



European Medicines Agency
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 elafin

for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

On 20 March 2007, orphan designation (EU/3/07/443) was granted by the European Commission to Proteo Biotech AG, Germany, for elafin 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 rare blood vessel disorder of the lung in which the pressure in the pulmonary artery (the blood vessel that leads from the heart to the lungs) rises above normal levels. The number of smooth muscle cells in the walls of small lung arteries increases (a phenomenon called proliferation) resulting in remodelling of these vessels. This may lead to obstructions in the microcirculation and then to an increase in the blood pressure.

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 clot or foreign material that has been transported by the blood), directly leading to pulmonary hypertension. Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension are chronically debilitating and life-threatening.

What are the methods of treatment?

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.

Elafin might be of potential significant benefit for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension in particular with regards to improved efficacy based on the new mechanism of action. This benefit will have to be confirmed at the time of marketing authorisation and 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 to affect 2.2 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 110,000 persons.

* 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.

How is this medicinal product expected to act?

One of the mechanisms that contribute to pulmonary arterial hypertension is the body's ability to increase the thickness of the pulmonary vessels. In pulmonary arterial hypertension this ability is not well regulated and the vessels become narrower. The disease worsens as the inner space of the vessels become smaller and it becomes increasingly difficult for the blood to move through the vessels.

Elafin is a protein that has an inhibitory activity over endogenous vascular elastase. Endogenous vascular elastase is a protein that has an important activity in the process of thickening of the blood vessel wall. By inhibiting this protein, elafin is expected to stop the thickening of the blood vessel wall, seen in pulmonary arterial hypertension.

What is the stage of development of this medicinal product?

At the time of submission, the effects of elafin were evaluated in experimental models.

Elafin was not authorised anywhere worldwide for pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension, 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 7 February 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.

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

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