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EMA/COMP/560372/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Nitric oxide for the treatment of cystic fibrosis

On 15 October 2014, orphan designation (EU/3/14/1344) was granted by the European Commission to PD Dr.med. Joachim Riethmüller, Germany, for nitric oxide 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 such as mucus and digestive juices. In cystic fibrosis, these fluids become thick and viscous, blocking the airways and the flow of digestive juices. This leads to long-term infection and inflammation of the lungs because of excess mucus not being cleared away, and to problems with the digestion and absorption of food, resulting in poor growth.

Cystic fibrosis is caused by defects ('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 0.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 36,000 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, lung infection in cystic fibrosis was mainly treated with antibiotics. Kalydeco (ivacaftor) was authorised to treat the subgroup of patients with cystic fibrosis who have certain mutations in the gene for the CFTR protein. Other medicines used to treat the lung disease included

*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 511,100,000 (Eurostat 2014).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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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 nitric oxide might be of significant benefit for patients with cystic fibrosis because it works in a different way to existing treatments and preliminary data show a broad anti-infective activity and an improvement of lung function in patients with this condition. 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?

Nitric oxide is a naturally-occurring chemical in the body that, when inhaled at high concentrations, is able to enter bacteria that are causing infection in the lungs of cystic fibrosis patients, even bacteria that are resistant to commonly used antibiotics. Once inside bacteria, nitric oxide starts a series of reactions that lead to their death. By killing the bacteria, treatment with nitric oxide helps to clear the infection and improve lung function in cystic fibrosis patients.

What is the stage of development of this medicine?

The effects of nitric oxide have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with nitric oxide in patients with cystic fibrosis had started.

At the time of submission, nitric oxide was authorised in the EU to help improve blood oxygen levels in newborn babies with breathing problems (neonatal respiratory distress syndrome) and in patients with pulmonary hypertension (high blood pressure in the lungs).

At the time of submission, nitric oxide was not authorised anywhere in the EU for cystic fibrosis. Orphan designation of nitric oxide had been granted in the United States for the treatment of cystic fibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 4 September 2014 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:

PD Dr.med. Joachim Riethmüller
Beethovenweg 7
72076 Tübingen
Germany
Tel. +49 7071 298 1442
Fax +49 7071 294 450
E-mail: joachim.riethmueller@med.uni-tuebingen.de

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	Nitric oxide	Treatment of cystic fibrosis
Bulgarian	Азотен оксид	Лечение на кистозна фиброза
Croatian	Dušikov(II) oksid	Liječenje cistične fibroze
Czech	Oxid dusnatý	Léčba cystické fibrózy
Danish	Nitrogenoxid	Behandling af cystisk fibrose
Dutch	Stikstofmonoxide	Behandeling van cystische fibrose
Estonian	Lämmastikoksiidi	Tsüstilise fibroosi ravi
Finnish	Typpioksidi	Kystisen fibroosin hoito
French	Oxyde nitrique	Traitement de la mucoviscidose
German	Stickstoffmonoxid	Behandlung zystischer Fibrose
Greek	Μονοξείδιο του αζώτου	Θεραπεία της κυστικής ίνωσης
Hungarian	Nitrogén oxid	Cisztikus fibrózis kezelése
Italian	Ossido nitrico	Trattamento della fibrosi cistica
Latvian	Slāpekļa oksīds	Cistiskās fibrozes ārstēšana
Lithuanian	Azoto oksidas	Cistinės fibrozės gydymas
Maltese	Ossidu nitriku	Kura tal-fibrożi ċistiku
Polish	Tlenek azotu	Leczenie zwłóknienia torbielowatego
Portuguese	Óxido nítrico	Tratamento da fibrose quística
Romanian	Oxid nitric	Tratamentul fibrozei chistice
Slovak	Oxid dusnatý	Terapia cystickej fibrózy
Slovenian	Dušikov oksid	Zdravljenje cistične fibroze
Spanish	Óxido nítrico	Tratamiento de la fibrosis quística
Swedish	Kväveoxid	Behandling av cystisk fibros
Norwegian	Nitrogenmonoksid	Behandling av cystisk fibrose
Icelandic	Nituroxíð	Meðferð við slímseigjusjúkdómi

[1] At the time of designation