11 March 2013
EMA/COMP/22635/2006 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Denufosol tetrasodium for the treatment of cystic fibrosis

On 23 December 2005, orphan designation (EU/3/05/342) was granted by the European Commission to Quintiles Limited, United Kingdom, for denufosol tetrasodium for the treatment of cystic fibrosis.

The sponsorship was transferred to Envestia Limited, United Kingdom, in May 2007 and subsequently to Merck Sharp & Dohme Limited, United Kingdom, in January 2013.

What is cystic fibrosis?

Cystic fibrosis is an inherited disease. The genetic information that determines the characteristics of each individual is carried by genes located on structures called chromosomes. In humans, each cell has 23 pairs of chromosomes. For each pair one chromosome is inherited from the mother and the other from the father. Cystic fibrosis is caused by abnormalities of a specific gene, called cystic CFTR, carried by the seventh pair of chromosomes. Cystic fibrosis appears only when the CFTR is abnormal on both chromosomes of the seventh pair. The CFTR gene is responsible for the production of a protein that regulates the outflow of water and salts (like chloride) from cells that cover internal and external surfaces of the body, the so-called epithelial cells. The defective transport of water and salts due to the lack of the regulatory protein, results in the thickening of the secretions (mucous) in several organs (e.g. lungs, pancreas). This leads to reduced functioning and chronic infection of the lungs and chronic inflammation (a body response to the injury caused to the tissue). In the long run, these events can induce damage to the lung tissue and the disease can become 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 was equivalent to a total of around 61,000 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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 466,600,000 (Eurostat 2005).

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What treatments are available?

At the time of submission of the application for the orphan drug designation lung infection and inflammation in cystic fibrosis were treated mainly with antibiotics. These can be taken in a number of ways such as through the mouth, through a vein or they can be inhaled as a fine mist of particles. Associated treatments included daily exercise and physical therapies and several other types of medications such as pancreatic enzymes and food supplements. Bronchodilators are medications that can enlarge the lumen of the airways. Mucolytics help to dissolve the secretions. Still other medications were used to fight the inflammation.

Denufosol tetrasodium might be of potential significant benefit for the treatment of cystic fibrosis because it might improve the long-term outcome of patients. 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?

Denufosol tetrasodium is expected to act on the cells of the lungs and stimulate them to secrete (sort out) ions and water resulting in decrease in mucus viscosity. In addition to this effect, it might enhance the movement of the 'hair' (cilia) at the surface of the lung cells. All these effects may result in an improvement of the so-called mucociliary clearance. Thus, the local administration of denufosol tetrasodium is expected to improve the mucociliary clearance and thereby it might contribute to an increase in the lung function in patients with cystic fibrosis.

What is the stage of development of this medicine?

The effects of denufosol tetrasodium were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with cystic fibrosis were ongoing.

Denufosol tetrasodium was not authorised anywhere worldwide for cystic fibrosis, at the time of submission.

Orphan designation of denufosol tetrasodium was granted in the United States for cystic fibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 November 2005 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	Denufosol tetrasodium	Treatment of cystic fibrosis
Bulgarian	Денуфосол тетрасодиум	Лечение на кистозна фиброза
Czech	Denufosol tetrasodný	Léčba cystické fibrózy
Danish	Denufosol tetranatrium	Behandling af cystisk fibrose
Dutch	Denufosol tetranatrium	Behandeling van cystische fibrose
Estonian	Denufosooltetranaatrium	Tsüstilise fibroosi ravi
Finnish	Tetranatrium denufosoli	Kystisen fibroosin hoito
French	Dénufosol tétrasodique	Traitement de la mucoviscidose
German	Denufosol-Tetranatrium	Behandlung der zystischen Fibrose
Greek	Τετρανατριούχος δενουφοσόλη	Θεραπεία της κυστικής ίνωσης
Hungarian	Denufosol tetranátrium	Cisztikus fibrózis kezelése
Italian	Tetrasodio denufosol	Trattamento della fibrosi cistica
Latvian	Denufosols tetranātrija sāls	Cistiskās fibrozes ārstēšana
Lithuanian	Tetranatrio denufosolis	Cistinės fibrozės gydymas
Maltese	Denufosol tetrasodium	Kura tal-fibrożi ċistiku
Polish	Denufozol czterosodowy	Leczenie zwłóknienia torbielowatego
Portuguese	Tetrassódio de denufosol	Tratamento da fibrose quística
Romanian	Denufosol tetrasodic	Tratamentul fibrozei chistice
Slovak	Denufosol tetrasodný	Terapia cystickej fibrózy
Slovenian	Tetranatrijev denufosol	Zdravljenje cistične fibroze
Spanish	Denufosol tetrasodio	Tratamiento de la fibrosis quística
Swedish	Denufosoltetranatrium	Behandling av cystisk fibros
Norwegian	Denufosoltetranatrium	Behandling av cystisk fibrose
Icelandic	Denúfosól tetranatríum	Meðferð við slímseigjusjúkdómi

[1] At the time of transfer of sponsorship