



## 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 Hodgkin's lymphoma

On 14 September 2007, orphan designation (EU/3/07/478) was granted by the European Commission to Pharmion Ltd, UK, for N-(2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide for the treatment of Hodgkin's lymphoma.

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 Hodgkin's lymphoma?

Hodgkin's lymphoma is a type of cancer that develops in the lymphatic system. The lymphatic system is part of the body's immune system: the body's natural defence against infection and disease. It is a complex system made up of organs such as bone marrow (the spongy tissue inside the large bones in the body), thymus and spleen, and a network of lymph nodes throughout the body that are connected by lymphatic vessels. As lymphatic tissue is found throughout the body, Hodgkin's lymphoma can begin in almost any part of the body and can spread to almost any tissue or organ in the body.

Normally, the growth and duplication of lymphatic cells takes place in a controlled manner, however in Hodgkin's lymphoma this process is out of control and the cells continue to divide, developing into a tumour. Hodgkin's lymphoma can occur in both adults and children; however, treatment for adults may be different from treatment for children. Hodgkin's lymphoma can usually be cured, if found and treated early. Despite the available treatments Hodgkin's lymphoma remains a serious and life-threatening condition in certain patients.

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

At the time of designation, Hodgkin's lymphoma affected approximately 2.4 in 10,000 people in the European Union (EU)\*. This is equivalent to a total of around 120,000 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?

Three different types of standard treatment are available and used: chemotherapy (using drugs to kill cancer cells), radiotherapy (using high-energy x-rays or other types of high-energy rays to kill cancer cells) and surgery (removing all possible cancer tissue in an operation). Bone marrow transplantation is also used. Several treatments had been authorised 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 could be of potential significant benefit for the treatment of Hodgkin's lymphoma, because it may act in a different way to other types of treatment. Further, the product can be given orally three times per week, instead of as an

\*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).

injection (as is necessary for many of the currently authorised products). This assumption of significant benefit will have to be confirmed at the time of marketing authorisation, as this is necessary to maintain the orphan status.

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

N-(2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide acts by blocking the action of a group of enzymes (a protein that speeds biochemical reactions in the body) called histone deacetylases, which are involved in the proliferation of cancer cells. By blocking some of the subtypes of this enzyme, the product is expected to block cancer growth.

#### **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 Hodgkin's lymphoma were ongoing.

N-(2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide was not authorised anywhere in the world for treatment of Hodgkin's lymphoma, or designated as orphan medicinal product anywhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 25 July 2007 a positive opinion recommending the grant of the above-mentioned 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.

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

<b>Language</b>	<b>Active Ingredient</b>	<b>Indication</b>
English	N-(2-Amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide	Treatment of Hodgkin's lymphoma
Bulgarian	N-(2-амино-фенил)-4-[(4-пиридин-3-ил-пиримидин-2-иламино)-метил] бензамид	Лечение на лимфом на Ходжкин
Czech	N-(2-amino-fenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamid	Léčba Hodgkinova lymfomu
Danish	N-(2-amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl]benzamid	Behandling af Hodgkin lymfom
Dutch	N-(2-aminofenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide	Behandeling van Hodgkin lymfoom
Estonian	N-(2-aminofenüül)-4-[(4-püridiin-3-üül-pürimidiin-2-üülamino)-metüül] bensamiid	Hodgkini lümfoomi ravi
Finnish	N-(2-aminofenyylä)-4-[(4-pyridiini-3-yyli-pyrimidiini-2-yyliamino)-metyyli]bentsamidi	Hodgkinin lymfooman hoito
French	N-(2-amino-phényl)-4-[(4-pyridine-3-yl-pyrimidine-2-ylamino)-méthyl] benzamide	Traitement du lymphome de Hodgkin
German	N-(2-Aminophenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl]benzamid	Behandlung des Hodgkin-Lymphoms
Greek	N-(2-Αμινο-φαινολ)-4-[(4-πυριδιν-3-υλ-πυριμιδιν-2-υλαμινο)-μεθυλ] βενζαμίδιο	Θεραπεία του λεμφώματος Hodgkin
Hungarian	N-(2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-il-amino)-metil] benzamid	Hodgkin lymphoma kezelése
Italian	N-(2-Ammino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilammino)-metil] benzammide	Trattamento del linfoma di Hodgkin
Latvian	N-(2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamīda	Hodžkina limfomas ārstēšana
Lithuanian	N-(2-aminofenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamidas	Hodžkino limfomos gydymas
Maltese	N-(2-Amino-phenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-methyl] benzamide	Kura tal-limfoma ta' Hodgkin
Polish	N-(2-amino-fenylo)-4-[(4-pirydyn-3-yl-pirymidyn-2-ylamino)-metylo]benzamid	Leczenie chłoniaka Hodgkina (ziarnicy złośliwej)
Portuguese	N-(2-Amino-fenil)-4-[(4-piridina-3-il-pirimidina-2-ilamino)-metil] benzamida	Tratamento do linfoma de Hodgkin
Romanian	N-(2-aminofenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil]-bensamidă	Tratamentul limfomului Hodgkin
Slovak	N-(2-amino-fenyl)-4-[(4-pyridín-3-yl-pyrimidín-2-yl-amino)-metyl]benzamid	Liečba lymfómu Hodgkinovho typu
Slovenian	N-(2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamid	Zdravljenje Hodgkinovega limfoma
Spanish	N-(2-amino-fenil)-4-[(4-piridin-3-il-pirimidin-2-ilamino)-metil] benzamida	Tratamiento del linfoma de Hodgkin

Swedish	N-(2-aminofenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-metyl]-bensamid	Behandling av Hodgkin lymfom
Norwegian	N- (2-aminofenyl)-4-[(4-pyridin-3-yl-pyrimidin-2-ylamino)-metyl] benzamid	Behandling av Hodgkin-lymfom
Icelandic	N- (2-amínó-fenýl)-4-[(4-pýridín-3-ýl-pýrimídín-2-ýlamínó)-metýl] benzamíð	Meðferð við Hodgkins sjúkdómi

Withdrawn