European Medicines Agency
*Pre-authorisation Evaluation of Medicines for Human Use*

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# Committee for Orphan Medicinal Products

## Public summary of positive opinion for orphan designation of ciprofloxacin (liposomal) for the treatment of cystic fibrosis

On 24 July 2009, orphan designation (EU/3/09/652) was granted by the European Commission to Interface International Consultancy Ltd, United Kingdom, for ciprofloxacin (liposomal) for the treatment of cystic fibrosis.

**What is cystic fibrosis?**
Cystic fibrosis is a hereditary disease that affects the production of secretions such as mucus in the body. It mainly affects the lungs and the digestive system (gut). Cystic fibrosis is caused by abnormalities in a gene called 'cystic fibrosis transmembrane conductance regulator' (CFTR). The CFTR gene is responsible for the production of the CFTR protein. This protein regulates the production of mucus and digestive juices by acting as a channel to allow the movement of salt and water in and out of cells in the lungs and other tissues.
In patients with cystic fibrosis, there is an overproduction of mucus in the lungs and a reduced production of digestive juices from the pancreas (an organ near the stomach). This leads to long-term infection and inflammation of the lungs and problems with the digestion and absorption of food resulting in poor growth.
Cystic fibrosis is a long-lasting and life-threatening disease because it severely damages the lung tissue and results in shortened life expectancy.

**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 is equivalent to a total of around 66,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

**What treatments are available?**
At the time of submission of the application for orphan drug designation, lung infection and inflammation in cystic fibrosis were mainly treated with antibiotics. Other medicines used to treat the lung disease included 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 medicine 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 ciprofloxacin (liposomal) might be of significant benefit for patients with cystic fibrosis because the medicine is a new formulation of the

[*]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 27), Norway, Iceland and Liechtenstein. This represents a population of 504,800,000 (Eurostat 2009).

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antibiotic ciprofloxacin to be inhaled. This formulation may allow delivery of higher amounts of ciprofloxacin directly into the lungs compared with existing formulations of ciprofloxacin. Also, the liposomal formulation is expected to reduce the bitterness of the medicine, allowing it to be given by inhalation. Ciprofloxacin (liposomal) may be used in patients who do not respond to other antibiotics or in the 'off' periods (periods without treatments) of treatment with other antibiotics. 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?**
Ciprofloxacin is an antibiotic that has been used in the treatment of many types of bacterial infections since the late 1980s. Ciprofloxacin is also authorised for the treatment of respiratory infections in patients with cystic fibrosis. It is available in different forms, such as tablets, solution for infusion and oral suspension.
Ciprofloxacin works by blocking some enzymes known as topoisomerases that are important for the production of DNA in bacteria. When these enzymes are blocked, the bacteria do not reproduce normally, slowing down the spread of infection.
Ciprofloxacin (liposomal) is made up of ciprofloxacin that is contained in small fatty particles called 'liposomes'. The medicine is expected to be inhaled using a nebuliser (a special machine that changes the solution into an aerosol that the patient can breathe in), so that ciprofloxacin is delivered directly into the lungs. Because ciprofloxacin is contained within liposomes, it is expected to remain in the patient's lungs for longer than free ciprofloxacin.

**What is the stage of development of this medicine?**
The effects of ciprofloxacin (liposomal) have been evaluated in experimental models.
At the time of submission of the application for orphan designation, clinical trials in patients with cystic fibrosis were ongoing.
At the time of submission, ciprofloxacin (liposomal) was not authorised anywhere in the EU for cystic fibrosis. Orphan designation of liposomal ciprofloxacin for inhalation had been granted in the United States of America for cystic fibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 4 June 2009 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 Community) 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.

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**Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic**

| Language | Active ingredient | Indication |
|---|---|---|
| English | Ciprofloxacin (liposomal) | Treatment of cystic fibrosis |
| Bulgarian | Ципрофлоксацин (липозомален) | Лечение на кистозна фиброза |
| Czech | Ciprofloxacin (liposomální) | Léčba cystické fibrózy |
| Danish | Ciprofloxacin (liposomal) | Behandling af cystisk fibrose |
| Dutch | Ciprofloxacin (liposomaal) | Behandeling van cystische fibrose |
| Estonian | Ciprofloxacin (liposomaalne) | Tsüstilise fibroosi ravi |
| Finnish | Ciprofloxacin (liposomaalinen) | Kystisen fibroosin hoito |
| French | Ciprofloxacine (liposomale) | Traitement de la mucoviscidose |
| German | Ciprofloxacin (liposomal) | Behandlung zystischer Fibrose |
| Greek | Σιπροφλοξασίνη (Λιποσωμική) | Θεραπεία της κυστικής ίνωσης |
| Hungarian | Ciprofloxacin (liposzómában) | Cisztikus fibrózis kezelése |
| Italian | Ciprofloxacina (liposomiale) | Trattamento della fibrosi cistica |
| Latvian | Ciprofloksacīns (liposomu) | Cistiskās fibrozes ārstēšana |
| Lithuanian | Ciprofloksacinas (liposominis) | Cistinės fibrozės gydymas |
| Maltese | Ciprofloxacin (liposomali) | Kura tal-fibrożi ċistiku |
| Polish | Cyprofloksacyna (liposomalna) | Leczenie zwłóknienia torbielowatego |
| Portuguese | Ciprofloxacina (liposomal) | Tratamento da fibrose quística |
| Romanian | Ciprofloxacin (inclusă în lipozomi) | Tratamentul fibrozei chistice |
| Slovak | Ciprofloxacín (lipozomálny) | Terapia cystickej fibrózy |
| Slovenian | Ciprofloksacin (liposomski) | Zdravljenje cistične fibroze |
| Spanish | Ciprofloxacina (liposomal) | Tratamiento de la fibrosis quística |
| Swedish | Ciprofloxacin (liposomal) | Behandling av cystisk fibros |
| Norwegian | Ciprofloksacin (liposomalt) | Behandling av cystisk fibrose |
| Icelandic | Cíprófloxacín (í lípósómum) | Meðferð við slímseigjusjúkdómi |