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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 alginate oligosaccharide (G-block) fragment for the treatment of cystic fibrosis

On 14 September 2007, orphan designation (EU/3/07/475) was granted by the European Commission to AlgiPharma AS, Norway, for alginate oligosaccharide (G-block) fragment for the treatment of cystic fibrosis.

What is cystic fibrosis?
Cystic fibrosis is an inherited disease caused by abnormalities in a specific gene called cystic fibrosis transmembrane regulator (CFTR). Cystic fibrosis appears only when the CFTR gene is abnormal on both chromosomes of the seventh chromosome pair (one inherited from the father, the other from the mother). In cystic fibrosis, defects of the CFTR gene decrease production of a protein that regulates outflow of water and ions such as chloride from the cells that line the internal and external surfaces of the body, the so-called epithelial cells. This defective transport of water and salts results in the thickening of the secretions (mucus) in several organs, including the lungs and the pancreas. In turn, this makes it harder for the body to fend off attacks on the respiratory tract and it leads to chronic and acute infections of the lungs by bacteria, chronic inflammation (a body response to the injury caused to the tissue by the bacteria), and digestive difficulties due to the decreased pancreas function. In the long term, these events can induce damage to the lung tissue and the disease becomes life-threatening.

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 65,000 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 treated mainly with antibiotics (drugs that kill bacteria). These can be taken in a number of ways; as tablets, as intravenous infusion or as inhalation. Other medications to treat the lung symptoms of cystic fibrosis included bronchodilators (medications that enlarge the width of the airways) and mucolytics (drugs that help to dissolve the lung secretions). Associated treatments included daily exercise and physiotherapy and several other types of medications such as pancreatic enzymes and food supplements for the digestive symptoms. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that alginate oligosaccharide (G-block) fragment might be of potential significant benefit for the treatment of cystic fibrosis mainly because it has a new mechanism of action and may possibly be used in combination

[*]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 498,000,000 (Eurostat 2006).

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with other treatments. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?
Patients affected by cystic fibrosis often develop chronic infection by bacteria called Pseudomonas aeruginosa. This bacterium produces a gelatinous compound called alginate that protects it from the body's immune system (the body's natural defence system). Alginate binds to the mucus in the patients' lungs and makes it even thicker and subsequently worsens the obstruction of the airwaves. Alginate oligosaccharide (G-block) fragment is designed to break the interactions between the mucus particles (mucin) and alginate. It is thought that alginate oligosaccharide (G-block) fragment will by this mechanism improve the symptoms of cystic fibrosis.

What is the stage of development of this medicine?
The effects of alginate oligosaccharide (G-block) fragment were evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with cystic fibrosis were initiated.

Alginate oligosaccharide (G-block) fragment was not authorised anywhere worldwide for the treatment of cystic fibrosis nor designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 25 July 2007 a positive opinion recommending the grant of the above-mentioned 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 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 EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Alginate oligosaccharide (G-block) fragment	Treatment of cystic fibrosis
Bulgarian	Фрагмент от олигозахарид алгинат) G-блок)	Лечение на кистозна фиброза
Czech	Fragment alginátu oligosacharidu (G-blok)	Léčba cystické fibrózy
Danish	Alginat oligosaccharid fragment (G blok)	Behandling af cystisk fibrose
Dutch	Alginaat-oligosaccharidefragment (G-blok)	Behandeling van cystische fibrose
Estonian	Alginaat-oligosahhariidi (G-blokk) fragment	Tsüstilise fibroosi ravi
Finnish	Alginaattioligosakkaridifragmentti (G-block)	Kystisen fibroosin hoito
French	Fragment d'oligosaccharide d'alginate (bloc G)	Traitement de la mucoviscidose
German	Oligosaccharid-Fragment (G-Block) eines Alginats	Behandlung zystischer Fibrose
Greek	Κλάσμα αλγινικού ολιγοσακχαρίτη (τμήμα γουλουρονικού οξέος)	Θεραπεία της κυστικής ίνωσης
Hungarian	Alginát oligoszaccharid (G-blokk) fragmens	Cisztikus fibrózis kezelése
Italian	Frammento oligosaccaridico di alginato (blocco G)	Trattamento della fibrosi cistica
Latvian	Alginmāta oligosaharīda (G-bloka) frakcija	Cistiskās fibrozes ārstēšana
Lithuanian	Alginato oligosacharido (G bloko) fragmentas	Cistinės fibrozės gydymas
Maltese	Framment ta' alginate oligosaccharide (G-block)	Kura tal-fibroži ċistiku
Polish	Oligosacharydowy (G-mer) fragment alginianu	Leczenie zwłóknienia torbielowatego
Portuguese	Fragmento de oligossacárido de alginato (bloco G)	Tratamento da fibrose quística
Romanian	Fragment oligozaharidic alginat (bloc G)	Tratamentul fibrozei chistice
Slovak	Fragment alginátu oligosaccharidu (blok G)	Terapia cystickej fibrózy
Slovenian	Fragment (G-blok) alginatnega oligosaharida	Zdravljenje cistične fibroze
Spanish	Fragmento de oligosacárido alginado (bloque G)	Tratamiento de la fibrosis quística
Swedish	Fragment av alginatoligosackarid (G-block)	Behandling av cystisk fibros
Norwegian	Alginat oligosakkarid (G-blokk) fragment	Behandling av cystisk fibrose
Icelandic	Algínat óligosakkaríð (G-blokk) brot	Meðferð við slímseigjusjúkdómi