrito de sódio e ácido etilenodiaminotetracético	Tratamento da fibrose quística
Romanian	Nitrit de sodiu şi acid etilendiaminotetraacetic	Tratamentul fibrozei chistice
Slovak	Dusitan sodný a kyselina etyléndiamíntetraoctová	Terapia cystickej fibrózy
Slovenian	Natrijev nitrit in etilendiamintetraocetna kislina	Zdravljenje cistične fibroze
Spanish	Nitrito de sodio y ácido etilenodiaminotetracético	Tratamiento de la fibrosis quística
Swedish	Natriumnitrit och etylendiamintetraättiksyra	Behandling av cystisk fibros
Norwegian	Natriumnitritt og etylendiamintetraeddiksyre	Behandling av cystisk fibrose
Icelandic	Natríum nítrít og etýlendíamíntetraediksýra	Meðferð við slímseigjusjúkdómi

[1] At the time of designation