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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Hypothiocyanite / lactoferrin for the treatment of cystic fibrosis

On 24 July 2009, orphan designation (EU/3/09/654) was granted by the European Commission to Alaxia, France, for hypothiocyanite / lactoferrin 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 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 was equivalent to a total of around 66,000 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 27), Norway, Iceland and Lichtenstein.
At the time of designation, this represented a population of 504,800,000 (Eurostat 2009).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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 disease's effects on the lungs 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 have physiotherapy.

The sponsor has provided sufficient information to show that the combination of hypothiocyanite and lactoferrin might be of significant benefit for patients with cystic fibrosis because it works in a different way to existing antibiotics. It might also be able to treat a wider range of bacterial infections than existing treatments used in cystic fibrosis. 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?

Because of the abnormalities in the CFTR gene, patients with cystic fibrosis are unable to produce hypothiocyanite. Hypothiocyanite is a substance produced in the airways by the immune system (the body's natural defences), which kills a wide range of bacteria.

Lactoferrin is a protein that is found naturally in milk, tears and saliva and can stop the growth of bacteria by preventing them forming 'biofilms' (when bacterial cells group together on a surface, such as the lining of the lung).

When they are given together, hypothiocyanite and lactoferrin are expected to be more effective than when they are used separately, and kill a wider range of bacteria that can cause lung infections in patients with cystic fibrosis, including *Pseudomonas aeruginosa, Burkholderia cepacia* and *Staphylococcus aureus*.

The combination medicine is expected to be given to patients by inhalation, using a device that first produces hypothiocyanite, before mixing it with lactoferrin to form a solution for inhalation.

What is the stage of development of this medicine?

The effects of hypothiocyanite and lactoferrin have been evaluated in experimental models.

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

At the time of submission, the combination of hypothiocyanite and lactoferrin was not authorised anywhere in the EU for cystic fibrosis or designated as 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 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 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:

Alaxia
60 avenue Rockefeller Bâtiment Adenine
69008 Lyon
France
Telephone: +33 4 37 53 26 40
Telefax: +33 4 37 53 26 40
E-mail: contact@bioalaxia.eu

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	Hypothiocyanite / lactoferrin	Treatment of cystic fibrosis
Bulgarian	Хипотиоцианат / лактоферин	Лечение на кистозна фиброза
Czech	Hypothiokyanit / lactoferin	Léčba cystické fibrózy
Danish	Hypothiocyanatopløsning / lactoferrin	Behandling af cystisk fibrose
Dutch	Hypothiocyaniet / lactoferrine	Behandeling van cystische fibrose
Estonian	Hüpotiotsünaat / laktoferriin	Tsüstilise fibroosi ravi
Finnish	Hypotiosyaniiti / laktoferriini	Kystisen fibroosin hoito
French	Hypothiocyanite / lactoferrine	Traitement de la mucoviscidose
German	Hypothiocyanite / lactoferrin	Behandlung der Mukoviszidose
Greek	Υποθειοκυανίτης / λακτοφερρίνη	Θεραπεία της κυστικής ίνωσης
Hungarian	Hypothiocyanite / lactoferrin	Cisztikus fibrózis kezelése
Italian	Ipotiocianito / lactoferrina	Trattamento della fibrosi cistica
Latvian	Hipotiocianīts / laktoferīns	Cistiskās fibrozes ārstēšana
Lithuanian	Hipotiocianitas / laktoferinas	Cistinės fibrozės gydymas
Maltese	Hypothiocyanite / lactoferrin	Kura tal-fibroži ċistiku
Polish	Hipotiocyjan / laktoferyna	Leczenie zwłóknienia torbielowatego
Portuguese	Hypothiocyanito / lactoferrina	Tratamento da fibrose quística
Romanian	Hipotiocianat / lactoferină	Tratamentul fibrozei chistice
Slovak	Hypotiocyanit / laktoferín	Terapia cystickej fibrózy
Slovenian	Hipotiocianit / laktoferin	Zdravljenje cistične fibroze
Spanish	Hypothiocyanitos / lactoferrina	Tratamiento de la fibrosis quística
Swedish	Hypotiocyanat / laktoferrin	Behandling av cystisk fibros
Norwegian	Hypotiocyanit / laktoferrin	Behandling av cystisk fibrose
Icelandic	Hypóthíócýanít / laktóferrín	Meðferð við slímseigjusjúkdómi

[1] At the time of designation