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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF terguride for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

On 29 November 2007, orphan designation (EU/3/07/499) was granted by the European Commission to Ergonex Licensing and Regulatory Services AG, Liechtenstein, for terguride for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

What is pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension?

Pulmonary arterial hypertension is a disorder of the blood vessels leading to and surrounding the lungs, in which the pressure in the pulmonary artery (the large blood vessel that leads blood from the heart to the lungs) rises above normal. For an unknown reason, the walls of the blood vessels are thickened and hardened, becoming less elastic and leading to a decrease in their diameter (less space for the blood to move through) which increases the pressure. This causes heart damage in the long run and a range of symptoms, such as shortness of breath, fatigue, chest pain, weakness, coughing and wheezing, and swelling. The vessel wall thickens through hypertrophy (increased size) and hyperplasia (increased number) of the smooth muscle cells in the blood vessels.

Chronic thromboembolic pulmonary hypertension is a complication representing less than 1% of all cases of acute pulmonary embolism (the sudden blocking of a lung artery by a blood clot), which directly leads to pulmonary hypertension. Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension are chronically debilitating and life-threatening.

What are the methods of treatment available?

Several medicinal products were authorised for the treatment of pulmonary arterial hypertension in the Community at the time of submission of the application for orphan drug designation. Chronic thromboembolic pulmonary hypertension can sometimes be treated by surgical removal of the blood clot.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that terguride might be of potential significant benefit for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension mainly because of its 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.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension was considered

* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

to affect less than 2 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 100,000 persons in total.

How is this medicinal product expected to act?

Serotonin is a signal molecule in the body with many functions. In the blood vessel walls it stimulates proliferation of smooth muscle cells and constriction of the vessel walls (narrowing of the blood vessels), which creates pulmonary arterial hypertension. According to the sponsor, terguride binds to the receptors intended for serotonin and inhibits its actions on the smooth muscle cells, thus counter-acting pulmonary arterial hypertension.

What is the stage of development of this medicinal product?

The effects of terguride were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with pulmonary arterial hypertension was ongoing.

Terguride was not authorised anywhere worldwide for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension 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 10 October 2007 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for 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 will be necessary before this product can be granted a marketing authorisation.

For more information:

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**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Terguride	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
Bulgarian	Тергурид	Лечение на белодробна артериална хипертония и хронична тромбоемболична белодробна хипертония
Czech	Tergurid	Léčba plicní arteriální hypertenze a chronické tromboembolické plicní hypertenze
Danish	Tergurid	Behandling af pulmonal arteriel hypertension og kronisk tromboembolisk pulmonal hypertension
Dutch	Terguride	Behandeling van pulmonale arteriële hypertensie en chronische trombo-embolische pulmonale hypertensie
Estonian	Terguriid	Pulmonaalhüpertensiooni ja kroonilise tromboemboolse pulmonaalhüpertensiooni ravi
Finnish	Terguridi	Keuhkoverenkierron hypertension ja kroonisen tromboembolisen keuhkoverenpainetaudin hoito
French	Terguride	Traitement de l'hypertension artérielle pulmonaire et de l'hypertension pulmonaire thromboembolique chronique
German	Tergurid	Behandlung der pulmonalen arteriellen Hypertonie und der chronisch thromboembolischen pulmonalen Hypertonie
Greek	Τεργουρίδη	Θεραπεία της πνευμονικής αρτηριακής υπέρτασης και της χρόνιας πνευμονικής υπέρτασης θρομβοεμβολικής αιτιολογίας
Hungarian	Tergurid	Pulmonáris arteriális hipertónia és krónikus thromboemboliás pulmonáris hipertónia kezelése
Italian	Terguride	Trattamento dell'ipertensione arteriosa polmonare e dell'ipertensione polmonare cronica tromboembolica
Latvian	Tergurīds	Plaušu arteriālās hipertensijas un hroniskās tromboemboliskās plaušu hipertensijas ārstēšanai
Lithuanian	Terguridas	Plaučių arterinės hipertenzijos ir lėtinės tromboembolinės plaučių hipertenzijos gydymas
Maltese	Terguride	Kura ta' pressjoni arterjali pulmonari għolja u ta' pressjoni pulmonari trombo-embolika għolja kronika
Polish	Terguryd	Leczenie tętniczego nadciśnienia płucnego oraz przewlekłego zakrzepowo-zatorowego nadciśnienia płucnego
Portuguese	Terguride	Tratamento da hipertensão arterial pulmonar e da hipertensão pulmonar tromboembólica crónica
Romanian	Terguridă	Tratamentul hipertensiunii arteriale pulmonare și al hipertensiunii pulmonare tromboembolice cronice
Slovak	Tergurid	Liečba pľúcnej arteriálnej hypertenzie a chronickej tromboembolickej pľúcnej hypertenzie
Slovenian	Tergurid	Zdravljenje pljučne arterijske hipertenzije in kronične tromboembolične pljučne hipertenzije
Spanish	Tergurida	Tratamiento de la hipertensión arterial pulmonar y de la hipertensión pulmonar tromboembólica crónica
Swedish	Tergurid	Behandling av pulmonell arteriell hypertension samt kronisk tromboembolisk pulmonell hypertension

Norwegian	Tergurid	Behandling av pulmonal arteriell hypertensjon og kronisk tromboembolisk pulmonal hypertensjon
Icelandic	Tergúrið	Meðferð við háþrýstingi í lungnablóðrás og langvinnum háþrýstingi í lungnablóðrás í kjölfar segareks