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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(R)-3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropanenitrile phosphate for the treatment of chronic idiopathic myelofibrosis

First publication	22 June 2009
Rev.1: sponsor's change of address	17 November 2010
Rev.2: transfer of sponsorship	3 March 2011
Rev.3: information about Marketing Authorisation	11 September 2013
Rev.4: sponsor's change of address	30 January 2015
Rev.5: withdrawal from the Community Register	13 April 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.	

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in February 2015 on request of the Sponsor.

On 7 November 2008, orphan designation (EU/3/08/572) was granted by the European Commission to Incyte Corporation Ltd, United Kingdom, for (R)-3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropanenitrile phosphate for the treatment of chronic idiopathic myelofibrosis.

The sponsorship was transferred to Novartis Europharm Limited, United Kingdom, in September 2010.

What is chronic idiopathic myelofibrosis?

Chronic idiopathic myelofibrosis is a disease in which cancer cells are found in the blood and in the bone marrow. The bone marrow is the spongy tissue inside the large bones in the body. Normally the bone marrow makes cells called "blasts" that mature into several different types of blood cells that have specific functions in the body. These include red cells, white cells and platelets. Red blood cells carry oxygen and other materials to all tissues of the body. White blood cells fight infection. Platelets make the blood clot. When myelofibrosis develops, the bone marrow produces large number of

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abnormal blood cells. In chronic idiopathic myelofibrosis the abnormal population of cells produce substances that alter the growth media of bone marrow and makes bone marrow very dense and rigid. As the abnormal bone marrow environment is no more adequate for the cells, some migrate to other sites where proliferation and maturation take place.

Chronic idiopathic myelofibrosis is life threatening, in particular due to the decreased life expectancy of patients.

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

At the time of designation, chronic idiopathic myelofibrosis affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 25,000 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).

What treatments are available?

At the time of submission, hydroxyurea was authorised in the Community for the treatment of the condition. Other drugs were used for the treatment of symptoms of the disease such as androgen, glucocorticoids or erythropoietin for anaemia; splenectomy (surgical removal of the spleen) was performed in case of excessive enlargement of the spleen (splenomegaly); and bone marrow transplantation in some patients.

How is this medicine expected to work?

Protein kinases are enzymes that regulate many functions in the cell. In chronic idiopathic myelofibrosis a chain of these molecules are involved in the development of the disease. This is known as JAK pathway. The product is an inhibitor of the JAK pathway and, by doing this, it is expected to inhibit the development of the disease and reverse some of the negative consequences derived form the condition.

What is the stage of development of this medicine?

The effects of (R)-3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropanenitrile phosphate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with chronic idiopathic myelofibrosis were ongoing.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 September 2008 recommending the granting of this designation.

Update: (R)-3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropanenitrile phosphate (Jakavi) has been authorised in the EU since 23 August 2012 for treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post-polycythaemia-vera myelofibrosis or post-essential-thrombocythaemia myelofibrosis.

[*]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 502,800,000 (Eurostat 2008).

