31 March 2014
EMA/COMP/26019/2014
Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dione for the treatment of cystic fibrosis

On 19 February 2014, orphan designation (EU/3/14/1239) was granted by the European Commission to Synovo GmbH, Germany, for 11-(4-dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dione 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. 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 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 in experimental models show that it might reduce the inflammation seen in patients with this condition. As a result, the medicine may improve the outcome of cystic fibrosis patients when used in combination with existing treatments. These assumptions 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 belongs to a class of substances called 'macrolides', but does not have antibacterial activity. It is expected to work by reducing the activity of substances in the body involved in the inflammation process, and thereby reducing the inflammation seen in patients with 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 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 January 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 | 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dione | Treatment of cystic fibrosis |
| Bulgarian | 11-(4-диметиламино-3-хидрокси-6-метил-тетрахидро-пиран-2-илокси)-2-етил-3,4,10-трихидрокси-3,5,6,8,10,12,14-хептаметил-1-окса-6-аза-циклопентадекан-13,15-дион | Лечение на кистозна фиброза |
| Czech | 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dion | Léčba cystické fibrózy |
| Croatian | 11-(4-dimetilamino-3-hidroksi-6-metil-tetrahidro-piran-2-iloksi)-2-etil-3,4,10-trihidroksi-3,5,6,8,10,12,14-heptametil-1-oksa-6-aza-ciklopentadekan-13,15-dion | Liječenje cistične fibroze |
| Danish | 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecan-13,15-dion | Behandling af cystisk fibrose |
| Dutch | 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dione | Behandeling van cystische fibrose |
| Estonian | 11-(4-dimetüülamino-3-hüdroksü-6-metüül-tetrahüdro-püraan-2-üüloksü)-2-ettüül-3,4,10-trihüdroksü-3,5,6,8,10,12,14-heptametüül-1-oksa-6-aza-tsüklopentadekaan-13,15-dioon | Tsüstilise fibroosi ravi |
| Finnish | 11-(4-dimetyyliamino-3-hydroksi-6-metyyli-tetrahydropyraani-2-yloksi)-2-etyyli-3,4,10-trihydroksi-3,5,6,8,10,12,14-heptametyyli-1-oksa-6-atsa-syklopentadekaani-13,15-dioni | Kystisen fibroosin hoito |
| French | 11-(4-Diméthylamino-3-hydroxy-6-méthyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptaméthyl-1-oxa-6-aza-cyclopentadécan-13,15-dione | Traitement de la mucoviscidose |
| German | 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dione | Behandlung zystischer Fibrose |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Greek | 11-(4-Διμεθυλαμινο-3-υδροξυ-6-μεθυλ-τραυδροπυρανο-2-υλοξυ)-2-αιθυλ-3,4,10-τριυδροξυ-3,5,6,8,10,12,14-επταμεθυλ-1-οξα-6-αζα-κυκλοπενταδεκανο-13,15-διόνη | Θεραπεία της κυστικής ίνωσης |
| Hungarian | 11-(4-dimetilamino-3-hidroxi-6-metil-tetrahidro-piran-2-iloxi)-2-etil-3,4,10-trihidroxi-3,5,6,8,10,12,14-heptametil-1-oxa-6-aza-ciklopentadekán-13,15-dion | Cisztikus fibrózis kezelése |
| Italian | 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dione | Trattamento della fibrosi cistica |
| Latvian | 11-(4-dimetilamino-3-hidroksi-6-metil-tetrahidro-pirān-2-iloksi)-2-etil-3,4,10-trihidroksi-3,5,6,8,10,12,14-heptametil-1-oksa-6-aza-ciklopentadekāna-13,15-dions | Cistiskās fibrozes ārstēšana |
| Lithuanian | 11-(4-imetilamino-3-hidroksi-6-metil-tetrahidro-piran-2-iloksi)-2-etil-3,4,10-trihidroksi-3,5,6,8,10,12,14-heptametil-1-oksa-6-aza-ciklopentadekano-13,15-dionas | Cistinės fibrozės gydymas |
| Maltese | 11-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecane-13,15-dione | Kura tal-fibrożi ċistiku |
| Polish | 11-(4-dimetyloamino-3-hydroksy-6-metylo-tetrahydro-piran-2-yloksy)-2-etylo-3,4,10-trihydroksy-3,5,6,8,10,12,14-heptametylo-1-oksa-6-azacyklopentadekan-13,15-dion | Leczenie zwłóknienia torbielowatego |
| Portuguese | 11-(4-Dimetilamino-3-hidroxi-6-metil-tetrahidro-piran-2-iloxyi)-2-etil-3,4,10-trihidroxi-3,5,6,8,10,12,14-heptametil-1-oxa-6-aza-ciclopentadecano-13,15-dione | Tratamento da fibrose quística |
| Romanian | 11-(4-Dimetilamino-3-hidroxi-6-metil-tetrahidro-piran-2-iloxi)-2-etil-3,4,10-trihidroxi-3,5,6,8,10,12,14-heptametil-1-oxa-6-aza-ciclopentadecan-13,15-dionă | Tratamentul fibrozei chistice |
| Slovak | 11-(4-dimetylamino-3-hydroxy-6-metyl-tetrahydro-pyrán-2-yloxy)-2-etyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptametyl-1-oxa-6-aza-cyclopentadekán-13,15-dión | Terapia cystickej fibrózy |
| Slovenian | 11-(4-dimetilamino-3-hidroksi-6-metil-tetrahidro-piran-2-iloksi)-2-etil -3,4,10-trihidroksi-3,5,6,8,10,12,14-heptametil-1-oksa-6-aza-ciclopentadekan-13,15-dione | Zdravljenje cistične fibroze |

| Language | Active ingredient | Indication |
|---|---|---|
| Spanish | 11-(4-Dimetilamino-3-hidroxi-6-metil-tetrahidro-piran-2-iloxyi)-2-etil-3,4,10-trihidroxi-3,5,6,8,10,12,14-heptametil-1-oxa-6-aza-ciclopentadecano-13,15-dione | Tratamiento de la fibrosis quística |
| Swedish | 11-(4-Dimetylamino-3-hydroxy-6-metyl-tetrahydro-pyran-2-yloxy)-2-etyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptametyl-1-oxa-6-aza-cyklopentadecan-13,15-dion | Behandling av cystisk fibros |
| Norwegian | 11-(4-Dimetylamino-3-hydroksy-6-metyl-tetrahydro-pyran-2-yloksy)-2-etyl-3,4,10-trihydroksy-3,5,6,8,10,12,14-heptametyl-1-oksa-6-aza-syklopentadekan-13,15-dion | Behandling av cystisk fibrose |
| Icelandic | 11-(4-Dímetýlamínó-3-hýdroxý-6-metýl-tetrahýdró-pýran-2-ýloxý)-2-etýl-3,4,10-tríhýdroxý-3,5,6,8,10,12,14-heptametýl-1-oxa-6-aza-cýklópentadekan-13,15-díón | Meðferð við slímseigjusjúkdómi |