



## Committee for Orphan Medicinal Products

### Public summary of positive opinion for orphan designation of

### 1-cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzoimidazol-2-yl)-1H-pyrazol-4-yl]- urea for the treatment of acute myeloid leukaemia

On 26 November 2009, orphan designation (EU/3/09/693) was granted by the European Commission to Astex Therapeutics Ltd, United Kingdom, for 1-cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzoimidazol-2-yl)-1H-pyrazol-4-yl]-urea for the treatment of acute myeloid leukaemia.

#### What is acute myeloid leukaemia?

Acute myeloid leukaemia (AML) is a cancer of the white blood cells (cells that fight against infections). In patients with AML, the bone marrow (the spongy tissue inside the large bones) produces large numbers of abnormal, immature white blood cells called 'blasts'. These abnormal cells quickly build up in large numbers in the bone marrow and are found in the blood.

AML is a life-threatening disease because these immature cells take the place of the normal white blood cells, reducing the patient's ability to fight infections.

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

At the time of designation, AML affected less than 2 in 10,000 people in the European Union (EU)\*. This is equivalent to a total of fewer than 101,000 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 knowledge of the Committee for Orphan Medicinal Products (COMP).

#### What treatments are available?

Treatment for AML is complex and depends on a number of factors including the extent of the disease, whether it has been treated before, and the patient's age, symptoms and general state of health. At the time of designation, the main treatments for AML were chemotherapy (medicines to treat cancer) and bone marrow transplantation (a complex procedure where the bone marrow of the patient is destroyed and replaced with bone marrow from a matched donor).

The sponsor has provided sufficient information to show that 1-cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzoimidazol-2-yl)-1H-pyrazol-4-yl]-urea might be of significant benefit for patients with AML because it works in a different way to existing treatments and because early studies indicate that it might represent an alternative treatment for patients with this condition. These assumptions will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

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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. This represents a population of 504,800,000 (Eurostat 2009).

**How is this medicine expected to work?**

1-Cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea is expected to work by blocking several types of enzymes known as protein kinases, including tyrosine kinases. Tyrosine kinases can be found in some receptors on the surface of AML cells that are involved in stimulating the cells to divide uncontrollably. By blocking these and other kinases, this medicine is expected to control cell division, slowing down the growth and spread of the cancer cells.

**What is the stage of development of this medicine?**

The effects of 1-cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the designated product in patients with AML were ongoing.

At the time of submission, 1-cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea was not authorised anywhere in the EU for AML 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 7 October 2009 recommending the granting of this designation.

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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 Community) 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:**

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Withdrawn

**Translations of the active ingredient and indication in all official EU languages,  
Norwegian and Icelandic**

Language	Active ingredient	Indication
English	1-Cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea	Treatment of acute myeloid leukaemia
Bulgarian	1-циклопропил-3-[3-(5-морфолин-4-илметил-1H-бензоимидазол-2-ил)-1H-пиразол-4-ил]-урея	Лечение на остра миелоидна левкемия
Czech	1-Cyklopropyl-3-[3-(5-morfolin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea	Léčba akutní myeloidní leukémie
Danish	1-Cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea	Behandling af akut myeloid leukæmi
Dutch	1-Cyclopropyl-3-[3-(5-morfoline-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-ureum	Behandeling van acute myeloïde leukemie
Estonian	1-tsüklopropüül-3-[3-(5-morfoliin-4-üülmetüül-1H-benzoimidasool-2-üül)-1H-pürasool-4-üül]-uurea	Akuutse müeloidse leukeemia ravi
Finnish	1-syklopropyyli-3-[3-(5-morfoliini-4-yylimetyyli-1H-bentsimidatsoli-2-yyli)-1H-pyratsoli-4-yyli]-urea	Akuutin myelooisen leukemian hoito
French	1-cyclopropyl-3-[3-(5-morpholin-4-ylméthyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urée	Traitement de la leucémie aiguë myéloïde
German	1-Cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-harnstoff	Behandlung der akuten myeloischen Leukämie
Greek	1-κυκλοπροπυλο-3-[3-(5-μορφολιν-4-υλομεθυλο-1H-βενζοϊμιδαζολ-2-υλο)-1H-πυραζολ-4-υλο]-ουρία	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	1-cyclopropil-3-[3-5-morfolin-4-ilmetil-1H-benzimidazol-2-il)-1H-pirazol-4-il]-urea	Akut myeloid leukaemia kezelése
Italian	1-ciclopropil-3-[3-(5-morfolin-4-il-metil-1H-benzimidazol-2-il)-1H-pirazol-4-il]-urea	Trattamento della leucemia mieloide acuta
Latvian	1-ciklopropil-3-[3-(5-morfolīn-4-ilmetil-1H-benzimidazol-2-il)-1H-pirazol-4-il]-karbamīds	Akūtas mieloleikozes ārstēšana
Lithuanian	1-ciklopropil-3-[3-(5-morfolin-4-ilmetil-1H-benzimidazol-2-il)-1H-pirazol-4-il]-urėja	Ūmios mieloleukozės gydymas
Maltese	1-Cyclopropyl-3-[3-(5-morpholin-4-ylmethyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea	Kura tal-lewkimja mjeloidja akuta
Polish	1-cyklopropylo-3-[3-(5-morfolino-4-ylometylo-1H-benzimidazol-2-ylo)-1H-pirazol-4-ylo]-mocznik	Leczenie ostrej białaczki szpikowej
Portuguese	1-ciclopropil-3-[3-(5-morfolin-4-ilmetil-1H-benzimidazol-2-il)-1H-pirazol-4-il]-ureia	Tratamento da leucémia mielóide aguda
Romanian	1-Ciclopropil-3-[3-(5-morfolin-4-ilmetil-1H-benzimidazol-2-il)-1H-pirazol-4-il]-uree	Tratamentul leucemiei mieloidice acute
Slovak	1-Cyklopropyl-3-[3-(5-morfolín-4-ylmetyl-1H-benzimidazol-2-yl)-1H-pyrazol-4-yl]-urea	Liečba akútnej myeloidkej leukémie
Slovenian	1-ciklopropil-3-[3-(5-morfolin-4-ilmetil-1H-benzimidazol-2-il)-1H-pirazol-4-il]-urea	Zdravljenje akutne mieloične levkemije

Spanish	1-ciclopropil-3-[3-(5-morfolina-4-ilmetilo-1H-benzoimidazola-2-il)-1H-pirazola-4-il]-urea	Tratamiento de la leucemia mieloide aguda
Swedish	1-Cyklopropyl-3-[3-(5-morfolin-4-ylmetyl-1H-benzoimidazol-2-yl)-1H-pyrazol-4-yl]-urea	Behandling av akut myeloisk leukemi
Norwegian	1-syklopropyl-3-[3-(5-morfolin-4-ylmetyl-1H-benzoimidazol-2-yl)-1H-pyrazole-4-yl]-urea	Behandling av akutt myelogen leukemi
Icelandic	1-cýklóprópýl-3-[3-(5-morfólín-4-ýlmetyl-1H-benzóimidazól-2-ýl)-1H-pýrazól-4-ýl]-þvagefni	Meðferð við bráðu kyrningahvítblæði

Withdrawn