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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

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

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in May 2012 at the end of the period of market exclusivity.

On 14 February 2001, orphan designation (EU/3/01/019) was granted by the European Commission to Actelion Pharmaceuticals, France, for bosentan for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

The sponsorship was transferred to Actelion Registration Limited, United Kingdom in July 2001.

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 0.95 in 10,000 people in the European Union (EU). This was

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equivalent to a total of around 36,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

One medicinal product was authorised for the treatment of pulmonary arterial hypertension in the Community at the time of submission of the application for orphan drug designation.

Bosentan might be of potential significant benefit for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension because it may be safer than the existing medicinal product and it might improve the quality of life for the patients. The benefit 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?

Bosentan opposes the effect of a substance called endothelin-1. Endothelin is a group of naturally produced substances, called hormones, released by the cells which are lining the inside surface of the blood vessels. Endothelin is known to be the most powerful substance that can cause narrowing of blood vessels. By blocking the effect of endothelin, the diameter of the blood vessel can normalise and this might induce a decrease of the blood pressure.

What is the stage of development of this medicine?

The effects of bosentan were evaluated in experimental models. 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 completed.

Bosentan was not marketed anywhere worldwide for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension, at the time of submission. Orphan designation of bosentan was granted in the United States for the same condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 December 2000 recommending the granting of this designation.

Update: Bosentan (Tracleer) has been authorised in the EU since 15 May 2002 for the treatment of pulmonary arterial hypertension (PAH) to improve exercise capacity and symptoms in patients with grade III functional status. Efficacy has been shown in:

- primary (idiopathic and familial) PAH;
- PAH secondary to scleroderma without significant interstitial pulmonary disease and
- PAH associated with congenital systemic-to-pulmonary shunts and Eisenmenger's physiology.

In 2008, some improvements have also been shown in patients with PAH WHO functional class II and the therapeutic indication was extended accordingly.

*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.
At the time of designation, this represented a population of 378,800,000 (Eurostat 2001).

More information on Tracleer can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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 EU) 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

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Bosentan	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
Danish	Bosentan	Behandling af pulmonal arteriel hypertension samt kronisk tromboembolisk pulmonal hypertension
Dutch	Bosentan	Behandeling van pulmonale arteriële hypertensie en chronische trombo-embolische pulmonale hypertensie
Finnish	Bosentaani	Kohonneen keuhkovaltimopaineen ja kroonisen tromboembolisen pulmonaarisen hypertension hoito
French	Bosentan	Traitement de l'hypertension artérielle pulmonaire et del'hypertension pulmonaire chronique thrombo-embolique
German	Bosentan	Behandlung der pulmonalen arteriellen Hypertonie und der chronischen thromboembolischen pulmonalen Hypertonie
Greek	Bosentan	Θεραπεια της αρτηριακής πνευμονικής υπέρτασης και της χρόνιας θρομβοεμβολικής πνευμονικής υπέρτασης
Italian	Bosentan	Trattamento dell'ipertensione arteriosa polmonare e l'ipertensione polmonare cronica tromboembolica
Portuguese	Bosentan	Tratamento da hipertensão arterial pulmonar e Hipertensão pulmonar tromboembólica crónica
Spanish	Bosentan	Tratamiento de la hipertensión arterial pulmonar y Hipertensión pulmonar tromboembólica crónica
Swedish	Bosentan	Behandling av förhöjt pulmonärartärtryck och kronisk tromboembolisk pulmonell hypertoni

[1] At the time of designation