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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-(cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamide, dihydrochloride salt for the treatment of post-polycythaemia vera myelofibrosis

First publication	16 August 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 5 August 2011, orphan designation (EU/3/11/886) was granted by the European Commission to Cres Pharmaceuticals Limited, United Kingdom, for N-(cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamide, dihydrochloride salt for the treatment of post-polycythaemia vera myelofibrosis.

The sponsorship was transferred to YM BioSciences (UK) Limited, United Kingdom, in February 2012 and subsequently to Gilead Sciences International Ltd, United Kingdom, in May 2013.

What is post-polycythaemia vera myelofibrosis?

Myelofibrosis is a disease in which the bone marrow (the spongy tissue inside the large bones where blood cells are produced) becomes dense and fibrous, and starts producing abnormal immature blood cells that replace the normal blood cells. It can develop following polycythaemia vera (overproduction of red blood cells), in which case the disease is known as post-polycythaemia vera myelofibrosis.

In this disease, some immature blood cells migrate from the bone marrow to other organs, such as the spleen and liver, where they mature. This causes the organs to become enlarged. Patients with the disease can develop several symptoms, including bone pain, fever, tiredness, weakness, weight loss, infections and bleeding.

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Post-polycythaemia vera myelofibrosis is a debilitating disease that is long lasting and life threatening because it can lead to severe anaemia (low red blood cell counts) and infections, and can result in leukaemia (cancer of the white blood cells).

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

At the time of designation, post-polycythaemia vera myelofibrosis affected less than 0.15 in 10,000 people in the European Union (EU). This is equivalent to a total of fewer than 8,000 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?

At the time of designation, although hydroxycarbamide and busulfan were authorised in the EU for primary myelofibrosis (myelofibrosis of unknown cause), there were no treatments authorised specifically for post-polycythaemia vera myelofibrosis. Medicines were authorised to treat the symptoms, including erythropoietin (a hormone that stimulates the production of red blood cells) to treat anaemia, and surgery or radiation to remove or shrink the enlarged spleen. In some patients, allogeneic stem-cell transplantation was used to treat the disease. This is a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow.

How is this medicine expected to work?

This medicine is thought to work by blocking some enzymes known as Janus kinases (JAKs). These enzymes can be found in some receptors on the surface of cells and are involved in the reproduction and growth of blood cells. In myelofibrosis, JAKs are more active than normal. By blocking these enzymes, this medicine is expected to slow down the abnormal growth of blood cells, reducing the symptoms of the disease.

What is the stage of development of this medicine?

The effects of N-(cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamide, dihydrochloride salt have been evaluated in experimental models.

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

At the time of submission, this medicine was not authorised anywhere in the EU for post-polycythaemia vera myelofibrosis. Orphan designation of the medicine had been granted in the United States of America for myelofibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 May 2011 recommending the granting of this designation.

