



Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of treprostinil diethanolamine (oral use) for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

On 26 August 2005, orphan designation (EU/3/05/310) was granted by the European Commission to United Therapeutics Europe Ltd., United Kingdom, for treprostinil diethanolamine (oral use) 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. An increase of the number of smooth muscle cells in the walls of small lung arteries (a phenomenon called proliferation) that are remodelling the vessels, may lead to obstructions in the microcirculation, which will then lead 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 which has been brought to its site by the blood current), which directly leads to pulmonary hypertension. Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension are chronically debilitating and life-threatening.

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

At the time of designation, pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension affected approximately 1.4 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 64,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are 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.

Treprostinil diethanolamine (oral use) might be of potential significant benefit for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension because it might improve the long-term outcome of the patients. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

*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. This represents a population of 459,700,000 (Eurostat 2004).

How is this medicine expected to work?

In pulmonary arterial hypertension there appears to be an imbalance between vasoconstrictors (substances produced by certain cells that help to narrow the blood vessels) and vasodilators (substances produced by other cells that help to widen the blood vessels, such as prostacyclin). This imbalance seems to be caused, at least in part, by the lack or reduction of a certain enzyme, prostacyclin synthase, responsible for producing prostacyclin. Prostacyclin causes vasodilatation and has also a strong effect in blocking the platelets (blood cells responsible to make the blood clot) to make the clot. Treprostinil diethanolamine (oral use) is a substance similar to prostacyclin and is expected to act in a similar way on the pulmonary arteries in patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

What is the stage of development of this medicine?

The effects of treprostinil diethanolamine (oral use) were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials were ongoing.

Treprostinil diethanolamine (oral use) was not authorised anywhere worldwide for pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension, at the time of submission.

Orphan designation of treprostinil has been granted in the United States for treatment of pulmonary arterial hypertension.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 13 July 2005 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;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the Community) 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.

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

Language	Active Ingredient	Indication
English	Treprostinil diethanolamine (oral use)	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
Czech	Treprostinil diethanolamin (perorální podání)	Léčba plicní arteriální hypertenze a chronické tromboembolické plicní hypertenze
Danish	Treprostinil diethanolamin (oral anvendelse)	Behandling af pulmonal arteriel hypertension og kronisk tromboembolisk pulmonal hypertension
Dutch	Treprostinil diethanolamin (oraal gebruik)	Behandeling van pulmonale arteriële hypertensie en chronische trombo-embolische pulmonale hypertensie
Estonian	Treprostiniil dietanolamiin (peroraalne)	Pulmonaalhüpertensiooni ja kroonilise tromboemboolse pulmonaalhüpertensiooni ravi
Finnish	Treprostiniili dietanoliamiini (ssun kautta)	Keuhkoverenkierron hypertension ja kroonisen tromboembolisen keuhkoverenpainetaudin hoito
French	Tréprostinil diéthanolamine (voie orale)	Traitement de l'hypertension artérielle pulmonaire et de l'hypertension pulmonaire thromboembolique chronique
German	Treprostinil Diethanolamin (zum Einnehmen)	Behandlung der pulmonalen arteriellen Hypertonie und der chronisch thromboembolischen pulmonalen Hypertonie
Greek	Τρεπροστινίλ-διαιθανολαμίνη (Από στόματος χρήση)	Θεραπεία της πνευμονικής αρτηριακής υπέρτασης και της χρόνιας πνευμονικής υπέρτασης θρομβοεμβολικής αιτιολογίας
Hungarian	Treprostinil dietanolamin (oralis alkalmazás)	Pulmonáris arteriális hipertónia és krónikus thromboemboliás pulmonáris hipertónia kezelése
Italian	Treprostinil dietanolamina (uso orale)	Trattamento dell'ipertensione arteriosa polmonare e dell'ipertensione polmonare cronica tromboembolica
Latvian	Treprostinildietanolamīns (iekšķīgai lietošanai)	Plaušu arteriālās hipertensijas un hroniskās tromboemboliskās plaušu hipertensijas ārstēšanai
Lithuanian	Treprostinilo dietanolaminas (gerti)	Plaučių arterinės hipertenzijos ir lėtinės tromboembolinės plaučių hipertenzijos gydymas
Polish	Treprostynylu dietanoloamina (podanie doustne)	Leczenie tętniczego nadciśnienia płucnego oraz przewlekłego zakrzepowo-zatorowego nadciśnienia płucnego
Portuguese	Dietanolamina de treprostinil (via oral)	Tratamento da hipertensão arterial pulmonar e da hipertensão pulmonar tromboembólica crónica
Slovak	Treptostinil dietanolamín (perorálne použitie)	Liečba pľúcnej arteriálnej hypertenzie a chronickej tromboembolickej pľúcnej hypertenzie.
Slovenian	Treprostinil dietanolamin (peroralna uporaba)	Zdravljenje pljučne arterijske hipertenzije in kronične tromboembolične pljučne hipertenzije

Spanish	Treprostinil dietanolamina (vía oral)	Tratamiento de la hipertensión arterial pulmonar y de la hipertensión pulmonar tromboembólica crónica
Swedish	Treprostinildietanolamin (oral användning)	Behandling av pulmonell arteriell hypertension samt kronisk tromboembolisk pulmonell hypertension
Norwegian	Treprostinil-dietanolamin (oral bruk)	Behandling av pulmonal arteriell hypertensjon og kronisk tromboembolisk pulmonal hypertensjon
Icelandic	Treprostiníl tvietanolamín (til inntöku)	Meðferð við háþrýstingi í lungnablóðrás og langvinnum háþrýstingi í lungnablóðrás í kjölfar segareks