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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

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

First publication	11 October 2005
Rev.1: transfer of sponsorship	6 March 2007
Rev.2: information about Marketing Authorisation	29 July 2008
Rev.3: sponsor's change of address	30 June 2014

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 11 April 2005, orphan designation (EU/3/05/273) was granted by the European Commission to Uppsala Medical Information System AB, Sweden, for ambrisentan for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

The sponsorship was trasferred to European Medical Advisory Services Limited, United Kingdom, in August 2005 and subsequently to Glaxo Group Limited, United Kingdom, in September 2006.

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 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 remoddeling 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.

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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 less than 2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 93,000 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?

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.

Ambrisentan might be of potential significant benefit for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension because it might act in a different way and thereby improve the long-term outcome of the patients. This benefit will have to be confirmed at the time of marketing authorisation and will be necessary to maintain the orphan status.

How is this medicine expected to work?

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

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, preliminary clinical trials in patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension had been performed and more studies were planned.

Ambrisentan 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.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 3 March 2005 recommending the granting of this designation.

Update: ambrisentan (Volibris) has been authorised in the EU since 21 April 2008 for the treatment of pulmonary arterial hypertension (PAH).

More information on Volibris 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

*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.
At the time of designation, this represented a population of 466,600,000 (Eurostat 2005).

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:

Glaxo Group Limited
980 Great West Road
Brentford
Middlesex TW8 9GS
United Kingdom
http://www.gsk.com/uk/about-us/contact-us.html

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	Ambrisentan	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
Bulgarian	Амбрисентан	Лечение на белодробна артериална хипертония и хронична тромбемболична белодробна хипертония
Czech	Ambrisentan	Léčba plicní arteriální hypertenze a chronické tromboembolické plicní hypertenze
Danish	Ambrisentan	Behandling af pulmonal arteriel hypertension og kronisk tromboembolisk pulmonal hypertension
Dutch	Ambrisentan	Behandeling van pulmonale arteriële hypertensie en chronische trombo-embolische pulmonale hypertensie
Estonian	Ambrisentan	Pulmonaalhüpertensiooni ja kroonilise tromboemboolse pulmonaalhüpertensiooni ravi
Finnish	Ambrisentaani	Keuhkoverenkierron hypertension ja kroonisen tromboembolisen keuhkoverenpainetaudin hoito
French	Ambrisentan	Traitement de l'hypertension artérielle pulmonaire et de l'hypertension pulmonaire thromboembolique chronique
German	Ambrisentan	Behandlung der pulmonalen arteriellen Hypertonie und der chronisch thromboembolischen pulmonalen Hypertonie
Greek	Αμπρισαντάν	Θεραπεία της πνευμονικής αρτηριακής υπέρτασης και της χρόνιας πνευμονικής υπέρτασης θρομβοεμβολικής αιτιολογίας
Hungarian	Ambrisentan	Pulmonáris arteriális hipertónia és krónikus tromboembólia okozta pulmonáris hipertónia kezelésére
Italian	Ambrisentan	Trattamento dell'ipertensione arteriosa polmonare e dell'ipertensione polmonare cronica tromboembolica
Latvian	Ambrisentan	Plaušu arteriālās hipertensijas un hroniskās tromboemboliskās plaušu hipertensijas ārstēšanai
Lithuanian	Ambrisentanas	Plaučių arterinės hipertenzijos ir lėtinės tromboembolinės plaučių hipertenzijos gydymas
Maltese	Ambrisentan	Kura ta' pressjoni arterjali pulmonari għolja u ta' pressjoni pulmonari trombo-embolika kronika
Polish	Ambrisentan	Leczenie tętniczego nadciśnienia płucnego oraz przewlekłego zakrzepowo-zatorowego nadciśnienia płucnego
Portuguese	Ambrisentan	Tratamento da hipertensão arterial pulmonar e da hipertensão pulmonar tromboembólica crónica
Romanian	Ambrisentan	Tratamentul hipertensiunii arteriale pulmonare şi al hipertensiunii pulmonare tromboembolice cronice
Slovak	Ambrisentan	Liečba pľúcnej arteriálnej hypertenzie a chronickej tromboembolickej pľúcnej hypertenzie.

[1] At the time of marketing authorisation

Language	Active Ingredient	Indication
Slovenian	Ambrisentan	Zdravljenje pljučne arterijske hipertenzije in kronične tromboembolične pljučne hipertenzije
Spanish	Ambrisentán	Tratamiento de la hipertensión arterial pulmonar y de la hipertensión pulmonar tromboembólica crónica
Swedish	Ambrisentan	Behandling av pulmonell arteriell hypertension samt kronisk tromboembolisk pulmonell hypertension
Norwegian	Ambrisentan	Behandling av pulmonal arteriell hypertensjon og kronisk tromboembolisk pulmonal hypertensjon
Icelandic	Ambrisentan	Ambrisentan hefur ábendingu við meðferð á lungnaslagæðaháþrýstingi og langvinnum lungnaháþrýstingi af völdum segareks