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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Tobramycin (liposomal) for the treatment of Pseudomonas aeruginosa lung infection in cystic fibrosis

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in February 2013 on request of the Sponsor.

On 11 April 2006, orphan designation (EU/3/06/366) was granted by the European Commission to EUCRO GmbH & Co. KG, Germany, for tobramycin (liposomal) for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis.

The sponsorship was transferred to Axentis Pharma Limited, United Kingdom, in October 2008.

What is Pseudomonas aeruginosa lung infection in 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. *Pseudomonas aeruginosa* is a species of bacteria (micro-organisms that can cause certain types of infections). Chronic infection of the lung with *Pseudomonas aeruginosa* is a typical feature of cystic fibrosis. It can induce further damage to the lung tissue and respiratory insufficiency, which is life threatening.

What is the estimated number of patients affected by the condition?

At the time of designation, *Pseudomonas aeruginosa* lung infection in cystic fibrosis affected approximately 1.3 in 10,000 people in the European Union (EU). This was equivalent to a total of

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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).

What treatments are available?

At the time of submission of the application for orphan designation, *Pseudomonas aeruginosa* lung infection in cystic fibrosis was treated mostly with antibiotics (drugs that kill micro-organisms) and several antibiotics had been authorised for the condition in some countries in the Community. These could be taken in a number of ways such as by mouth, intravenous infusion or they could be inhaled as a fine mist of particles. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that tobramycin (liposomal) might be of potential significant benefit for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis, particularly because it could improve the long-term outcome of the patients and because it may contribute to the patient care. This assumption 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?

Tobramycin is an antibiotic with activity against a wide range microorganisms including *Pseudomonas aeruginosa*. Tobramycin is going to be administered directly into the lungs by inhalation. In addition, tobramycin is going to be incorporated in so called liposomes. The liposomes are structures made of phospholipids (the main components of the cell membrane) that create three-dimensional structures that can incorporate drugs. This liposomal formulation could then help tobramycin to be delivered in a more efficient way to the bacteria.

What is the stage of development of this medicine?

The effects of tobramycin (liposomal) were evaluated in experimental models.

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

Tobramycin (liposomal) was not authorised anywhere worldwide for the treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 March 2006 recommending the granting of this designation.

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*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 468,900,000 (Eurostat 2006).

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	Tobramycin (liposomal)	Treatment of *Pseudomonas aeruginosa* lung infection in cystic fibrosis
Czech	Tobramycin (liposomální)	Léčba plicních infekcí vyvolaných Pseudomonádou *aeruginosa* při cystické fibróze
Danish	Tobramycin (liposomal)	Behandling af lungeinfektion med *Pseudomonas aeruginosa* ved cystisk fibrose
Dutch	Tobramycine (liposomal)	Behandeling van *Pseudomonas aeruginosa* longinfectie bij cystische fibrosis
Estonian	Tobramütsiin (liposomaalne)	*Pseudomonas aeruginosa* poolt põhjustatud kopsuinfektsiooni ravi tsüstilise fibroosi korral
Finnish	Tobramysiini (liposomaalinen)	*Pseudomonas aeruginosan* aiheuttaman keuhkoinfektion hoito kystisessä fibroosissa
French	Tobramycine (liposomale)	Traitement des infections pulmonaires à *Pseudomonas aeruginosa* dans la mucoviscidose
German	Tobramycin (liposomal)	Therapie der *Pseudomonas aeruginosa*-Infektion der Lunge bei zystischer Fibrose
Greek	Τομπραμυκίνη (λιποσωμική)	θεραπεία λοιμώξεων των πνευμόνων με *Pseudomonas aeruginosa* κατά την κυστική ίνωση
Hungarian	Tobramycin (liposzómába)	*Pseudomonas aeruginosa* okozta tüdőfertőzés kezelése cisztikus fibrózisban
Italian	Tobramicina (liposomale)	Trattamento di infezione polmonare da *Pseudomonas aeruginosa* nella fibrosi cistica
Latvian	(Liposomu) tobramicīns	*Pseudomonas aeruginosa* izraisītas plaušu infekcijas ārstēšana cistiskās fibrozes gadījumā
Lithuanian	Tobramicinas (liposomų)	Plaučių infekcijos, sukeltos *Pseudomonas aeruginosa*, gydymas, sergant cistine fibroze
Polish	Tobramycyna (liposomalna)	Leczenie zapalenia płuc wywołanych przez *Pseudomonas aeruginosa* w przebiegu zwłóknienia torbielowatego
Portuguese	Tobramicina (lipossómica)	Tratamento de infecção pulmonar por *Pseudomonas aeruginosa* na fibrosa quística
Slovak	Tobramycín (lipozomálny)	Ošetrovanie infekcií pľúc s *Pseudomonas aeruginosa* pri cystickej fibróze
Slovenian	Tobramicin (liposomska)	Zdravljenje pljučnice povzročene s *Pseudomonasom aeruginosa* pri cistični fibrozi
Spanish	Tobramicina (liposomal)	Tratamiento de infecciones pulmonares por *Pseudomonas aeruginosa* en la fibrosis quística
Swedish	Tobramycin (liposomal)	Behandling av lunginflammation orsakad av *Pseudomonas aeruginosa* vid cystisk fibros

[1] At the time of designation

Language	Active Ingredient	Indication
Norwegian	Tobramycin (liposomal)	Behandling av lungeinfeksjon forårsaket av *Pseudomonas aeruginosa* ved cystisk fibrose
Icelandic	Tobramýcín (í fitukorna)	Meðferð á *Pseudomonas aeruginosa* lungnasýkingum í slímseigjusjúkdómi