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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Antisense oligonucleotide targeting the F508delta mutation of CFTR for the treatment of cystic fibrosis

On 7 October 2013, orphan designation (EU/3/13/1195) was granted by the European Commission to ProQR Therapeutics BV, The Netherlands, for antisense oligonucleotide targeting the F508delta mutation of CFTR 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 abnormalities 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 this 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).

*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 512,200,000 (Eurostat 2013).

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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 correct the defect of the CFTR protein in a subgroup of patients with cystic fibrosis with 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 based on data from laboratory studies suggesting that it may lead to the production of a normal CFTR protein in patients with the F508delta mutation in their CFTR genes. 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 an 'anti-sense oligonucleotide', a very short piece of synthesized RNA (a type of genetic material involved in the production of proteins). This anti-sense RNA specifically attaches to the 'sense' RNA with the F508delta mutation which is responsible for the production of the abnormal CFTR protein in cystic fibrosis. As a result, the anti-sense RNA is expected to induce the repair of the genetic RNA abnormality, leading to the production of a fully functional CFTR protein. When given by inhalation, 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 the medicinal product have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicinal product in patients with cystic fibrosis had been started.

At the time of submission, the medicinal product 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 4 September 2013 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	Antisense oligonucleotide targeting the F508delta mutation of CFTR	Treatment of cystic fibrosis
Bulgarian	Антисенс олигонуклеотиди с таргет делта-F508 мутации в CFTR	Лечение на кистозна фиброза
Czech	Antisense oligonukleotid cílený na mutaci F508delta CFTR	Léčba cystické fibrózy
Croatian	Protusmisleni oligonukleotid koji cilja F508delta mutaciju u CFTR	Liječenje cistične fibroze
Danish	Antisense oligonukleotid, rettet mod F508delta mutationen i CFTR	Behandling af cystisk fibrose
Dutch	Antisense oligonucleotide gericht tegen de F508delta mutatie in CFTR	Behandeling van cystische fibrose
Estonian	CFTR-geeni F508delta mutatsiooni vastu suunatud antisense-oligonukleotiid	Tsüstilise fibroosi ravi
Finnish	Antisense-oligonukleotidi, jonka kohteena on CFTR:n F508delta-mutaatio	Kystisen fibroosin hoito
French	Oligonucléotides antisens ciblant la mutation Delta F508 du CFTR	Traitement de la mucoviscidose
German	Antisense-Oligonukleotide, die auf die F508del-Mutation des CFTR-Gens abzielen.	Behandlung zystischer Fibrose
Greek	Αντιπληροφοριακό ολιγονουκλεοτιδίο με στόχο την μετάλλαξη F508delta της CFTR	Θεραπεία της κυστικής ίνωσης
Hungarian	CFTR gén F508delta mutációját célzó antiszensz oligonukleotid	Cisztikus fibrózis kezelése
Italian	Oligonucleotide antisenso che si lega alla mutazione F508delta del CFTR	Trattamento della fibrosi cistica
Latvian	Antisenses oligonukleotīds, kas darbojas uz cistiskās fibrozes transmembrānu vadītspējas regulatora (*CFTR*) F508-delta mutāciju	Cistiskās fibrozes ārstēšana
Lithuanian	Priešprasminis oligonukleotidas nukreiptas į *CFTR* geno F508 delta mutaciją	Cistinės fibrozės gydymas
Maltese	Oligonukleotide antisens immirat għall-mutazzjoni F508delta ta' CFTR	Kura tal-fibrożi ċistiku
Polish	Oligonukleotyd antysensowny skierowany w mutację F508delta CFTR	Leczenie zwłóknienia torbielowatego
Portuguese	Oligonucleotídeo antisense direcionado para a mutação delta F508 no gene CFTR	Tratamento da fibrose quística
Romanian	Oligonucleotidă antisens care vizează mutaţia F508delta a CFTR	Tratamentul fibrozei chistice
Slovak	Protismerný oligonukleotid cielený na Delta F508 mutáciu CFTR	Terapia cystickej fibrózy

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Protismerni oligonukleotid, usmerjen proti mutaciji delta F508 CFTR gena	Zdravljenje cistične fibroze
Spanish	Oligonucleótido antisentido dirigido a la mutación delta F508 del CFTR	Tratamiento de la fibrosis quística
Swedish	Antisense-oligonukleotid riktad mot F508delta-mutationen i CFTR	Behandling av cystisk fibros
Norwegian	Antisense-oligonukleotid rettet mot F508delta mutasjoner i CFTR	Behandling av cystisk fibrose
Icelandic	Andþáttar-ólígónúkleótíð sem virkar á F508 delta stökkbreytingu í CFTR	Meðferð við slímseigjusjúkdómi