



EUROPEAN MEDICINES AGENCY
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Macitentan for the treatment of pulmonary arterial hypertension

First publication	13 October 2011
Rev.1: information about Marketing Authorisation	17 March 2014
Rev.2: sponsor's change of address	5 March 2015
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 27 September 2011, orphan designation (EU/3/11/909) was granted by the European Commission to Actelion Registration Limited, United Kingdom, for macitentan for the treatment of pulmonary arterial hypertension.

What is pulmonary arterial hypertension?

Pulmonary arterial hypertension is a condition where there is high blood pressure in the arteries that supply the lungs. In patients with pulmonary arterial hypertension, there is a thickening of the muscles in the walls of the arteries and a narrowing of the arteries in the lungs, making it harder for blood to flow to the lungs. Pulmonary arterial hypertension is a long-term debilitating and life-threatening condition that shortens patients' life expectancy because it may lead to heart failure and difficulty breathing.

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

At the time of designation, pulmonary arterial hypertension affected less than 1.8 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 91,000 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).

*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 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).



What treatments are available?

Several medicines were authorised for the treatment of pulmonary arterial hypertension in the EU at the time of designation. They included bosentan, ambrisentan, tadalafil, sildenafil, iloprost, epoprostenol, and treprostinil sodium. Surgery was also used in some patients to carry out a lung transplant or atrial septostomy (where a small hole is created between the upper two chambers of the heart, the atria).

The sponsor has provided sufficient information to show that macitentan might be of significant benefit for patients with pulmonary arterial hypertension because it may penetrate the diseased tissue more effectively than current treatments with a similar mechanism of action, which may improve the outcome of patients with pulmonary arterial hypertension, particularly when used in combination with existing treatments. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Macitentan is expected to work as an 'endothelin receptor antagonist'. This means that it is expected to block the receptors (type A and B) which the substance called 'endothelin-1' normally attaches to and activates. Endothelin is a naturally occurring substance that is released from lining of the blood vessels. It is present at raised levels in patients with pulmonary arterial hypertension, causing the blood vessels to constrict and the blood vessel walls to thicken. By blocking endothelin receptors, macitentan is expected to stop endothelin from constricting the blood vessels, thereby leading to a decrease in the blood pressure and a reduction of the symptoms of pulmonary arterial hypertension.

What is the stage of development of this medicine?

The effects of macitentan have been evaluated in experimental models.

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

At the time of submission, macitentan was not authorised anywhere in the EU for pulmonary arterial hypertension. Orphan designation of macitentan had been granted in the United States for the treatment of pulmonary arterial hypertension.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 July 2011 recommending the granting of this designation.

Update: Macitentan (Opsumit) has been authorised in the EU since 20 December 2013. Opsumit, as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease

More information on Opsumit 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

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Macitentan	Treatment of pulmonary arterial hypertension
Bulgarian	мацитентан	Лечение на белодробна артериална хипертония
Czech	Macitentan	Léčba plicní arteriální hypertenze
Danish	Macitentan	Behandling af pulmonal arteriel hypertension
Dutch	Macitentan	Behandeling van pulmonale arteriële hypertensie
Estonian	Macitentan	Arteriaalse pulmonaalhüpertensiooni ravi
Finnish	Macitentan	Keuhkoverenkierron hypertension hoito
French	Macitentan	Traitement de l'hypertension artérielle pulmonaire
German	Macitentan	Behandlung der pulmonalen arteriellen Hypertonie
Greek	Μασιτένταν	Θεραπεία της πνευμονικής αρτηριακής υπέρτασης
Hungarian	Macitentan	Pulmonáris arteriális hipertónia kezelése
Italian	Macitentan	Trattamento dell'ipertensione arteriosa polmonare
Latvian	Macitentāns	Plaušu arteriālās hipertensijas ārstēšana
Lithuanian	Macitentanas	Plaučių arterinės hipertenzijos gydymas
Maltese	Macitentan	Kura ta' pressjoni arterjali pulmonari għolja
Polish	Macitentan	Leczenie tętniczego nadciśnienia płucnego
Portuguese	Macitentan	Tratamento da hipertensão arterial pulmonar
Romanian	Macitentan	Tratamentul hipertensiunii arteriale pulmonare
Slovak	Macitentan	Liečba pľúcnej arteriálnej hypertenzie vrátane
Slovenian	Macitentan	Zdravljenje pljučne arterijske hipertenzije vključno
Spanish	Macitentan	Tratamiento de la hipertensión arterial pulmonar
Swedish	Macitentan	Behandling av pulmonell arteriell hypertension
Norwegian	Macitentan	Behandling av pulmonal arteriell hypertensjon
Icelandic	Macítentan	Meðferð við háþrýstingi í lungnablóðrás

¹ At the time of designation