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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Fixed-dose combination of fosfomycin disodium and tobramycin for the treatment of cystic fibrosis

On 10 August 2015, orphan designation (EU/3/15/1538) was granted by the European Commission to CURx Pharma (UK) Limited, United Kingdom, for a fixed-dose combination of fosfomycin disodium and tobramycin 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 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 512,900,000 (Eurostat 2015).

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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) was authorised to treat a 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 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 fixed-dose combination of fosfomycin disodium and tobramycin might be of significant benefit for patients with cystic fibrosis because early results from studies suggest it can help prevent infection and maintain lung function after treatment with another antibiotic. In addition, the medicine is expected to target more types of infections than the authorised medicine tobramycin alone. 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?

The medicine is a solution for inhalation that contains a combination of two antibiotics: tobramycin, which is already approved for the treatment of lung infections in cystic fibrosis caused by the bacterium *Pseudomonas aeruginosa*, and fosfomycin, an antibiotic which is active against various types of bacteria including MRSA. By combining these two antibiotics with two different actions, the medicine is expected to act against a wider range of infections, and reduce the risk of bacteria becoming resistant to treatment.

What is the stage of development of this medicine?

The effects of the fixed-dose combination of fosfomycin disodium and tobramycin 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, this medicine was not authorised anywhere in the EU for cystic fibrosis. Orphan designation of the medicine had been granted in the United States for control of bacterial infections in cystic fibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 July 2015 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:

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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	Fixed-dose combination of fosfomycin disodium and tobramycin	Treatment of cystic fibrosis
Bulgarian	Фиксирана комбинация на фосфомицин натрий и тобрамицин	Лечение на кистозна фиброза
Croatian	Fiksna kombinacija dinatrijevog fosfomicina i tobramicina	Liječenje cistične fibroze
Czech	Fixní kombinace disodné soli fosfomycinu a tobramycin	Léčba cystické fibrózy
Danish	Fast dosis kombination af fosfomycin dinatrium og tobramycin	Behandling af cystisk fibrose
Dutch	Vast combinatiepreparaat van fosfomycin dinatrium en tobramycine	Behandeling van cystische fibrose
Estonian	Fikseeritud doosiga fosfomütsiin dinaatriumi ja tobramütsiini kombinatsioon	Tsüstilise fibroosi ravi
Finnish	Fosfomysiinidinatriumin ja tobramysiinin kiinteä yhdistelmä	Kystisen fibroosin hoito
French	Combinaison de fosfomycine disodique et tobramycine à dose fixe	Traitement de la mucoviscidose
German	Kombinationspräparat aus Dinatrium-Fosfomyzin und Tobramycin	Behandlung zystischer Fibrose
Greek	Συνδυασμός σταθερής δόσης δινατριούχου φωσφομυκίνης και τομπραμυκίνης	Θεραπεία της κυστικής ίνωσης
Hungarian	Foszfomicin dinátrium és tobramicin fix-dózisú kombinációja	Cisztikus fibrózis kezelése
Italian	Combinazione a dosaggio fisso di fosfomicina sale disodico e tobramicina	Trattamento della fibrosi cistica
Latvian	Fosfomicīna dinātrija sāls un tobramicīna fiksētu devu kombinācija	Cistiskās fibrozes ārstēšana
Lithuanian	Fosfomicino dinatrio ir tobramicino fiksuotos dozės derinys	Cistinės fibrozės gydymas
Maltese	Fosfomycin disodium u tobramycin magħqudin f'doża fissa	Kura tal-fibrożi ċistiku
Polish	Preparat złożony o ustalonych dawkach fosfomycyna dwusodowa i tobramycyna	Leczenie zwłóknienia torbielowatego
Portuguese	Combinação fixa de fosfomicina dissódica e tobramicina	Tratamento da fibrose quística
Romanian	Combinaţie cu doză fixă de fosfomicină disodică si tobramicină	Tratamentul fibrozei chistice
Slovak	Kombinácia fixnej dávky fosfomycinu dijsodného a tobramycínu	Terapia cystickej fibrózy

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Kombiniran fiksni odmerek dinatrijevega fosfomicina in tobramicina	Zdravljenje cistične fibroze
Spanish	Compuesto de fosfomicina disódica e tobramicina	Tratamiento de la fibrosis quística
Swedish	Kombinationspreparat innehållande fosfomycin dinatrium och tobramycin	Behandling av cystisk fibros
Norwegian	Kombinasjonspreparat med fosfomycin dinatrium og tobramycin	Behandling av cystisk fibrose
Icelandic	Blanda í föstum skammti af fosfómýsín tvínatríum og tóbramýcíni	Meðferð við slímseigjusjúkdómi