11 July 2014
EMA/COMP/304418/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide for the treatment of cystic fibrosis

On 4 July 2014, orphan designation (EU/3/14/1281) was granted by the European Commission to Vertex Pharmaceuticals (UK) Limited, United Kingdom, for 1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide 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 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 511,100,000 (Eurostat 2014).

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What treatments are available?

At the time of designation, lung infection in cystic fibrosis was mainly treated with antibiotics. Ivacaftor is authorised to treat the subgroup of patients with cystic fibrosis who have the G551D mutation. 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 early results in patients with the condition have suggested that it can improve lung function when given in combination with another authorised treatment. 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 CFTR protein functions as a channel across the membrane of mucus-secreting cells, regulating the transport of chloride in and out of these cells. The transport of chloride helps to control the movement of water, which is necessary to produce thin, normal mucus.

This medicine is expected to work in a group of patients with cystic fibrosis whose disease is caused by a genetic defect called the F508D mutation. This defect causes the CFTR protein not to be present in sufficient amounts on the cell surface, resulting in inadequate transfer of chloride and water and abnormally thick secretions. The medicine is expected to increase the amount of and stabilise CFTR on the cell surface, improving the transport of chloride. When given in combination with another medicine that improves functioning of CFTR, it is expected to thin the abnormal secretions, reduce symptoms of the disease and improve lung function.

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, this medicine was not authorised anywhere in the EU for cystic fibrosis. Orphan designation had been granted in the United States for treatment of cystic fibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 14 May 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:

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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	1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide	Treatment of cystic fibrosis
Bulgarian	1-(2,2-дифлуоро-1,3-бензодиоксол-5-ил)-N-{1-[(2R)-2,3-дихидроксипропил]-6-флуоро-2-(1-хидрокси-2-метилпропан-2-ил)-1H-индол-5-ил}циклопропанкарбоксамид	Лечение на кистозна фиброза
Croatian	1-(2,2-difluoro-1,3-benzodioksol-5-il)-N-{1-[(2R)-2,3-dihidroksipropil]-6-fluoro-2-(1-hidroksi-2-metilpropan-2-il)-1H-indol-5-il}ciklopropankarboksamid	Liječenje cistične fibroze
Czech	1-(2,2-difluoro-1,3-benzodioksol-5-il)-N-{1-[(2R)-2,3-dihidroksipropil]-6-fluoro-2-(1-hidroksi-2-metilpropan-2-il)-1H-indol-5-il}ciklopropankarboksamid	Léčba cystické fibrózy
Danish	1-(2,2-difluor-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluor-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyklopropancarboxamid	Behandling af cystisk fibrose
Dutch	1-(2,2-difluor-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluor-2-(1-hydroxy-2-methylpropaan-2-yl)-1H-indol-5-yl}cyclopropaancarboxamide	Behandeling van cystische fibrose
Estonian	1-(2,2-difluoro-1,3-bensodioksool-5-üül)-N-{1-[(2R)-2,3-dihüdroksüpropüül]-6-fluoro-2-(1-hüdroksü-2-metüülpropaan-2-üül)-1H-indool-5-üül}tsüklopropaankarboksamiid	Tsüstilise fibroosi ravi
Finnish	1-(2,2-difluoro-1,3-bentsodioksoli-5-yyli)-N-{1-[(2R)-2,3-dihydroksipropyyli]-6-fluoro-2-(1-hydroksi-2-metyylipropaani-2-yyli)-1H-indoli-5-yyli}syklopropaanikarboksamidi	Kystisen fibroosin hoito
French	1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-méthylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide	Traitement de la mucoviscidose
German	1-(2,2-Difluor-1,3-Benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluor-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropancarboxamid	Behandlung zystischer Fibrose

