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

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in August 2008 on request of the Sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of 8-cyclopentyl-1,3-dipropylxanthine for the treatment of cystic fibrosis

On 13 February 2001, orphan designation (EU/3/01/030) was granted by the European Commission to SciClone Pharmaceuticals Italy S.r.l., Italy, for 8-cyclopentyl-1,3-dipropylxanthine for the treatment of cystic fibrosis.

What is cystic fibrosis?
Cystic fibrosis is a hereditary (genetic) disease that affects the production of secretions (such as mucus) from the glands in the body. It affects the lungs and the digestive system (gut) in particular. 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 CFTR, a protein that regulates the production of mucus and digestive juices by acting as a chloride ion channel to allow proper movement of salt and water in and out of certain 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.

What is the estimated number of patients affected by the condition[*]?
At the time of designation cystic fibrosis affected approximately 0.5 to 1.3 in 10,000 people in the European Union (EU)*.This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 19,000 to 49,000 people.

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 physiotherapy and 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 are often given other types of medicine such as pancreatic enzymes (substances that help to digest and absorb food) and food supplements. They are also advised to exercise and to undergo physiotherapy.
8-cyclopentyl-1,3-dipropylxanthine might be of potential significant benefit for the treatment of cystic

[*] Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition.

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fibrosis, because it has a new mechanism of action. 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?
8-cyclopentyl-1,3-dipropylxanthine is expected to bind to the CFTR protein close to a specific mutation (ΔF508). The binding will change the form of the CFTR protein and thereby restoring its function, i.e. the water and salt transport will return to normal. This is expected to lead to improvement of symptoms. The product is not expected to work in cystic fibrosis patients with other mutations.

What is the stage of development of this medicine?
In the United States orphan drug status was granted on 24 March 1997 for management of cystic fibrosis. 8-cyclopentyl-1,3-dipropylxanthine had not been marketed anywhere worldwide for cystic fibrosis, 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 9 February 2001 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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the 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

Language	Active Ingredient	Indication
English	8-cyclopentyl-1,3-dipropyl xanthine	Treatment of cystic fibrosis
Danish	8-cyclopentyl-1, 3-dipropylxanthin	Behandling af cystisk fibrose
Dutch	8-cyclopentyl-1, 3-dipropylxanthine	Behandeling van mucoviscidosis
Finnish	8-syklopentyyli-1, 3 dipropyyliksantiini	kystisen fibroosin hoito
French	8-cyclopentyle-1, 3-dipropylxanthine	Traitement de la mucoviscidose
German	8-cyclopentyl-1, 3-dipropylxanthin	Behandlung der zystischen Fibrose
Greek	8-κυκλοπεντυλ-1, 3-διπροπυλξανθινη	Θεραπεια της κυστικης ινωσης
Italian	8-cyclopentile-1, 3-dipropylxanthina	Trattamento della fibrosi cistica
Portuguese	8-ciclopentil-1, 3-dipropilxantina	Tratamento da fibrose quística
Spanish	8-ciclopentil-1, 3-dipropilxantina	Tratamiento de la fibrosis quística
Swedish	8-cyclopentyl-1, 3-dipropylxanthin	Behandling av cystisk fibros