More information on Jakavi 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 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 languages[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	(R)-3-(4-(7H-pyrrolol[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropanenitrile phosphate	Treatment of chronic idiopathic myelofibrosis
Bulgarian	(R)-3-(4-(7H-пиролол[2,3-d]пиримидин-4-ил)-1H-пиразол-1-ил)-3-циклопентил пропаненитрил фосфат	Лечение на хронична идеопатична миелофиброза
Czech	(R)-3-(4-(7H-pyrrolol[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyklopentylpropanonitril fosfát	Léčba chronické idiopatické myelofibrózy
Danish	(R)-3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropannitril fosfat	Behandling af kronisk idiopatisk myelofibrose
Dutch	(R)-3-(4-(7H-pyrrolo[2,3-d]pyrimidine-4-yl)-1H-pyrazool-1-yl)-3-cyclopentylpropaannitrielfosfaat	Behandeling van chronische idiopathische myelofibrose
Estonian	(R)-3-(4-(7H-pürrolool[2,3-d]pürimidiin-4-üül)-1H-pürasool-1-üül)-3-tsüklopentüülpropaannitriilfosfaat	Kroonilise idiopaatilise müelofibroosi ravi
Finnish	(R)-3-(4-(7H-pyrrololi[2,3-d]pyrimidin-4-yyli)-1H-pyratsol-1-yyli)-3-syklopentyylipropaanitriilifosfaatti	Kroonisen idiopaattisen myelofibroosin hoito
French	Phosphate de (R)-3-(4-(7H-pyrrolol[2,3-d]pyrimidine-4-yl)-1H-pyrazol-1-yl)-3-cyclopentyl-propanenitrile	Traitement de la splénomégalie myéloïde chronique
German	(R)-3-(4-(7H-Pyrrolol[2,3-d]pyrimidin-4-yl)-1H-Pyrazol-1-yl)-3-Cyclopentylpropannitrilphosphat	Behandlung der chronischen idiopathischen Myelofibrose
Greek	φωσφορικό (R)-3-(4-(7H-πυρολολ[2,3-d]πυριμιδιν-4-υλ)-1H-πυραζολ-1-υλ)-3-κυκλοπεντυλπροπανονιτρίλιο	Θεραπεία της χρόνιας ιδιοπαθούς μυελοσκλήρυνσης
Hungarian	(R)-3-(4-(7H-pirrolol[2,3-d]pirimidin-4-il)-1H-pirazol-1-il)-3-ciklopentilpropánnitril-foszfát	Krónikus idiopátiás mielofibrózis kezelése
Italian	(R)-3-(4-(7H-pirrolol[2,3-d]pirimidin-4-il)-1H-pirazol-1-il)-3-ciclopentil-propanonitrile fosfato	Trattamento della mielofibrosi idiopatica cronica
Latvian	(R)-3-(4-(7H-pirol[2,3-d]pirimidīn-4-il)-1H-pirazol-1-il)-3-ciklopentilpropānnitrila fosfāts	Hroniskas idiopātiskas mielofibrozes ārstēšana
Lithuanian	(R)-3-(4-(7H-pirolol[2,3-d]pirimidin-4-il)-1H-pirazol-1-il)-3-ciklopentil propano nitrilo fosfatas	Lėtinės idiopatinės mielofibrozės gydymas

[1] At the time of designation

Language	Active Ingredient	Indication
Maltese	(R)-3-(4-(7H-pyrrolol[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyclopentylpropanenitrile phosphate	Kura tal-mjelofibrożi idjopatika kronika
Polish	fosforan (R)-3-(4-(7H-pirolol[2,3-d]pirymidyn-4-il)-1H-pirazol-1-il)-3-cyklopentylo-propanonitrylu	Leczenie pacjentów z przewlekłą idiopatyczną mielofibrozą
Portuguese	Fosfato de (R)-3-(4-(7H-pirrolol[2,3-d]pirimidina-4-il)-1H-pirazol-1-il)-3-ciclopentilpropanonitrilo	Tratamento da mielofibrose idiopática crónica
Romanian	Fosfat de (R)-3-(4-(7H-pirolol[2,3-d]pirimidin-4-il)-1H-pirazol-1-il)-3-ciclopentil-propionitril	Tratamentul mielofibrozei idiopatice cronice
Slovak	(R)-3-(4-(7H-pyrolol[2,3-d]pyrimidín-4-yl)-1H-pyrazol-1-yl)-3-cyklopentylpropánnitril fosfát	Liečba chronickej idiopatickej myelofibrózy
Slovenian	(R)-3-(4-(7H-pirolol[2,3-d]pirimidin-4-il)-1H-pirazol-1-il)-3-ciklopentil-propan-nitril fosfat	Zdravljenje kronične idiopatične mielofibroze
Spanish	Fosfato de (R)-3-(4-(7H-pirrolol[2,3-d]pirimidina-4-il)-1H-pirazol-1-il)-3-ciclopentil propanonitrilo	Tratamiento de la mielofibrosis idiopática crónica
Swedish	(R)-3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-cyklopentylpropan-nitrilfosfat	Behandling av kronisk idiopatisk myelofibros
Norwegian	(R)-3-(4-(7H-pyrrolol[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-syklopentylpropannitrilfosfat	Behandling av kronisk idiopatisk myelofibrose
Icelandic	(R)-3-(4-(7H-pýrrolól (2,3-d]pýrimidín-4-ýl)-1H-pýrazól-1-ýl)-3-sýklópentýlprópannítríl fosfat	Meðhöndlun sjúklinga með beinmergsnetjuhersli (myelofibrosis)