



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Document Date: London, 12 August 2009
Doc.Ref.: EMEA/COMP/577292/2007 Rev.1

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of

N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide for the treatment of acute myeloid leukaemia

On 31 January 2008, orphan designation EU/3/07/526 was granted by the European Commission to Pharmion Ltd, United Kingdom, for N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide for the treatment of acute myeloid leukaemia.

The sponsorship was transferred to Celgene Europe Limited, United Kingdom, in November 2008 and subsequently to CanReg (Europe) Limited, Ireland, in March 2009.

What is acute myeloid leukaemia?

Acute myeloid leukaemia is a disease in which cancer cells are found in the blood and 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 leukaemia develops, the bone marrow produces large numbers of abnormal blood cells. There are several types of leukaemias. In myeloid leukaemia blasts that are developing into white blood cells called granulocytes are affected. These blasts do not mature but multiply abnormally and accumulate in the bone marrow. Then, they are also found in the blood. Leukaemia can be acute (when it develops quickly with many blasts). Acute myeloid leukaemia is life-threatening.

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

At the time of designation, acute myeloid leukaemia affected less than 2.4 people in 10,000 per year in the European Union (EU)*. This is equivalent to a total of fewer than 120,000 people per year, which was considered to be below the threshold for orphan designation. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatment are available?

Treatment for leukaemia is complex and depends on a number of factors including the type of leukaemia, the extent of the disease and whether the leukaemia has been treated before. It also depends on the age, the symptoms, and the general health of the patient. The primary treatment of acute myeloid leukemia is chemotherapy (using drugs to kill cancer cells). Several products were authorised for the condition in the Community at the time of submission of the application for orphan drug designation. N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide might be of potential significant benefit for the treatment of acute myeloid leukaemia. The assumption will

*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 498,000,000 (Eurostat 2006).

have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

The genetic material of cells (DNA) is normally tightly bound around structures called histones. When histones are acetylated (a specific chemical status) the effect of this on DNA is that its information cannot be accessible for protein synthesis. N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide appears to block the activity of an enzyme, called histone deacetylase. Inhibition of the histone deacetylases has been linked to a decrease in multiplication of tumour cells and suppression of some tumours.

What is the stage of development of this medicine?

The effects of N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with acute myeloid leukaemia were ongoing.

N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide has received orphan designation in the European Union for treatment of Hodgkin's lymphoma on 14 September 2007. Orphan drug designation was granted in the United States for the treatment of Hodgkin's lymphoma.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 5 December 2007 a positive opinion recommending the grant of the above-mentioned 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 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:

Sponsor's contact details:

CanReg (Europe) Limited

Templetown

Carlingford

County Louth

Ireland

Telephone: +353 42 937 67 40

Telefax: +353 42 937 67 40

Patients associations' contact points:

Leukaemia Care

2 Shrubbery Avenue

Worcester

WR1 1QH

United Kingdom

0800 169 6680 (freephone for UK residents)

Telephone: +44 19 05 33 00 03 / +44 84 57 67 32 03

Telefax: +44 19 05 33 00 90

E-mail: enquiries@leukaemiaCARE.org.uk

DLH : Deutsche Leukämie- und Lymphom-Hilfe e.V.

Thomas-Mann-Straße 40

53111 Bonn

Germany

Telephone: +49 22 83 90 440

Telefax: +49 22 83 90 44 22

E-mail: info@leukaemie-hilfe.de

Associazione Italiana contro le Leucemie-linfomi e mieloma ONLUS

Via Ravenna 34

00161 Roma

Italy

Telephone: +39 06 44 03 763

Telefax: +39 06 44 04 226

E-mail: ail@ail.it

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

Language	Active Ingredient	Indication
English	N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide	Treatment of acute myeloid leukaemia
Bulgarian	N-(2-амино-фенил)-4-[(4-пиридин-3-ил-пиримидин-2-иламино)-метил] бензамид	Лечение на остра миелоидна левкемия
Czech	N- (2-amino-fenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamid	Léčba akutní myeloidní leukémie
Danish	N- (2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl]benzamid	Behandling af akut myeloid leukæmi
Dutch	N-(2-aminofenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide	Behandeling van acute myeloïde leukemie
Estonian	N-(2-aminofenüül)-4-[(4-püridiin-3-üül-pürimidiin-2-üülamino)-metüül] bensamiid	Akuutse müeloidse leukeemia ravi
Finnish	N-(2-aminofenyylä)-4-[(4-pyridiini-3-yyli-pyrimidiini-2-yyliamino)-metyyli]bentsamidi	Akuutin myelooisen leukemian hoito
French	N-(2-amino-phényl)-4-[(4-pyridine-3-yl-pyrimidine-2-ylamino)-méthyl] benzamide	Traitement de la leucémie aiguë myéloïde
German	N-(2-Aminophenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl]benzamid	Behandlung der akuten myeloischen Leukämie
Greek	N- (2-Αμινο-φαινύλ)-4-[(4-πυριδίν-3-ύλ-πυριμιδίν-2-ύλαμινο)-μεθύλ] βενζαμίδιο	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	N - (2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-il-amino)-metil] benzamid	Akut myeloid leukaemia kezelése
Italian	N- (2-Ammino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilammino)-metil] benzammide	Trattamento della leucemia mieloide acuta
Latvian	N- (2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamīda	Akūtas mieloleikozes ārstēšana
Lithuanian	N- (2-aminofenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamidas	Ūmios mieloleukozės gydymas
Maltese	N- (2-Amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide	Kura tal-lewkimja mjelojda akuta
Polish	N-(2-amino-fenyl)-4-[(4-pirydyn-3-yl-pyrimidin-2-ylamino)-metylo]benzamid	Leczenie ostrej białaczki szpikowej
Portuguese	N- (2-Amino-fenil)-4-[(4-piridina-3-il-pirimidina-2-ilamino)-metil] benzamida	Tratamento da leucemia mielóide aguda
Romanian	N-(2-aminofenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil]-bensamidă	Tratamentul leucemiei mieloide acute
Slovak	N-(2-amino-fenyl)-4-[(4-pyridín-3-yl-pyrimidín-2-yl-amino)-metyl]benzamid	Liečba akútnej myeloickej leukémie
Slovenian	N- (2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamid	Zdravljenje akutne mieloične levkemije
Spanish	N- (2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamida	Tratamiento de la leucemia mieloide aguda
Swedish	N-(2-aminofenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-metyl]-bensamid	Behandling av akut myeloisk leukemi

Norwegian	N- (2-aminofenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-metyl] benzamid	Behandling av akutt myelogen leukemi
Icelandic	N- (2-amínó-fenýl)-4-[(4-pýridín-3-ýl-pýrimídín-2-ýlamínó)-metýl] benzamíð	Meðferð við bráðu kyrringahvítblæði