6 May 2019
EMADOC-628903358-642

# Public summary of opinion on orphan designation

## Codon-optimised human cystic fibrosis transmembrane conductance regulator messenger ribonucleic acid complexed with lipid-based nanoparticles for the treatment of cystic fibrosis



On 1 April 2019, orphan designation (EU/3/19/2150) was granted by the European Commission to Real Regulatory Limited, Ireland, for codon-optimised human cystic fibrosis transmembrane conductance regulator messenger ribonucleic acid complexed with lipid-based nanoparticles (also known as MRT5005) for the treatment of cystic fibrosis.

### What is cystic fibrosis?

Cystic fibrosis is an inherited disease that affects the secretion of fluids from cells in the lungs and from the glands in the gut and pancreas. In cystic fibrosis, these fluids become thick, blocking the airways in the lungs and the flow of digestive juices in the gut and pancreas. This leads to inflammation and long-term infection of the lungs because of the build-up of thick mucus, and to poor growth and nutrition because of problems with the digestion and absorption of food.

Cystic fibrosis is caused by changes (mutations) 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 less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 52,000 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 518,400,000 (Eurostat 2019).

**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**Address for visits and deliveries** Refer to www.ema.europa.eu/how-to-find-us
**Send us a question** Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

## What treatments are available?

At the time of designation, Kalydeco (ivacaftor), Orkambi (ivacaftor and lumacaftor) and Symkevi (tezacaftor and ivacaftor) were authorised in the EU to treat patients with cystic fibrosis who have certain mutations in the gene for CFTR. Lung infection in cystic fibrosis was mainly treated with antibiotics. Other medicines used to treat the lung disease included anti-inflammatory medicines, bronchodilators (medicines that help to open up the airways in the lungs) and mucolytics (medicines that help break down 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 have physiotherapy.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with cystic fibrosis. Laboratory studies showed that the medicine may improve the movement of chloride particles across the cell membrane and thus help to regulate the production of fluids from cells. In addition, the medicine could be used in patients in whom the CFTR protein is completely lacking, for whom no treatment is authorised.

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 genetic material (mRNA) responsible for making the CFTR protein, which is enclosed in tiny fatty particles that allow the genetic material to enter into cells. When the medicine is given to the patient by inhalation, the cells in the lungs are expected to produce a functioning CFTR, resulting in normal regulation and production of mucus. This is expected to prevent the lung infections 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, no clinical trials with the medicine in patients with cystic fibrosis had been started.

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 February 2019 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:

Contact details of the current sponsor for this orphan designation can be found on the EMA website.

