



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-C]pyridine-3,6(2H,5H)-dione for the treatment of idiopathic pulmonary fibrosis

On 26 November 2010, orphan designation (EU/3/10/802) was granted by the European Commission to Fulcrum Pharma (Europe) Ltd, United Kingdom, for 2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-C]pyridine-3,6(2H,5H)-dione for the treatment of idiopathic pulmonary fibrosis.

The sponsorship was transferred to GenKyoTex Innovation S.A.S, France, in August 2011.

What is idiopathic pulmonary fibrosis?

Idiopathic pulmonary fibrosis is a long-term disease of the lungs characterised by the progressive formation of hard tissue in the lining of the lungs. 'Idiopathic' means that the cause of the disease is unknown. As the tissue becomes thicker and forms scars, the lungs become unable to work normally, reducing the transfer of oxygen from the air into the blood. Patients with idiopathic pulmonary fibrosis have a persistent cough, frequent lung infections and severe shortness of breath that worsens over time.

Idiopathic pulmonary fibrosis is a long-term debilitating disease that may be life-threatening because the lungs gradually lose their ability to work properly.

What is the estimated number of patients?

At the time of designation, idiopathic pulmonary fibrosis affected approximately 3 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 152,000 people, and is below the threshold 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. This represents a population of 506,500,000 (Eurostat 2010).



What treatments are available?

At the time of designation, corticosteroids (anti-inflammatory medicines) were authorised in the EU for the treatment of idiopathic pulmonary fibrosis. Medicines that reduce the activity of the immune system (the body's natural defences) were also used. In some patients, the disease needed to be treated with a lung transplant.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with idiopathic pulmonary fibrosis because early studies in experimental models show that it works in a different way to existing treatments and might improve the outcome of patients with this condition. 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?

The medicine is expected to work by blocking the action of an enzyme called 'NADPH oxidase 4'. This enzyme is thought to be responsible for the production of toxic molecules containing oxygen, which are involved in causing the lung damage seen in idiopathic pulmonary fibrosis. By blocking the actions of NADPH oxidase 4, the medicine is expected to reduce lung damage, thereby slowing down or reversing the symptoms of the disease.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with idiopathic pulmonary fibrosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for idiopathic pulmonary fibrosis. Orphan designation of the medicine had been granted in the United States of America for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 September 2010 recommending the granting of this designation.

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 European Union) 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	2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-C]pyridine-3,6(2H,5H)-dione	Treatment of idiopathic pulmonary fibrosis
Bulgarian	2-(2-хлорфенил)-4-[3-(диметиламино)фенил]-5-метил-1H-пиразоло[4,3-с]пиридин-3,6(2H, 5H)-дион	Лечение на идиопатична белодробна фиброза
Czech	2-(2-chlorfenyl)-4-[3-(dimethylamino)fenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Léčba idiopatické plicní fibrózy
Danish	2-(2-klorofenyl)-4-[3-(dimethylamino)fenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandling af idiopatisk lungefibrose
Dutch	2-(2-chloorfenyl)-4-[3-(dimethylamino)fenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H, 5H)-dion	Behandeling van idiopathische longfibrose
Estonian	2-(2-klorofenüül)-4-[3-(dimetüülamino)fenüül]-5-metüül-1H-pürasolo[4,3-c]püridiin-3,6(2H, 5H)-dioon	Idiopaatilise kopsufibroosi ravi
Finnish	2-(2-kloorifenyyl)-4-[3-(dimetyyliamino)fenyyl]-5-metyyli-1H-pyratsolo[4,3-c]pyridiini-3,6(2H, 5H)-dioni	Idiopaattisen keuhkofibroosin hoito
French	2-(2-chlorophényl)-4-[3-(diméthylamino)phényl]-5-méthyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H, 5H)-dione	Traitement de la fibrose pulmonaire idiopathique
German	2-(2-chlorphenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandlung von Idiopathischer Pulmonaler Fibrose
Greek	2-(2-χλωροφαινυλο)-4-[3-(διμεθυλάμινο)φαινύλ]-5-μεθυλο-1H-πυραζολο[4,3-с]πυριδινό-3,6(2H, 5H)-διόνη	Θεραπεία της ιδιοπαθούς πνευμονικής ίνωσης
Hungarian	2-(2-klorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridin-3,6(2H, 5H)-dion	Idiopathiás tüdőfibrózis kezelése
Italian	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridin-3,6(2H, 5H)-dione	Trattamento della fibrosi polmonare idiopatica
Latvian	2-(2-hlorofenil)-4-[3-(dimetilamīn)fenil]-5-metil-1H-pirazolo[4,3-c]piridīn-3,6(2H, 5H)-dions	Idiopātiskās plaušu fibrozes ārstēšana
Lithuanian	2-(2-chlorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridino-3,6(2H, 5H)-dionas	Idiopatinės plaučių fibrozės gydymas
Maltese	2-(2-chlorophenyl)-4-[3-(dimethylamino)phenyl]-5-methyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H, 5H)-dione	Kura tal-fibrozi pulmonari idjopatika
Polish	2-(2-chlorofenyl)-4-[3-(dimetyloamino)fenyl]-5-metylo-1H-pirazolo[4,3-c]pirydyno-3,6(2H,5H)-dion	Leczenie idiopatycznego zwłóknienia płuc
Portuguese	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazol[4,3-c]piridina-3,6(2H, 5H)-diona	Tratamento da fibrose pulmonar idiopática

¹ At the time of designation

Romanian	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazolo[4,3-c]piridin-3,6(2H, 5H)-dionă	Tratamentul fibrozei pulmonare idiopatice
Slovak	2-(2-chlórfenyl)-4-[3-(dimetylaminó)fenyl]-5-metyl-1H-pyrazolo[4,3-c]pyridín-3,6(2H, 5H)-dión	Liečba idiopatickej pľúcnej fibrózy
Slovenian	2-(2-klorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pyrazolo[4,3-c]piridin-3,6(2H, 5H)-dion	Zdravljenje idiopatske pljučne fibroze
Spanish	2-(2-clorofenil)-4-[3-(dimetilamino)fenil]-5-metil-1H-pirazol [4,3-c]piridina-3,6(2H, 5H)-diona	Tratamiento de la fibrosis pulmonar idiopática
Swedish	2-(2-klorfenyl)-4-[3-(dimetylaminó)fenyl]-5-metyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandling av idiopatisk lungfibros
Norwegian	2-(2-klorfenyl)-4-[3-(dimetylaminó)fenyl]-5-metyl-1H-pyrazolo[4,3-c]pyridin-3,6(2H, 5H)-dion	Behandling av idiopatisk lungefibrose
Icelandic	2-(2-klórófenýl)-4-[3-(tvímetylaminó)fenýl]-5-metýl-1H-pýrazóló[4,3-c]pýridín-3,6(2H, 5H)-díón	Meðferð sjálfvakinnar bandvefsmýndunar í lungum