5 March 2013
EMA/COMP/325798/2010 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

3-(6-(1-(2,2-difluorobenzo [d] [1,3] dioxol-5-yl)cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid for the treatment of cystic fibrosis

On 4 August 2010, orphan designation (EU/3/10/761) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for 3-(6-(1-(2,2-difluorobenzo [d] [1,3] dioxol-5-yl)cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid for the treatment of cystic fibrosis.

The sponsorship was transferred to Vertex Pharmaceuticals (U.K.) Limited, United Kingdom, in November 2012.

What is cystic fibrosis?

Cystic fibrosis is a hereditary disease that affects the production of secretions such as mucus in the body. It mainly affects the lungs and the digestive system (gut). Cystic fibrosis is caused by abnormalities in a gene called 'cystic fibrosis transmembrane conductance regulator' (CFTR). The CFTR gene is responsible for the production of the CFTR protein. This protein regulates the production of mucus and digestive juices by acting as a channel to allow the movement of salt and water in and out of cells in the lungs and other tissues.

In patients with cystic fibrosis, there is an overproduction of mucus in the lungs and a reduced production of digestive juices from the pancreas (an organ near the stomach). This leads to long-term infection and inflammation of the lungs and problems with the digestion and absorption of food resulting in poor growth.

Cystic fibrosis is a long-lasting and life-threatening disease because it severely damages the lung tissue, which leads to problems with breathing and results in shortened life expectancy.

What is the estimated number of patients affected by the condition?

At the time of designation, cystic fibrosis affected approximately 1.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 61,000 people*, and is below the threshold for

*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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 506,300,000 (Eurostat 2010).

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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 submission of the application for orphan drug designation, lung infection and inflammation in cystic fibrosis were mainly treated with antibiotics. Other medicines used to treat the lung disease included 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 it works in a different way to existing treatments, and early studies indicate that it might improve the outcome of patients with this condition. 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?

This medicine is expected to work inside the cells that produce secretions and repair the CFTR protein, which is defective in patients with cystic fibrosis. By restoring the normal function of this protein, the medicine is expected to slow down or stop further damage to the lungs and relieve the symptoms of cystic fibrosis.

What is the stage of development of this medicine?

The effects of 3-(6-(1-(2,2-difluorobenzo [d] [1,3] dioxol-5-yl)cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid have been evaluated in experimental models.

At the time of submission of the application for orphan designation, two clinical trials with the medicine in patients with cystic fibrosis had been completed.