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 | Codon-optimised human cystic fibrosis transmembrane conductance regulator messenger ribonucleic acid complexed with lipid-based nanoparticles | Treatment of cystic fibrosis |
| Bulgarian | Кодон-оптимизирана човешка информационна рибонуклеинова киселина, носеща информация за синтеза на трансмембранния регулатор на проводимостта при кистозна фиброза, с комплекси наночастици, базирани на липиди | Лечение на кистозна фиброза |
| Croatian | Glasnička ribonukleinska kiselina s optimiziranim kodonom za ljudski transmembranski regulator provodljivosti u cističnoj fibrozi u kompleksu s nanočesticama na bazi lipida | Liječenje cistične fibroze |
| Czech | Humánní mediátorová ribonukleová kyselina pro transmembránový regulátor vodivosti u cystické fibrózy s optimalizovaným kodonem v komplexu s nanočásticemi na bázi lipidů | Léčba cystické fibrózy |
| Danish | Kodonoptimeret human cystisk fibrose-transmembrankonduktansregulator-messenger-ribonukleinsyre kompleksbundet med lipidbaserede nanopartikler | Behandling af cystisk fibrose |
| Dutch | Codongeoptimaliseerd 'messenger'-ribonucleïnezuur van menselijke cystische fibrose transmembraan geleidingsregulator gecomplexeerd met nanopartikels op basis van lipiden | Behandeling van cystische fibrose |
| Estonian | Lipiidipõhiste nanoosakestega kompleksi moodustanud koodonoptimeeritud inimese tsüstilise fibroosi transmembraanse juhtivuse regulaatori informatsiooni-ribonukleiinhape | Tsüstilise fibroosi ravi |
| Finnish | Kodonioptimoitu, lipidinanopartikkeleilla kompleksoitu ihmisperäinen kystisen fibroosin transmembraanisen konduktansin säätelijä mRNA | Kystisen fibroosin hoito |
| French | Complexe d’acide ribonucléique messager codant pour la protéine cystic fibrosis transmembrane conductance regulator humaine avec optimisation des codons et de nanoparticules lipidiques | Traitement de la mucoviscidose |
| German | Codon-optimierte humane Boten-Ribonukleinsäure komplexiert mit lipidbasierten Nanopartikeln gegen cystic fibrosis transmembrane conductance | Behandlung zystischer Fibrose |
| Greek | Βελτιστοποιημένων κωδικονίων ανθρώπινο αγγελιοφόρο ριβονουκλεϊκό οξύ του ρυθμιστή της διαμεμβρανικής αγωγιμότητας της κυστικής ίνωσης συμπλοκοποιημένο με λιπιδικά νανοσωματίδια | Θεραπεία της κυστικής ίνωσης |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Hungarian | Lipid alapú nanorészecskékkel komplexált, kodonoptimalizált humán cysticus fibrosis transzmembrán konduktancia-regulátor messenger ribonukleinsav | Cisztikus fibrózis kezelése |
| Italian | Acido ribonucleico messaggero, con codoni ottimizzati, codificante il regolatore della conduttanza transmembrana della fibrosi cistica umano, complessato con nanoparticelle a base lipidica | Trattamento della fibrosi cistica |
| Latvian | Cilvēka cistiskās fibrozes transmembrānas vadītspējas regulatora matricas ribonukleīnskābe ar optimizētu kodonu kompleksā ar lipīdu bāzes nanodaļiņām | Cistiskās fibrozes ārstēšana |
| Lithuanian | Žmogaus cistinės fibrozės transmembraninio laidumo reguliatoriaus informacinė ribonukleino rūgštis optimizuota kodonu, komplekse su lipidų pagrindo nanodalelėmis | Cistinės fibrozės gydymas |
| Maltese | Regolatur tal-konduttanza transmembranja tal-fibrożi ċistika uman ottimizzat b'kodon b'messaġġier kumpless ta' aċidu ribonuklejku b'nanopartiċelli bbażati fuq il-lipidi | Kura tal-fibrożi ċistiku |
| Polish | Matrycowy kwas rybonukleinowy ze zoptymalizowanym kodonem kodujący ludzki mukowiscydozowy błonowy regulator przewodnictwa skompleksowany z nanocząstkami na bazie lipidów | Leczenie zwłóknienia torbielowatego |
| Portuguese | Codão otimizado composto por um complexo de ácido ribonucleico mensageiro com nanopartículas à base de lípidos que codifica o regulador de condutância transmembrana na fibrose cística humana | Tratamento da fibrose quística |
| Romanian | Complex de acid ribonucleic mesager cu codoni optimizaţi ce codifică reglatorului uman al conductanței transmembranare în fibroza chistică, şi nanoparticule pe bază lipidică | Tratamentul fibrozei chistice |
| Slovak | Ľudská mediátorová ribonukleová kyselina pre transmembránový regulátor vodivosti u cystickej fibrózys optimalizovaným kodónom v komplexe s nanočasticami na báze lipidov | Terapia cystickej fibrózy |
| Slovenian | Informacijska ribonukleinska kislina z optimiziranim kodonom za regulator transmembranske prevodnosti pri cistični fibrozi pri človeku, združena z nanodelci na podlagi lipidov | Zdravljenje cistične fibroze |
| Spanish | Complejo formado por ácido ribonucleico mensajero con codones optimizados para el regulador de la conductancia transmembrana de la fibrosis quística humano y nanopartículas lipídicas | Tratamiento de la fibrosis quística |
| Swedish | Kodonoptimerad human cystic fibrosis transmembran konductans-regulator-budbärarribonukleinsyra sammansatt med lipidbaserade nanopartiklar | Behandling av cystisk fibros |

| Language | Active ingredient | Indication |
|---|---|---|
| Norwegian | Kodonoptimalisert human cystisk fibrose transmembran konduktansregulator budbringer ribonukleinsyre i kompleks med lipidbaserte nanopartikler | Behandling av cystisk fibrose |
| Icelandic | Táknahámörkuð miðlandi ríbósakjarnsýra manna, sem stýrir leiðni himnupróteina í slímseigjusjúkdómi, fléttuð með nanóögnum með lípíðgrunni | Meðferð við slímseigjusjúkdómi |