



COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

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

On 12 December 2003, orphan designation (EU/3/03/178) was granted by the European Commission to Pfizer Limited, United Kingdom, for sildenafil citrate 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 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.

Sildenafil citrate 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 and preliminary preclinical and clinical results. 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?

According to the information provided by the sponsor, pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension was considered to affect not more than 38,500 persons in the European Union.

How is this medicinal product expected to act?

Sildenafil citrate has vasodilating (enlargement of the vessel) properties, including an effect on pulmonary arteries. Furthermore, information deriving from some preclinical tests suggests that sildenafil citrate inhibits the proliferation of smooth muscle cells in the vessels, which might have a beneficial effect on the changes in the pulmonary microcirculation.

What is the stage of development of this medicinal product?

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

Sildenafil citrate was not marketed anywhere worldwide for pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension or 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 2003 a positive opinion recommending the grant of the above-mentioned designation.

Update: Sildenafil citrate (Revatio) is authorised in the European Union as of 28 October 2005 for the treatment of patients with pulmonary arterial hypertension classified as WHO functional class III, to improve exercise capacity.

Efficacy has been shown in primary pulmonary hypertension and pulmonary hypertension associated with connective tissue disease.

For more information please see www.emea.europa.eu

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:

Sponsor's contact details:

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*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. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients associations' contact points:

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Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Sildenafil citrate	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
Danish	Sildenafil citrat	Behandling af pulmonal hypertension og kronisk tromboembolisk pulmonal hypertension
Dutch	Sildenafil citraat	Behandeling van pulmonale arteriële hypertensie en chronische trombo-embolische pulmonale hypertensie
Finnish	Sildenafilisiitraatti	Keuhkoverenkierron hypertensio ja krooninen tromboembolinen keuhkoverenpainetauti
French	Citrate de sildénafil	Traitement de l'hypertension artérielle pulmonaire et de l'hypertension pulmonaire thromboembolique chronique
German	Sildenafil citrat	Behandlung der pulmonalen arteriellen Hypertonie und der chronisch thromboembolischen pulmonalen Hypertonie
Greek	Κιτρική σιλντεναφίλη	θεραπεία της πνευμονικής αρτηριακής υπέρτασης και της χρόνιας πνευμονικής υπέρτασης θρομβοεμβολικής αιτιολογίας
Italian	Sildenafil citrato	Trattamento dell'ipertensione arteriosa polmonare e dell'ipertensione polmonare cronica tromboembolica
Portuguese	Citrato de sildenafil	Tratamento da hipertensão arterial pulmonar e da hipertensão pulmonar tromboembólica crónica
Spanish	Citrato de sildenafilo	Tratamiento de la hipertensión arterial pulmonar y de la hipertensión pulmonar tromboembólica crónica
Swedish	Sildenafilcitrat	Behandling av pulmonell arteriell hypertension samt kronisk tromboembolisk pulmonell hypertension