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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)phenoxy]phenyl]methyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]benzoic acid for the treatment of cystic fibrosis

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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 19 November 2014, orphan designation (EU/3/14/1363) was granted by the European Commission to Coté Orphan Consulting UK Limited, United Kingdom, for 4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)phenoxy]phenyl]methyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]benzoic 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 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.

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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 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 the medicine might be of significant benefit for patients with cystic fibrosis because it works in a different way to existing treatments and could potentially be used in combination with these treatments. 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?

The medicine is expected to block the leukotriene A4 hydrolase (LTA4H) enzyme. This enzyme triggers the production of a substance called leukotriene B4. Leukotrienes are substances released by white blood cells as part of the inflammatory response in cystic fibrosis. By blocking the LTA4H enzyme and thereby the production of leukotriene B4, the medicine is expected to reduce or slow down the damage to the lung tissue caused by inflammation, 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, clinical trials with the medicine in patients with cystic fibrosis were ongoing.

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 9 October 2014 recommending the granting of this designation.

*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.
At the time of designation, this represented a population of 512,900,000 (Eurostat 2014).

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	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)phenoxy]phenyl]methyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]benzoic acid	Treatment of cystic fibrosis
Bulgarian	4-[[(1S,4S)-5-[[4-[4-(оксазол-2-ил)феноксифенил]метил]-2,5-диазабицикло[2.2.1]хепт-2-ил]метил]бензоена киселина	Лечение на кистозна фиброза
Croatian	4-[[(1S,4S)-5-[[4-[4-(oksazol-2-il)fenoksi]fenil]metil]-2,5-diazabiciklo[2.2.1]hept-2-il]metil]benzoatna kiselina	Liječenje cistične fibroze
Czech	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)fenoxy]fenyl]methyl]-2,5-diazabicyklo[2.2.1]hept-2-yl]methyl]benzoová kyselina	Léčba cystické fibrózy
Danish	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)phenoxy]phenyl]methyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]benzoesyre	Behandling af cystisk fibrose
Dutch	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)fenoxy]fenyl]methyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]benzoëzuur	Behandeling van cystische fibrose
Estonian	4-[[(1S,4S)-5-[[4-[4-(oksasool-2-üül)fenoksü]fenüül]metüül]-2,5-diasabitsüklo[2.2.1]hept-2-üül]metüül]bensoehape	Tsüstilise fibroosi ravi
Finnish	4-[[(1S,4S)-5-[[4-[4-(oksatsol-2-yyli)fenoksi]fenyyli]metyyli]-2,5-diatsabisyklo[2.2.1]hept-2-yyli]metyyli]bentsoehappo	Kystisen fibroosin hoito
French	Acide 4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)phénoxy]phényl]méthyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]méthyl]benzoïque	Traitement de la mucoviscidose
German	4-[[(1S,4S)-5-[[4-[4-(Oxazol-2-yl)phenoxy]phenyl]methyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]benzoesäure	Behandlung zystischer Fibrose
Greek	4-[[(1S,4S)-5-[[4-[4-(οξαζολ-2-υλο)φαινοξυ]φαινυλο]μεθυλο]-2,5-διαζαδικυκλο[2.2.1]επτ-2-υλο]μεθυλο]βενζοϊκό οξύ	Θεραπεία της κυστικής ίνωσης
Hungarian	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-il)fenoxi]fenil]metil]-2,5-diazabiciklo[2.2.1]hept-2-il]metil]benzoesav	Cisztikus fibrózis kezelése

[1] At the time of designation

Language	Active ingredient	Indication
Italian	Acido 4-[[(1S,4S)-5-[[4-[4-(ossazol-2-il)fenossi]fenil]metil]-2,5-diazabiciclo[2.2.1]ept-2-il]metil]benzoico	Trattamento della fibrosi cistica
Latvian	4-[[(1S,4S)-5-[[4-[4-(oksazol-2-il)fenoksi]fenil]metil]-2,5-diazabiciklo[2.2.1]hept-2-il]metil]benzoskābe	Cistiskās fibrozes ārstēšana
Lithuanian	4-[[(1S,4S)-5-[[4-[4-(oksazol-2-il)fenoksi]fenil]metil]-2,5-diazabiciklo[2.2.1]hept-2-il]metil]benzoinė rūgštis	Cistinės fibrozės gydymas
Maltese	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)phenoxy]phenyl]methyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]benzoic acid	Kura tal-fibrożi ċistiku
Polish	Kwas 4-[[(1S,4S)-5-[[4-[4-(oksazol-2-ilo)fenoksy]fenylo]metylo]-2,5-diazabicyklo[2.2.1]hept-2-ylo]metylo]benzoesowy	Leczenie zwłóknienia torbielowatego
Portuguese	Ácido 4-[[(1S,4S)-5-[[4-[4-(oxazol-2-il)fenoxi]fenil]metil]-2,5-diazabiciclo[2.2.1]hept-2-il]metil]benzóico	Tratamento da fibrose quística
Romanian	Acid 4-[[(1S,4S)-5-[[4-[4-(oxazol-2-il)fenoxi]fenil]metil]-2,5-diazabiciclo[2.2.1]hept-2-il]metil] benzoic	Tratamentul fibrozei chistice
Slovak	Kyselina 4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)fenoxy]fenyl]metyl]-2,5-diazabicyklo[2.2.1]hept-2-yl]metyl]benzoová	Terapia cystickej fibrózy
Slovenian	4-[[(1S,4S)-5-[[4-[4-(oksazol-2-il)fenoksi]fenil]metil]-2,5-diazabiciklo[2.2.1]hept-2-il]metil]benzojska kislina	Zdravljenje cistične fibroze
Spanish	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-il)fenoxi]fenil]metil]-2,5-diazabiciclo[2.2.1]hept-2-il]metil]ácido benzoico	Tratamiento de la fibrosis quística
Swedish	4-[[(1S,4S)-5-[[4-[4-(oxazol-2-yl)fenoxy]fenyl]metyl]-2,5-diazabicyclo[2.2.1]hept-2-yl]metyl]bensoesyra	Behandling av cystisk fibros
Norwegian	4-[[(1S,4S)-5-[[4-[4-(oksazol-2-yl)fenoksy]fenyl]metyl]-2,5-diazabisyklo[2.2.1]hept-2-yl]metyl]benzosyre	Behandling av cystisk fibrose
Icelandic	4-[[(1S,4S)-5-[[4-[4-(oxasól-2-ýl)fenoxý]fenýl]metýl]-2,5-díasabísýkló[2.2.1]hept-2-ýl]metýl]bensósýra	Meðferð við slímseigjusjúkdómi