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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Iloprost for the for the treatment of primary and of the following forms of secondary pulmonary hypertension: connective tissue disease pulmonary hypertension, drug-induced pulmonary hypertension, portopulmonary hypertension, pulmonary hypertension associated with congenital heart disease and chronic thromboembolic pulmonary hypertension

First publication	12 March 2009
Rev.1: sponsor's name change	3 May 2011
Rev.2: sponsor's name change	17 November 2011
Rev.3: withdrawal from the Community Register	3 October 2013
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.	

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in September 2013 at the end of the period of market exclusivity.

On 29 December 2000, orphan designation (EU/3/00/014) was granted by the European Commission to Schering AG , Germany, for iloprost for the treatment of primary and of the following forms of secondary pulmonary hypertension: connective tissue disease pulmonary hypertension, drug-induced pulmonary hypertension, portopulmonary hypertension, pulmonary hypertension associated with congenital heart disease and chronic thromboembolic pulmonary hypertension.

Schering AG changed name to Bayer Schering Pharma AG in February 2008 and subsequently to Bayer Pharma AG in October 2011.

What is the condition?

Primary pulmonary hypertension (PPH) is a disease of unknown cause. The condition seriously restricts physical capacity, and in turn, the patient's quality of life. Its symptoms include shortness of breath

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(that occurs or gets worse with exercise), chest pain, and syncope (fainting, a sudden, temporary, loss of consciousness generally caused by insufficient oxygen in the brain).

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

At the time of designation, primary and certain forms of secondary pulmonary hypertension affected approximately 2.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 83,000 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?

Current medications for the management of the condition include calcium channel blockers (drugs that stop calcium entering the cells) and vasodilators (drugs that widen blood vessels).

Satisfactory argumentation has been submitted by the sponsor to justify assumption that iloprost might be of potential significant benefit for the treatment of the condition because it could cause fewer side-effects than the current treatment and improve the quality of life of the patients. 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?

According to the sponsor, iloprost acts by stopping thrombosis (the formation of a blood clot, thrombus inside a blood vessel). Furthermore, it is expected to protect endothelial cells that line the inner wall of blood vessels from narrowing (vasoconstriction) and also widen constricted blood vessels. The effects are thought to improve the symptoms of primary and certain forms of secondary pulmonary hypertension.

What is the stage of development of this medicine?

The effects of Iloprost have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with primary and secondary pulmonary hypertension forms of interest were ongoing.

At the time of submission, iloprost was not authorised anywhere in the world for the treatment of primary and of the following forms of secondary pulmonary hypertension: connective tissue disease pulmonary hypertension, drug-induced pulmonary hypertension, portopulmonary hypertension, pulmonary hypertension associated with congenital heart disease and chronic thromboembolic pulmonary hypertension or designated as orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 27 October 2000 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.
At the time of designation, this represented a population of 375,500,000 (Eurostat 2000).

Update: Iloprost (Ventavis) has been authorised in the EU since 16 September 2003 for the treatment of patients with primary pulmonary hypertension, classified as NYHA functional class III, to improve exercise capacity and symptoms.

More information on Ventavis 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	Iloprost	Treatment of primary and of the following forms of secondary pulmonary hypertension: connective tissue disease pulmonary hypertension drug-induced pulmonary hypertension portopulmonary hypertension pulmonary hypertension associated with congenital heart disease chronic thromboembolic pulmonary hypertension
Danish	Iloprost	Behandling af primær samt visse former for sekundær pulmonal hypertension: Bindevævssygdom associeret med pulmonal hypertension Medikamentel pulmonal hypertension Portal pulmonal hypertension Pulmonal hypertension associeret med medfødt hjertesygdom Kronisk tromboembolisk pulmonal hypertension
Dutch	Iloprost	Behandeling van primaire en onderstaande vormen van secundaire pulmonale hypertensie: pulmonale hypertensie in samenhang met een bindweefselaandoening door geneesmiddelen geïnduceerde pulmonale hypertensie portale pulmonaire hypertensie met aangeboren hartaandoening samenhangende pulmonaire hypertensie chronische trombo-embolische pulmonale hypertensie
Finnish	Iloprosti	Primaarisen keuhkoverenpaineen sekä eräiden sekundaaristen keuhkoverenpaineen muotojen hoito, kuten Sidekudossairauden aiheuttama pulmonaarinen hypertensio Lääkkeen indusoima kohonnut keuhkoverenpaine Porto-pulmonaarinen hypertensio Synnynnäiseen sydänvikaan liittyvä kohonnut keuhkoverenpaine Krooninen tromboembolinen pulmonaarinen hypertensio
French	iloprost	traitement d'hypertension artérielle pulmonaire primitive (HTAP) et de certaines formes d'hypertension artérielle pulmonaire secondaire telles que: hypertension pulmonaire associée aux connectivites hypertension artérielle pulmonaire iatrogène hypertension pulmonaire portale hypertension pulmonaire associée à une cardiopathie congénitale hypertension artérielle pulmonaire thrombo-embolique chronique

[1] At the time of designation

Language	Active Ingredient	Indication
German	Iloprost	Behandlung der primären und folgender Formen der sekundären pulmonalen Hypertonie: pulmonale Hypertonie in Zusammenhang mit Bindegewebserkrankungen arzneimittelinduzierte pulmonale Hypertonie portal bedingte Hypertonie pulmonale pulmonale Hypertonie in Zusammenhang mit einer angeborenen Herzkrankheit chronische thromboembolische pulmonale Hypertonie
Greek	Ιλοπρόστη	Θεραπεία της πρωτοπαθούς και των ακόλουθων μορφών δευτεροπαθούς πνευμονικής υπέρτασης: Πνευμονική υπέρταση σχετιζόμενη με νόσο συνδετικών ιστών Πνευμονική υπέρταση προκαλούμενη από φάρμακα Πυλαία πνευμονική υπέρταση Πνευμονική υπέρταση σχετιζόμενη με συγγενή καρδιακή νόσο Χρόνια θρομβοεμβολική πνευμονική υπέρταση
Italian	Iloprost	Trattamento dell' ipertensione polmonare primaria e delle seguenti forme di ipertensione polmonare secondaria quali: l'ipertensione polmonare in malattie del tessuto connettivo l'ipertensione polmonare iatrogena l'ipertensione porto-polmonare l'ipertensione polmonare associata a cardiopatia congenita l'ipertensione polmonare cronica tromboembolica
Portuguese	Iloproste	Tratamento de hipertensão pulmonar primária e das seguintes formas secundárias de hipertensão pulmonar: Hipertensão pulmonar associada a doença dos tecidos conjuntivos Hipertensão pulmonar induzida por fármacos Hipertensão pulmonar portal Hipertensão pulmonar associada a doença cardíaca congénita Hipertensão pulmonar tromboembólica crónica
Spanish	Iloprost	Tratamiento de hipertensión pulmonar primaria y de las siguientes formas de hipertensión pulmonar secundaria: Enfermedad del tejido conjuntivo asociada a hipertensión pulmonar Hipertensión pulmonar inducida por fármacos Hipertensión pulmonar portal Hipertensión pulmonar asociada a cardiopatía congénita Hipertensión pulmonar tromboembólica crónica
Swedish	Iloprost	Behandling av primär och av f öljande former av sekundär pulmonell hypertoni: Pulmonell hypertoni i samband med Bindvävssjukdom Pulmonell hypertoni inducerad av läkemedel Portal pulmonell hypertoni Pulmonell hypertoni i samband med kongenital hjärtsjukdom Kronisk tromboembolisk pulmonell hypertoni