



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

11 November 2011  
EMA/COMP/23533/2010 Rev.1  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-methyl-4-(4-methylpiperazin-1-yl)-phenylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-ene-2-carboxamide benzoate for the treatment of acute myeloid leukaemia

*Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in October 2011 on request of the sponsor.*

On 23 March 2010, orphan designation (EU/3/10/729) was granted by the European Commission to Merck KGaA, Germany, for (1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-methyl-4-(4-methylpiperazin-1-yl)-phenylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-ene-2-carboxamide benzoate 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).

---

\*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?**

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 (1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-methyl-4-(4-methylpiperazin-1-yl)-phenylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-ene-2-carboxamide benzoate might be of significant benefit for patients with AML because early studies show that it might improve the treatment 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?**

This medicine is expected to work by blocking enzymes called 'aurora kinases'. These enzymes play an essential role in the division of cells, by controlling the movement of chromosomes. By blocking aurora kinases, the medicine is expected to disrupt the division of cancerous cells in AML, slowing down the development of the disease.

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

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

At the time of submission of the application for orphan designation, clinical trials with this medicine that included patients with AML were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for AML or designated as an 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 6 January 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 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:

Merck KGaA  
Frankfurter Str. 250  
64293 Darmstadt  
Germany  
Telephone: +49 61 51 72 70 0  
Telefax: +49 61 51 72 20 00  
E-mail: [service@merck.de](mailto:service@merck.de)

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-methyl-4-(4-methylpiperazin-1-yl)-phenylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-ene-2-carboxamide benzoate	Treatment of acute myeloid leukaemia
Bulgarian	(1S, 2S, 3R,4R)-3-(5-флуоро-2-(3-метил-4-(4-метилпиперазин-1-ил)-фениламино)-пиримидин-4-иламино)-бицикло[2.2.1]хепт-5-ен-2-карбоксамид бензоат	Лечение на остра миелоидна левкемия
Czech	(1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-metyl-4-(4-metyl-piperazin-1-yl)-fenylamino)-pyrimidin-4-ylamino)-bicyklo[2.2.1]hept-5-en-2-karboxamidbenzoát	Léčba akutní myeloidní leukémie
Danish	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-methyl-4-(4-methylpiperazin-1-yl)-phenylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-ene-2-carboxamidbenzoat	Behandling af akut myeloid leukæmi
Dutch	(1S, 2S, 3R, 4R)-3-(5-Floor-2-(3-methyl-4-(4-methylpiperazine-1-yl)-fenylamino)-pyrimidine-4-ylamino)-bicyclo[2.2.1]hept-5-ene-2-carboxamide benzoaat	Behandeling van acute myeloïde leukemie
Estonian	(1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-metüül-4-(4-metüülpiperasiin-1- üül)-fenüülamino)-pürimidiin-4-üülamino)-bitsüklo[2.2.1]hept-5-een-2-karboksamiidbensoaat	Akuutse müeloidse leukeemia ravi
Finnish	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-metyyli-4-(4-metyyลิปiperatsiini-1-yyli)-fenyylimino)-pyrimidiini-4-yyliamino)-bisyklo[2.2.1]hept-5-eeni-2-karboksiamidibentsoatti	Akuutin myelooisen leukemian hoito
French	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-méthyl-4-(4-méthylpipérazine-1-yl)-phénylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-ène-2-carboxamide benzoate	Traitement de la leucémie aiguë myéloïde
German	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-methyl-4-(4-methylpiperazin-1-yl)-phenylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-en-2-carboxamid benzoat	Behandlung der akuten myeloischen Leukämie
Greek	(1S, 2S, 3R, 4R)-3-(5-Φθόρο-2-(3-μεθυλ-4-(4-μεθυλπιπεραζίνη-1-γλ)-φαινυλάμινο)-πυριμιδίνη-4-γλ-άμινο)-δικύκλο[2.2.1]επτ-5-εν-2- βενζοϊκό καρβοξαμίδιο	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	(1S,2S,3R,4R)-3-(5-fluor-2-(3-metil-4-(4-metilpiperazin-1-il)-fenilamino)-pirimidin-4-ilamino)-biciklo[2.2.1]hept-5-én-2-karboxamidbenzoát	Akut myeloid leukaemia kezelése
Italian	(1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-metil-4-(4-metilpiperazina-1-il)-fenilamino)-pirimidin-4-ilamino)-biciclo[2.2.1]ept-5-en-2-carbossamide benzoato	Trattamento della leucemia mieloide acuta

