



Committee for Orphan Medicinal Products

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

On 14 April 2004, orphan designation (EU/3/04/197) was granted by the European Commission to LungRx Limited, United Kingdom, for treprostinil sodium (inhalation use) for the treatment of pulmonary artery hypertension and chronic thromboembolic pulmonary hypertension. The sponsorship was transferred to United Therapeutics Europe Ltd, United Kingdom, in January 2008.

What are 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 vessel that leads blood 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 in 10,000 people in the European Union (EU) *. This is equivalent to a total of around 39,000 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 sodium for inhalation use might be of potential significant benefit for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension because it

*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 385,000,000 (Eurostat 2002) and may differ from the true number of patients affected by the condition.

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.

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 sodium 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 sodium for inhalatory use have been evaluated in experimental models.

At the time of submission of the application for orphan designation, some clinical trials in patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension were completed.

Treprostinil sodium, for inhalatory use, was not marketed anywhere worldwide for pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension, at the time of submission. A formulation of treprostinil sodium, for subcutaneous use, is marketed in Australia, Canada, Israel, Switzerland and United States. Orphan designation of treprostinil sodium, for subcutaneous use, has also 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 16 March 2004 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.

For more information:

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Translations of the active ingredient and indication in all EU languages

| Language | Active Ingredient | Indication |
|------------|-------------------------|---|
| English | Treprostinil sodium | Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension |
| Danish | Treprostinil natrium | Behandling af pulmonal hypertension og kronisk tromboembolisk pulmonal hypertension |
| Dutch | Treprostinil natrium | Behandeling van pulmonale arteriële hypertensie en chronische trombo-embolische pulmonale hypertensie |
| Finnish | Treprostinil natrium | Keuhkoverenkierron hypertensio ja krooninen tromboembolinen keuhkoverenpainetauti |
| French | Treprostinil sodium | Traitement de l'hypertension artérielle pulmonaire et de l'hypertension pulmonaire thromboembolique chronique |
| German | Treprostinil Natrium | Behandlung der pulmonalen arteriellen Hypertonie und der chronisch thromboembolischen pulmonalen Hypertonie |
| Greek | Νατριούχα τρεπτοστιλίνη | Θεραπεία της πνευμονικής αρτηριακής υπέρτασης και της χρόνιας πνευμονικής υπέρτασης θρομβοεμβολικής αιτιολογίας |
| Italian | Treprostinil sodio | Trattamento dell'ipertensione arteriosa polmonare e dell'ipertensione polmonare cronica tromboembolica |
| Portuguese | Treprostinil sódico | Tratamento da hipertensão arterial pulmonar e da hipertensão pulmonar tromboembólica crónica |
| Spanish | Treprostinil sódico | Tratamiento de la hipertensión arterial pulmonar y de la hipertensión pulmonar tromboembólica crónica |
| Swedish | Treprostinil natrium | Behandling av pulmonell arteriell hypertension samt kronisk tromboembolisk pulmonell hypertension |