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[*]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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	N-(cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamide, dihydrochloride salt	Treatment of post-polycythaemia vera myelofibrosis
Bulgarian	N-(цианометил)-4-(2-{[4-(морфолин-4-ил)фенил]амино}пиримидин-4-ил)бензамид дихидрохлорид сол	Лечение на миелофиброза след полицитемия вера
Czech	N-(kyanomethyl)-4-(2-{[4-(morfolin-4-yl)fenyl]amino}pyrimidin-4-yl)benzamid dihydrochlorid sůl	Léčba post-polycytemické myelofibrózy
Danish	N-(cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamid-dihydrochlorid-salt	Behandling af post polycythæmia vera myelofibrose
Dutch	N-(cyanomethyl)-4-(2-{[4-(morfoline-4-yl)fenyl]amino}pyrimidine-4-yl)benzamidedihydrochloridezout	Behandeling van myelofibrosis volgend op polycythaemia vera
Estonian	N-(tsüanometüül)-4-(2-{[4-(morfoliin-4-üül)fenüül]amiino}pürimidiin-4-üül)bensamiid dihüdrokloriid sool	Post- polycythemia vera müelofibroosi ravi
Finnish	N-(syanometyyli)-4-(2-{[4-(morfoliini-4-yyli)fenyyli]amino}pyrimidiini-4-yyli)bentsamididihydrokloridisuola	Polysytemia veran jälkeisen myelofibroosin hoito
French	N-(cyanométhyle)-4-(2-{[4-(morpholine-4-yle)phényle]amino}pyrimidine-4-yle)benzamide dichlorhydrate	Traitement de la myélofibrose consécutive à une polyglobulie de Vaquez
German	N-(Cyanomethyl)-4-(2-{[4-(Morpholin-4-yl)Phenyl]amino}pyrimidin-4-yl)Benzamid Dihydrochloridsalz	Behandlung einer Myelofibrose nach Polycythämia vera
Greek	N-(κυανομέθυλ)-4(2-{[4-(μορφολινο-4-υλ)φαινυλ]αμινο}πυριμίδινο-4-υλ)βενζαμίδιο άλας διυδροχλωρικό	Θεραπεία της μυελοϊνωσης από αληθή πολυκυτταραιμία
Hungarian	N-(cianometil)-4-(2-{[4-(morfolin-4-yl)fenil]amino}pirimidin-4-yl)benzamid dihidroklorid só	Polycythaemia vera-t követő mielofibrózis kezelésére
Italian	N-(cianometil)-4-(2-{[4-(morfolin-4-ile)fenil]ammino}pirimidin-4-ile)benzamide sale dicloridrato	Terapia della mielofibrosi post-policitemia vera
Latvian	N-(ciānmetil)-4-(2-{[4-(morfolīn-4-il)fenil]amino}pirimidin-4-il)benzamīda dihidrohlorīda sāls	Pēc-polycythemia vera mielofibrozes ārstēšana
Lithuanian	N-(cianometil)-4-(2-{[4-(morfolin-4-il)fenil]amino}pirimidin-4-il)benzamidas dihidrochlorido druska	Mielofibrozės gydymas po tikrosios policitemijos

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Melħ dihydrochloride ta' N-(cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamide	Kura tal-mjelofibrożi konsegwenti għal policitemija vera
Polish	N-(cyjanometylo)-4-(2-{[4-(morfolin-4-ylo)fenylo]amino}pirymidyn-4-ylo)benzamid dichlorowodorek	Leczenie mielofibrozy wywołanej czerwienicą prawdziwą
Portuguese	N-(cianometil)-4-(2-{[4-(morfolina-4-il)fenil]amino}pirimidina-4-il)cloridrato de benzamida	Tratamento da mielofibrose devida a policitemia vera
Romanian	Diclorhidrat de N-(cianometil)-4-(2-{[4-(morfolin-4-yl)fenil]amino}pirimidin-4-yl)benzamidă	Tratamentul mielofibrozei post-policitemie vera
Slovak	N-(cyanometyl)-4-(2-{[4-(morfolín-4-yl)fenyl]amino}pyrimidín-4-yl)benzamid dihydrochlorid	Liečba myelofibrózy po pravej polycytémii
Slovenian	N-(cianometil)-4-(2-{[4-(morfolin-4-il)fenil]amino}pirimidin-4-il)benzamid dihidroklorid soli	Zdravljenje mielofibroze, nastale po pravi policitemiji
Spanish	N-(cianometil)-4-(2-{[4-(morfolina-4-il)fenil]amino}pirimidina-4-il)benzamida sal de dihidrocloruro	Tratamiento de la mielofibrosis secundaria a policitemia vera
Swedish	N-(cyanometyl)-4-(2-{[4-(morfolin-4-yl)fenyl]amino}pyrimidin-4-yl)benzamid dihydrokloridsalt	Behandling av post-polycytemia vera myelofibros
Norwegian	N-(cyanometyl)-4-(2-{[4-(morfolin-4-yl)fenyl]amino}pyrimidin-4-yl)benzamid dihydroklorid	Behandling av myelofibrose sekundært til polycytemia vera
Icelandic	N-(sýanómetýl)-4-(2-{[4-(morfoólín-4-ýl)fenýl]amínó}pýrimídín-4-ýl)benzamíð díhýdróklóríð salt	Til meðferðar á mýelófíbrósu í kjölfar polycythemia vera