[1] At the time of designation

Language	Active ingredient	Indication
Greek	1-(2,2-διφθορο-1,3-βενζοδιοξολ-5-υλο)-N-{1-[(2R)-2,3-διυδροξυπροπυλο)]-6-φθορο-2-(1-υδροξυ-2-μεθυλοπροπαν-2-υλο)-1H-ινδολ-5-υλο}κυκλοπροπανοκαρβοξαμίδιο	Θεραπεία της κυστικής ίνωσης
Hungarian	1-(2,2-difluor-1,3-benzodioxol-5-il)-N-{1-[(2R)-2,3-dihidroxipropil]-6-fluoro-2-(1-hidroxi-2-metilpropán-2-il)-1H-indol-5-il}ciklopropán-karboxamid	Cisztikus fibrózis kezelése
Italian	1-(2,2-difluoro-1,3-benzodiossol-5-il)-N-{1-[(2R)-2,3-diidrossipropil]-6-fluoro-2-(1-idrossi-2-metilpropan-2-il)-1H-indol-5-il}ciclopropancarbossammide	Trattamento della fibrosi cistica
Latvian	1-(2,2-difluor-1,3-benzodioksol-5-il)-N-{1-[(2R)-2,3-dihidroksipropil]-6-fluor-2-(1-hidroksi-2-metilpropān-2-il)-1H-indol-5-il}ciklopropānkarboksamīds	Cistiskās fibrozes ārstēšana
Lithuanian	1-(2,2-difluoro-1,3-benzodioksol-5-il)-N-{1-[(2R)-2,3-dihidroksipropil]-6-fluoro-2-(1-hidroksi-2-metilpropan-2-il)-1H-indol-5-il}ciklopropankarboksamidas	Cistinės fibrozės gydymas
Maltese	1-(2,2-difluoro-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl}cyclopropanecarboxamide	Kura tal-fibrożi ċistiku
Polish	1-(2,2-difluoro-1,3-benzodioksol-5-yl)-*N*-{1-[(2R)-2,3-dihydroksypropylo]-6-fluoro-2-(1-hydroksy-2-metylopropan-2-yl)-1*H*-indol-5-yl}cyklopropanokarboksamid	Leczenie zwłóknienia torbielowatego
Portuguese	1-(2,2-difluoro-1,3-benzodioxol-5-il)-N-{1-[(2R)-2,3-dihidroxipropil]-6-fluoro-2-(1-hidroxi-2-metilpropan-2-il)-1H-indol-5-il}ciclopropanocarboxamida	Tratamento da fibrose quística
Romanian	1-(2,2-difluoro-1,3-benzodioxol-5-il)-N-{1-[(2R)-2,3-dihidroxipropil]-6-fluoro-2-(1-hidroxi-2-metilpropan-2-il)-1H-indol-5-il}ciclopropancarboxamidă	Tratamentul fibrozei chistice
Slovak	1-(2,2-difluór-1,3-benzodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxypropyl]-6-fluór-2-(1-hydroxy-2-metylpropán-2-yl)-1H-indol-5-yl}cyklopropánkarboxamid	Terapia cystickej fibrózy
Slovenian	1-(2,2-difluoro-1,3-benzodioksol-5-il)-N-{1-[(2R)-2,3-dihidroksipropil]-6-fluoro-2-(1-hidroksi-2-metilpropan-2-il)-1H-indol-5-il}ciklopropankarboksamid	Zdravljenje cistične fibroze

Language	Active ingredient	Indication
Spanish	1-(2,2-difluoro-1,3-benzodioxol-5-il)-N-{1-[(2R)-2,3-dihidroxipropil]-6-fluoro-2-(1-hidroxi-2-metilpropano-2-il)-1H-indol-5-il}ciclopropancarboxamida	Tratamiento de la fibrosis quística
Swedish	1-(2,2-difluoro-1,3-bensodioxol-5-yl)-N-{1-[(2R)-2,3-dihydroxipropyl]-6-fluoro-2-(1-hydroxi-2-metylpropan-2-yl)-1H-indol-5-yl}cyklopropankarboxamid	Behandling av cystisk fibros
Norwegian	1-(2,2-difluoro–1,3–benzodioksol-5-yl)-N-{1-[(2R)-2,3-dihydroksypropyl]-6-fluoro-2-(1-hydroksy-2-metylpropan-2-yl)-1H-indol-5-yl}syklopropankarboksamid	Behandling av cystisk fibrose
Icelandic	1-(2,2-díflúóró-1,3-bensódíoxól-5-ýl)-N-{1-[(2R)-2,3-díhýdroxýprópýl]-6-flúóró-2-(1-hýdroxý-2-metýlprópan-2-ýl)-1H-indól-5-ýl}sýklóprópankarboxamíð	Meðferð við slímseigjusjúkdómi