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Latvian	(1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-metil-4-(4-metilpiperazīn-1-il)-fenilamino)-pirimidīn-4-ilamino)-bīciklo[2.2.1]hept-5-ēn-2-karboksamīda benzoāts	Akūtas mieloleikozes ārstēšana
Lithuanian	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-metil-4-(4-metilpiperazīn-1-il)-fenilamin)-pirimidin-4-ilamin)-bīciklo[2.2.1]hept-5-ene-2-karboksiamido benzoatas	Ūmios mieloleukozės gydymas
Maltese	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-methyl-4-(4-methylpiperazīn-1-yl)-phenylamino)-pyrimidin-4-ylamino)-bicyclo[2.2.1]hept-5-ene-2-carboxamide benzoate	Kura tal-lewkimja mjeloidja akuta
Polish	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-metylo-4-(4-metylopiperazyn-1-ylo)-fenylamino)-pīrymidyn-4-yloamino)-bīcyklo[2.2.1]hept-5-en-2-karboksamīdu benzoesan	Leczenie ostrej białaczki szpikowej
Portuguese	Benzoato de (1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-metil-4-(4-metilpiperazina-1-il)-fenilamino)-pirimidina-4-ilamino)-bīcīclo[2.2.1]hept-5-eno-2-carboxamida	Tratamento da leucémia mielóide aguda
Romanian	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-metil-4-(4-metilpiperazīn-1-il)-fenilamino)-pirimidīn-4-ilamino)-bīcīclo[2.2.1]hept-5-enă-2-carboxamīdă benzoat	Tratamentul leucemiei mieloidice acute
Slovak	(1S,2S,3R,4R)-3-(5-fluoro-2-(3-metyl-4-(4-metylpiperazín-1-yl)-fenylamino)-pyrimidín-4-ylamino)-bīcyklo[2.2.1]hept-5-én-2-karboxamīdbenzoát	Liečba akútnej myeloidkej leukémie
Slovenian	(1S, 2S, 3R, 4R)-3-(5-fluoro-2-(3-metil-4-(4-metilpiperazīn-1-il)fenilamino)pirimidīn-4-ilamino)bīcīklo[2.2.1]hept-5-en-2-karboksamīd benzoat	Zdravljenje akutne mieloične levkemije
Spanish	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-metil-4-(4-metil-1-piperacīnīl)-fenilamino)-4-pīrimidīnīlamino)-bīcīclo[2.2.1]5-hepteno-2-carboxamīda benzoato	Tratamiento de la leucemia mieloidice aguda
Swedish	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-metyl-4-(4-metylpiperazīn-1-yl)-fenylamino)-pyrimidīn-4-ylamino)-bīcyklo[2.2.1]hept-5-ene-2-karboxamīdbensoat	Behandling av akut myeloidisk leukemi
Norwegian	(1S, 2S, 3R, 4R)-3-(5-Fluoro-2-(3-metyl-4-(4-metylpiperazīn-1-yl)-fenylamino)-pyrimidīn-4-ylamino)-bīsyklo[2.2.1]hept-5-en-2-karboksamīd benzoat	Behandling av akutt myelogen leukemi
Icelandic	(1S, 2S, 3R, 4R)-3-(5- flúóró -2-(3-metýl-4-(4-metýlpíperazín-1-ýl)-fenýlamínó)-pýrimídín-4-ýlamínó)-bícýkló[2.2.1]hept-5-en-2-karboxamíð benzóat	Meðferð við bráðu kyrningahvítblæði