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 of America 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 6 May 2010 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	3-(6-(1-(2,2-difluorobenzo [d] [1,3] dioxol-5-yl)cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid	Treatment of cystic fibrosis
Bulgarian	3-(6-(1-(2,2-дифлуоробензо [d] [1,3]диоксол-5-yl)циклопропанкарбоксамидо)-3-метилпиридин-2-yl)бензоева киселина	Лечение на кистозна фиброза
Czech	3-(6-(1-(2,2-difluorobenzo [d] [1,3]dioxol-5-yl)cyklopropankarboxamido)-3-methylpyridin-2-yl)benzoová kyselina	Léčba cystické fibrózy
Danish	3-(6-(1-(2,2-difluorbenzo [d] [1,3]dioxol-5-yl)cyclopropancarboxamido)-3-methylpyridin-2-yl) benzoesyre	Behandling af cystisk fibrose
Dutch	3-(6-(1-(2,2-difluorbenzo [d] [1,3]dioxol-5-yl)cyclopropaancarboxamido)-3-methylpyridin-2-yl) benzoëzuur	Behandeling van cystische fibrose
Estonian	3-(6-(1-(2,2-difluorobenso [d] [1,3]dioksool-5-üül)tsüklopropaankarboksamido)-3-metüülpüridiin-2-üül) bensoehape	Tsüstilise fibroosi ravi
Finnish	3-(6-(1-(2,2-difluoribentso [d] [1,3]dioksol-5-yyli)syklopropaanikarboksamido)-3-metyylipyridin-2-yyli) bentsoehappo	Kystisen fibroosin hoito
French	3-(6-(1-(2,2-difluorobenzo [d] [1,3]dioxol-5-yl)cyclopropanecarboxamido)-3-méthylpyridine-2-yl) acide benzoïque	Traitement de la mucoviscidose
German	3-(6-(1-(2,2-difluorbenzo [d] [1,3]dioxol-5-yl)cyclopropancarboxamido)-3-Methylpyridin-2-yl) Benzoesäure	Behandlung zystischer Fibrose
Greek	3-(6-(1-(2,2-διχλωροβενζο [d] [1,3]διοξολ-5-yl)κυκλοπροπανοκαρβοξαμιδο)-3-μεθυλοπυριδίνη-2-yl)βενζοϊκό οξύ	Θεραπεία της κυστικής ίνωσης
Hungarian	3-(6-(1-(2,2-difluórbenzo [d] [1,3]dioxol-5-il)ciklopropánkarboxamid)-3-metilpiridin-2-il)benzoésav	Cisztikus fibrózis kezelése
Italian	Acido 3-(6-(1-(2,2-difluorobenzo [d] [1,3]dioxol-5-il) ciclopropancarbossammido)-3- metilpiridin-2-il) benzoico	Trattamento della fibrosi cistica
Latvian	3-(6-(1-(2,2-difluorbenzo [d] [1,3]dioksol-5-il)ciklopropānkarboksamido)-3-metilpiridīn -2-il) benzoskābe	Cistiskās fibrozes ārstēšana
Lithuanian	3-(6-(1-(2,2-difluorobenzo [d] [1,3] dioksol-5-il)ciklopropanekarboksamido)-3-metilpiridin-2-il) benzenkarboksirūgštis	Cistinės fibrozės gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	3-(6-(1-(2,2-difluorobenzo [d] [1,3] dioxol-5-yl)cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid	Kura tal-fibroża ċistiku
Polish	3-(6-(1-(2,2-difluorobenzo [d] [1,3]dioksol-5-yl)cyklopropanokarboksamido)-3-metylopirydyn-2-yl)kwas benzoesowy	Leczenie zwłóknienia torbielowatego
Portuguese	Ácido 3-(6-(1-(2,2-diflúorbenzo [d] [1,3]dioxol-5-il)ciclopropanocarboxamido)-3-metilpiridin-2-il) benzóico	Tratamento da fibrose quística
Romanian	Acid 3-(6-(1-(2,2-difluorobenzo [d] [1,3]dioxol-5-il)ciclopropan carboxamido)-3-metilpiridin-2-il) benzoic	Tratamentul fibrozei chistice
Slovak	3-(6-(1-(2,2-difluórobenzo [d] [1,3]dioxol-5-yl)cyklopropánkarboxamido)-3-methylpyridín-2-yl)benzoová kyselina	Terapia cystickej fibrózy
Slovenian	3-(6-(1-(2,2-difluorobenzo [d] [1,3]dioksol-5-il)ciklopropankarboksamido)-3-metilpiridin-2-il)benzojska kislina	Zdravljenje cistične fibroze
Spanish	Ácido 3-(6-(1-(2,2-difluorobenzo [d] [1,3]dioxol-5-yl)ciclopropanocarboxamido)-3-metilpiridin-2-il) benzoico	Tratamiento de la fibrosis quística
Swedish	3-(6-(1-(2,2-difluorbenzo [d] [1,3]dioksol-5-yl)cyklopropankarboxamido)-3-metylpyridin-2-yl) bensoesyra	Behandling av cystisk fibros
Norwegian	3-(6-(1-(2,2-difluorbenzo [d] [1,3]dioksol-5-yl)syklopropankarboxamido)-3-metylpyridin-2-yl) benzosyre	Behandling av cystisk fibrose
Icelandic	3-(6-(1-(2,2-díflúorbensó [d] [1,3]díoxól-5-ýl)cýklóproópankarboxamíð-)-3-methýlpýridín-2-ýl) bensónsýra	Meðferð við slímseigjusjúkdómi