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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lisuride hydrogen maleate for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

First publication	19 May 2011
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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 13 May 2011, orphan designation (EU/3/11/869) was granted by the European Commission to Sinoxa Pharma UG, Germany, for lisuride hydrogen maleate for the treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

In November 2012, Sinoxa Pharma UG changed name to Sinoxa Pharma GmbH.

What are pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension?

Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension are two conditions where there is high blood pressure in the arteries that supply the lungs.

In patients with pulmonary arterial hypertension, there is a narrowing of the arteries in the lungs and a thickening in the muscles in the walls of the arteries, making it harder for blood to flow to the lungs.

In chronic thromboembolic pulmonary hypertension, the increased blood pressure in the arteries of the lungs is caused by a blockage due to a blood clot or foreign material.

Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension are long-term debilitating and life-threatening conditions that shorten patients' life expectancy because they may lead to heart failure.



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

At the time of designation, pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension affected between 1.4 and 2 in 10,000 people in the European Union (EU). This was equivalent to a total of between 71,000 and 102,000 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 medicines were authorised for the treatment of pulmonary arterial hypertension in the EU at the time of designation.

The sponsor has provided sufficient information to show that lisuride hydrogen maleate might be of potential significant benefit to patients because of its new mode of action which could lead to better outcomes for patients, as supported by early studies in experimental models. 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?

Lisuride is a substance that has been used in medicine to treat Parkinson's disease for a number of years. In pulmonary hypertension, lisuride given as a continuous infusion under the skin is expected to work by stopping a substance called serotonin to attach to some receptors called 5-HT_{2B}. When serotonin attaches to these receptors, it causes the narrowing of the arteries in the lungs and the growth of muscle cells and connective tissue in the walls of arteries. By blocking the action of serotonin at these receptors, lisuride is expected to cause the arteries in the lungs to widen and to prevent blood clots from forming, thereby reducing blood pressure in the lungs. Blockade of the serotonin receptors by lisuride is also expected to prevent and reverse the growth of muscle cells and connective tissue in the walls of the lung arteries.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of lisuride hydrogen maleate in experimental models was ongoing.

At the time of submission, no clinical trials with lisuride hydrogen maleate in patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension had been started.

At the time of submission, lisuride hydrogen maleate was not authorised anywhere in the EU for pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension or designated as an orphan medicinal product elsewhere for these conditions.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 February 2011 recommending the granting of this designation.

*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).

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	Lisuride hydrogen maleate	Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
Bulgarian	Хидрогенмалеат на лизурид	Лечение на белодробна артериална хипертония и хронична тромбемболична белодробна хипертония
Czech	Lisurid hydrogenmaleát	Léčba plicní arteriální hypertenze a chronické tromboembolické plicní hypertenze
Danish	Lisuridhydrogenmaleat	Behandling af pulmonal arteriel hypertension og kronisk tromboembolisk pulmonal hypertension
Dutch	Lisuride hydrogeenmaleaat	Behandeling van pulmonale arteriële hypertensie en chronische trombo-embolische pulmonale hypertensie
Estonian	Lisuriidvesinikmaleaat	Pulmonaalhüpertensiooni ja kroonilise tromboemboolse pulmonaalhüpertensiooni ravi
Finnish	Lisuridivetymaleaatti	Keuhkoverenkierron hypertension ja kroonisen tromboembolisen keuhkoverenpainetaudin hoito
French	Maléate acide de lisuride	Traitement de l'hypertension artérielle pulmonaire et de l'hypertension pulmonaire thromboembolique chronique
German	Lisurid-Hydrogenmaleat	Behandlung der pulmonalen arteriellen Hypertonie und der chronisch thromboembolischen pulmonalen Hypertonie
Greek	Άλας λισουρίδης υδρογονωμένου μηλεϊκού οξέως	Θεραπεία της πνευμονικής αρτηριακής υπέρτασης και της χρόνιας πνευμονικής υπέρτασης θρομβοεμβολικής αιτιολογίας
Hungarian	Lisurid hidrogénmaleát	Pulmonáris arteriális hipertónia és krónikus thromboemboliás pulmonáris hipertónia kezelése
Italian	Lisuride idrogenomaleato	Trattamento dell'ipertensione arteriosa polmonare e dell'ipertensione polmonare cronica tromboembolica
Latvian	Lisurīda hidrogēnmaleāts	Plaušu arteriālās hipertensijas un hroniskās tromboemboliskās plaušu hipertensijas ārstēšanai
Lithuanian	Lizurido hidrogenmaleatas	Plaučių arterinės hipertenzijos ir lėtinės tromboembolinės plaučių hipertenzijos gydymas
Maltese	Lisuride hydrogen maleate	Kura ta' pressjoni arterjali pulmonari għolja u ta' pressjoni pulmonari trombo-embolika għolja kronika
Polish	Wodoromaleinian lizurydu	Leczenie tętniczego nadciśnienia płucnego oraz przewlekłego zakrzepowo-zatorowego nadciśnienia płucnego
Portuguese	Hidrogenomaleato de lisurida	Tratamento da hipertensão arterial pulmonar e da hipertensão pulmonar tromboembólica crónica
Romanian	Hidrogenmaleat de lisurid	Tratamentul hipertensiunii arteriale pulmonare și al hipertensiunii pulmonare tromboembolice cronice
Slovak	Lizurid hydrogénmaleát	Liečba pľúcnej arteriálnej hypertenzie a chronickej tromboembolickej pľúcnej hypertenzie

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	Lizuridijev maleat	Zdravljenje pljučne arterijske hipertenzije in kronične tromboembolične pljučne hipertenzije
Spanish	Maleato de hidrógeno de lisurida	Tratamiento de la hipertensión arterial pulmonar y de la hipertensión pulmonar tromboembólica crónica
Swedish	Lisuridvätemaleat	Behandling av pulmonell arteriell hypertension samt kronisk tromboembolisk pulmonell hypertension
Norwegian	Lisuridhydrogenmaleat	Behandling av pulmonal arteriell hypertensjon og kronisk tromboembolisk pulmonal hypertensjon
Icelandic	Lísúríð-hýdrógenmaleat	Meðferð við háþrýstingi í lungnablóðrás og langvinnum háþrýstingi í lungnablóðrás í kjölfar segareks