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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl) acetamide for treatment of cystic fibrosis

On 21 May 2015, orphan designation (EU/3/15/1498) was granted by the European Commission to Clinical Network Services (UK) Ltd, United Kingdom, for 2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide 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 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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 this medicine might be of significant benefit for patients with cystic fibrosis because early studies in experimental models suggest that the medicine may correct the function of the defective CFTR protein in patients with the most common form of mutation (F508d). 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 due to the most common CFTR mutation, F508d, produce badly shaped CFTR protein which does not work properly and is quickly broken down and destroyed. The medicine is expected to help correct the way in which the protein is shaped and allow it to work better and be more stable. This should reduce the thickness of mucus and digestive juices, thereby improving the symptoms of the disease.

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 or designated as an orphan medicinal product elsewhere for this condition.

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

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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	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Treatment of cystic fibrosis
Bulgarian	2-(7-етокси-4-(3-флуорофенил)-1-оксофталазин-2(1H)-yl)-N-метил-N-(2-метилбензо[d]оксазол-6-ил)ацетамид	Лечение на кистозна фиброза
Croatian	2-(7-etoksi-4-(3-fluorofenil)-1-oksoftalazin-2(1H)-il)-N-metil-N-(2-metilbenzo[d]oksazol-6-il)acetamid	Liječenje cistične fibroze
Czech	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Léčba cystické fibrózy
Danish	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Behandling af cystisk fibrose
Dutch	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Behandeling van cystische fibrose
Estonian	2-(7-etoksüy-4-(3-fluorofenüüll)-1-oksoftalaziin-2(1H)-üül)-N-metüül-N-(2-metüülbenso[d]oksasool-6-üül)atsetamiid	Tsüstilise fibroosi ravi
Finnish	2-(7-etoksi-4-(3-fluorofenyyli)-1-oksophtalasiini-2(1H)-yl)-N-metyyli-N-(2-metyylibentso[d]oksatsoli-6-yl)asetamidi	Kystisen fibroosin hoito
French	2-(7-éthoxy-4-(3-fluorophényl)-1-oxophthalazin-2(1H)-yl)-N-méthyl-N-(2-méthylbenzo[d]oxazol-6-yl)acétamide	Traitement de la mucoviscidose
German	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamid	Behandlung zystischer Fibrose
Greek	2-(7-αιθοξυ-4-(3-φθοροφαινυλ)-1-οξοφθαλαζιν-2(1H)-υλ)-N-μεθυλ-N-(2-μεθυλβενζο[d]οξαζολ-6-yl)ακεταμίδη	Θεραπεία της κυστικής ίνωσης
Hungarian	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Cisztikus fibrózis kezelése

[1] At the time of designation

Language	Active ingredient	Indication
Italian	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Trattamento della fibrosi cistica
Latvian	2-(7-etoksi-4-(3-fluorofenil)-1-oksoftalazīn-2(1H)-il)-N-metil-N-(2-metilbenzo[d]oksazol-6-il)acetamīds	Cistiskās fibrozes ārstēšana
Lithuanian	2-(7-etoksi-4-(3-fluorofenil)-1-oksoftalazin-2(1H)-il)-N-metil-N-(2-metilbenzo[d]oksazol-6-il)acetamidas	Cistinės fibrozės gydymas
Maltese	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Kura tal-fibrożi ċistiku
Polish	2-(7-etoksy-4-(3-fluorofenylo)-1-oksoftalazyn-2(1H)-yl)-N-metyl-N-(2-metylbenzo[d]oksazol-6-ylo)acetamid	Leczenie zwłóknienia torbielowatego
Portuguese	2-(7-etoxi-4-(3-fluorofenil)-1-oxoftalazin-2(1H)-yl)-N-metil-N-(2-metilbenzo[d]oxazol-6-yl)acetamida	Tratamento da fibrose quística
Romanian	2-(7-etoxi-4-(3-fluorofenil)-1-oxoftalazin-2(1H)-yl)-N-metil-N-(2-metilbenzo[d]oxazol-6-il)acetamidă	Tratamentul fibrozei chistice
Slovak	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Terapia cystickej fibrózy
Slovenian	2-(7-etoksi-4-(3-fluorofenil)-1-oksoftalazin-2(1H)-il)-N-metil-N-(2-metilbenzo[d]oksazol-6-il)acetamide	Zdravljenje cistične fibroze
Spanish	2-(7-ethoxi-4-(3-fluorofenil)-1-oxofthalazin-2(1H)-il)-N-methil-N-(2-methilbenzo[d]oxazol-6-il)acetamide	Tratamiento de la fibrosis quística
Swedish	2-(7-ethoxy-4-(3-fluorophenyl)-1-oxophthalazin-2(1H)-yl)-N-methyl-N-(2-methylbenzo[d]oxazol-6-yl)acetamide	Behandling av cystisk fibros
Norwegian	2-(7-etoksy-4-(3-fluorofenyl)-1-oksoftalazin-2(1H)-yl)-N-metyl-N-(2-metylbenzo[d]oksazol-6-yl)acetamid	Behandling av cystisk fibrose
Icelandic	2-(7-ethoxý-4-(3-flúórófenýl)-1-oxóphthalazín-2(1H)-ýl)-N-metýl-N-(2-metýlbenzó[d]oxazól-6-ýl)acetamíð	Meðferð við slímseigjusjúkdómi