6 March 2015
EMA/COMP/123054/2005 Rev.5
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid for the treatment of cystic fibrosis

First publication	29 June 2005
Rev.1: text correction	1 July 2005
Rev.2: sponsor's contact details updated	13 October 2005
Rev.3: transfer of sponsorship	3 July 2007
Rev.4: transfer of sponsorship	5 June 2013
Rev.5: sponsor's change of address	6 March 2015
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.	

Withdrawn

On 27 May 2005, orphan designation (EU/3/05/277) was granted by the European Commission to The Matthews consultancy Ltd, UK, for 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid for the treatment of cystic fibrosis.

The sponsorship was transferred to Voisin Consulting S.A.R.L., France, in May 2007 and subsequently to PTC Therapeutics Limited, United Kingdom, in May 2013.

What is cystic fibrosis?

Cystic fibrosis is a genetic disease. Genes located on structures (the so-called chromosomes) carry the genetic information that determines the characteristics of each individual. In humans, each cell has 23 pairs of chromosomes. For each pair one chromosome is inherited from the mother, and the other from the father. Cystic fibrosis is caused by abnormalities of a specific gene, called CFTR, carried by the seventh pair of chromosomes. Cystic fibrosis appears only when the CFTR gene is abnormal on both chromosomes of the seventh pair. The CFTR gene is responsible for the production of a protein that regulates the outflow of water and salts (like chloride) from cells that cover internal and external surfaces of the body, the so-called epithelial cells. The defective transport of water and salts, due to the lack of the regulatory protein, results in the thickening of the secretions (mucous) in several organs (e.g. lungs, pancreas). This leads to reduced functioning, chronic infection of the lungs and

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chronic inflammation (a body response to the injury caused to the tissue). In the long run, these events can induce damage to the lung tissue and the disease can become life threatening.

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

At the time of designation, cystic fibrosis affected approximately 1.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 61,000 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 submission of the application for the orphan drug designation lung infection and inflammation in cystic fibrosis were treated mainly with antibiotics. These can be taken in a number of ways such as through the mouth, through a vein or they can be inhaled as a fine mist of particles. Associated treatments included daily exercise and physical therapies and several other types of medications such as pancreatic enzymes and food supplements. Bronchodilators are medications that can enlarge the lumen of the airways. Mucolytics help to dissolve the secretions. Still other medications were used to fight the inflammation. 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid might be of potential significant benefit in the treatment of cystic fibrosis, because it is expected to act differently from existing treatments, and because it can be taken orally. This assumption remains to be proven at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid is a medicinal product which in theory might overcome a specific type of abnormality present in the CFTR gene of some cistic fibrosis patients. Thus, it could enable the production of the protein that regulates the outflow of water and salts (like chloride) from cells.

What is the stage of development of this medicine?

The evaluation of the effects of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid in experimental models is ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with cystic fibrosis were initiated.

3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid was not marketed anywhere worldwide for cystic fibrosis, at the time of submission.

Orphan designation of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid was granted in the United States for use in the treatment of cystic fibrosis resulting fron a nonsense (premature stopcodon) mutation in the cystic fibrosis transmembrane conductance regulatory gene.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 April 2005 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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 466,600,000 (Eurostat 2005).

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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.

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Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Treatment of cystic fibrosis
Bulgarian	(3-[5-(2-флуоро-фенил)-[1,2,4]оксадиазол-3-ил]-бензоена киселина	Лечение на кистозна фиброза
Czech	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Léčba cystické fibrózy
Danish	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Behandling af cystisk fibrose
Dutch	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic zuur	Behandeling van cystische fibrose
Estonian	(3-[5-(2-floorfenüül-phenyl)-[1,2,4]oksadiasool-3-üül]-benzoiinhape	Tsüstilise fibroosi ravi
Finnish	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-bentsoehappo	Kystisen fibroosin hoito
French	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Traitement de la mucoviscidose
German	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Behandlung von zystischer Fibrose
Greek	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Θεραπεία της κυστικής ίνωσης
Hungarian	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoesav	Cisztikus fibrózis kezelése
Italian	(3-[5-(2-fluoro-fenil)-[1,2,4]ossadiazolo-3-il]- acido benzoico	Trattamento della fibrosi cistica
Latvian	(3-[5-(2-fluoro-fenil)-[1,2,4]oksadiazol-3-il]-benzoskābe	Cistiskās fibrozes ārstēšana
Lithuanian	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Cistinės fibrozės gydymas
Maltese	3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Kura tal-fibrożi ċistiku
Polish	kwas(3-[5-(2-fluoro-fenylo)-[1,2,4]oksadiazol-3-ylo]-benzoesowy	Leczenie zwłóknienia torbielowatego
Portuguese	Acido (3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]benzoico	Tratamento da fibrose quística
Romanian	(3-[5-(2-fluor-fenil)-[1,2,4]oxadiazol-3-il]-acid benzoic	Tratamentul fibrozei chistice
Slovak	(3-[5-(2-fluoro-fenyl)-[1,2,4]oxadiazol-3-yl]-benzoová kyselina	Terapia cystickej fibrózy

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Slovenian	(3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoic acid	Zdravljenje cistične fibroze
Spanish	Àcido (3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazole-3-yl]-benzoico	Tratamiento de la fibrosis quística
Swedish	(3-[5-(2-fluoro-fenyl)-[1,2,4]oxadiasol-3-yl]-bensoesyra	Behandling av cystisk fibros
Norwegian	(3-[5-(2-fluoro-fenyl)-[1,2,4]oksadiazol-3-yl]-benzosyre	Behandling av cystisk fibrose
Icelandic	(3-[5-(2-flúoró-fenýl)-[1,2,4]oxadíazól-3-yl]-benzósýra	Meðferð við slímseigjusjúkdómi

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