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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene complexed with a non-viral, cationic lipid based gene transfer agent for the treatment of cystic fibrosis

On 4 June 2014, orphan designation (EU/03/14/1277) was granted by the European Commission to Imperial Innovations Limited, United Kingdom, for plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene complexed with a non-viral, cationic lipid based gene transfer agent 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 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).

[*]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 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 this medicine might be of significant benefit for patients with cystic fibrosis because early studies suggest that it may lead to the production of a normal CFTR protein. 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 contains the gene (DNA) responsible for making the CFTR protein, which is combined with a lipid (fat) mixture to make a complex that can enter the cell. When given to the patient, the gene is expected to then allow these cells to produce properly functioning CFTR, resulting in normal regulation and production of mucus and digestive juices. This is expected to prevent the lung infections and the problems with absorption of nutrients characteristic of cystic fibrosis.

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 April 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	Plasmid DNA encoding the human cystic fibrosis transmembrane conductance regulator gene complexed with a non-viral, cationic lipid based gene transfer agent	Treatment of cystic fibrosis
Bulgarian	Плазмидна ДНК, кодираща човешкия ген за белтъка трансмембранен регулатор на проводимостта при кистозна фиброза в комплекс с невирусен, катионен липид-базиран ген-трансферен агент	Лечение на кистозна фиброза
Croatian	Plazmidna DNK koja kodira ljudski gen za transmembranski regulator provodljivosti u cističnoj fibrozi u kompleksu s nevirusnim, kationskim agensom za prijenos gena na bazi lipida	Liječenje cistične fibroze
Czech	Plasmidová DNA kódující lidský gen pro transmembránový regulátor vodivosti u cystické fibrózy v komplexu s nevirovým přípravkem pro genový přenos na bázi kationtových lipidů	Léčba cystické fibrózy
Danish	Plasmid DNA, der koder for det humane CFTR-gen som har dannet kompleks med et non-viralt, kationisk lipidbaseret middel til genoverførsel	Behandling af cystisk fibrose
Dutch	Plasmide DNA dat codeert voor het humaan cystic fibrosis transmembrane conductance regulator gen in complex met een niet-viraal agens voor gentransfer op basis van kationische lipiden	Behandeling van cystische fibrose
Estonian	Inimese tsüstilise fibroosi transmembraanse juhtivuse regulaatori geeni kodeeriv plasmiidi DNA kompleksis mitteviirusliku katioonsete lipiidide põhise geeniülekande ainega	Tsüstilise fibroosi ravi
Finnish	Plasmidi-DNA, joka koodittaa ihmisen kystisen fibroosin transmembraanista konduktanssin säädingeeniä kompleksissa ei-virusperäisen, kationisen lipidipohjaisen geenin siirtoaineen kanssa	Kystisen fibroosin hoito
French	ADN plasmidique codant pour le gène CFTR humain complexé à un agent de transfert de gène non viral composé d'un lipide cationique	Traitement de la mucoviscidose
German	Für das humane CRTR-Gen (Regulator der transmembranen Leitfähigkeit bei cystischer Fibrose) kodierende Plasmid-DNA, komplexiert mit einem nicht-viralen, kationischen lipidbasierten Gentransfer-Agens	Behandlung zystischer Fibrose

[1] At the time of designation

Language	Active ingredient	Indication
Greek	Πλασμιδιακό DNA που κωδικοποιεί το γονίδιο του ρυθμιστή της διαμεμβρανικής αγωγιμότητας της κυστικής ίνωσης συμπλοκοποιημένο με έναν μη ιογενή, βασισμένο σε κατιονικά λιπίδια, παράγοντα γονιδιακής μεταφοράς	Θεραπεία της κυστικής ίνωσης
Hungarian	Humán cisztás fibrózis transzmembrán konduktancia regulátor gént kódoló plazmid DNS és egy nem virális, kationos lipid-bázisú géntranszfer ágens komplexe	Cisztikus fibrózis kezelése
Italian	DNA plasmidico codificante per il gene CFTR umano, complessato con un vettore non virale basato su lipidi cationici	Trattamento della fibrosi cistica
Latvian	Cilvēka cistiskās fibrozes transmembrānu vadītspējas regulatora gēnu kodējoša plazmīdu DNS kompleksā ar nevīrusu izcelsmes gēnu pārneses līdzekli uz katjonisko lipīdu bāzes	Cistiskās fibrozes ārstēšana
Lithuanian	Plazmidžių DNR, koduojanti žmogaus cistinės fibrozės transmembraninio laidumo reguliatoriaus geną, komplekse su nevirusine, katijoniniais lipidais paremta genų perdavimo medžiaga	Cistinės fibrozės gydymas
Maltese	Plasmid ta' DNA li jikkodifika il-ġene tar-regolatur tal-konduttanza tat-transmembrana tal-fibrożi ċistiku uman magħqud m'aġent li jittrasferixxi l-ġeni bbażat fuq lipidi katjoniċi, mhux virali	Kura tal-fibrożi ċistiku
Polish	Plazmidowy DNA kodujący ludzki gen błonowego regulatora przewodnictwa swoisty dla mukowiscydozy w kompleksie z niewirusowym nośnikiem genów na bazie kationowych lipidów	Leczenie zwłóknienia torbielowatego
Portuguese	ADN plasmídico codificando o gene humano regulador da condutância transmembrana na fibrose cística complexado com um agente de transferência genética não viral, com base lipídica catiónica	Tratamento da fibrose quística
Romanian	ADN plasmidic codificator al genei umane care reglează conducerea transmembranară în fibroza chistică, în combinaţie cu un agent de transfer de genă neviral pe bază de lipide cationice	Tratamentul fibrozei chistice
Slovak	Plazmidová DNA kódujúca ľudský gén transmembránového regulátoru vodivosti pri cystickej fibróze v komplexe s nevírusovým elementom na prenos génu s kationickým lipidovým základom.	Terapia cystickej fibrózy
Slovenian	Plazmidna DNK za kodiranje gena za humani cistično fibrozni transmembranski regulator prevodnosti, kompleksirana z nevirusnim agensom za prenos genov na osnovi kationskih lipidov	Zdravljenje cistične fibroze

Language	Active ingredient	Indication
Spanish	ADN plasmídico codificante para el gen humano regulador de la conductancia transmembrana de la fibrosis quística en forma de complejo con un agente de transferencia génica no viral basado en lípidos catiónicos	Tratamiento de la fibrosis quística
Swedish	Plasmid-DNA som kodar för den mänskliga "cystic fibrosis transmembrane conductance regulator"-genen i komplex med ett icke-viralt, katjoniskt lipidbaserat genöverföringsmedel	Behandling av cystisk fibros
Norwegian	Plasmid DNA som koder for det humane cystisk fibrose-transmembrankonduktansregulatorgenet sammen med et ikke-viralt, kationisk lipidbasert genoverføringsmiddel	Behandling av cystisk fibrose
Icelandic	Plasmíð-DNA sem kóðar fyrir manna geni fyrir klóríðjónagöng slímseigjusjúkdóms tengt við katjónagenaferju sem grundvallast á lípíðum en er ekki af veiruuppruna	Meðferð við slímseigjusjúkdómi