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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl] for the treatment of chronic myeloid leukaemia

First publication	2 March 2010
Rev.1: information about Marketing Authorisation	11 September 2013
Rev.2: sponsor's change of address	9 March 2015
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 2 February 2010, orphan designation (EU/3/09/716) was granted by the European Commission to ARIAD Pharma Ltd, United Kingdom, for benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl] for the treatment of chronic myeloid leukaemia.

What is chronic myeloid leukaemia?

Chronic myeloid leukaemia (CML) is a cancer of the white blood cells (cells that fight against infections). In patients with CML, the bone marrow (the spongy tissue inside the large bones) produces large numbers of abnormal, immature white blood cells called 'blasts', so there are too many of them circulating in the blood. These blast cells are not fully developed and do not work properly. Over a period of time, they replace the normal white blood cells, red blood cells and platelets in the bone marrow.

CML is most common in adults and older people, but children may also be affected. The disease usually develops very slowly, which is why it is called 'chronic'. However, when it progresses, CML is a severe and life-threatening disease that is associated with poor overall survival.



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

At the time of designation, CML affected approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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 CML 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 CML 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 healthy bone marrow from a matched donor).

The sponsor has provided sufficient information to show that benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl] might be of significant benefit for patients with CML because it may represent an alternative treatment for patients with this condition, and because early studies indicate that it might be used in patients who do not respond to existing treatments. These assumptions 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?

Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl] belongs to a group of medicines called 'protein tyrosine kinase inhibitors'. These medicines work by blocking enzymes known as protein kinases. This medicine is expected to work mainly by blocking the protein kinase called 'BCR-ABL' kinase. This enzyme is produced by leukaemia cells, and causes them to multiply uncontrollably. By blocking BCR-ABL kinase, as well as other kinases, the medicine is expected to help to control the spread of leukaemia cells.

What is the stage of development of this medicine?

The effects of benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl] 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 CML were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for CML 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 3 December 2009 recommending the granting of this designation.

*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 506,300,000 (Eurostat 2010).

Update: Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl] (Iclusig) has been authorised in the EU since 01 July 2013. Iclusig is indicated in adult patients with chronic-phase, accelerated-phase or blast-phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib, who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate, or who have the T315I mutation;

More information on Iclusig can be found in the European public assessment report (EPAR) on the Agency's website: [ema.europa.eu/Find_medicine/Human_medicines/European Public Assessment Reports](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports)

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:

ARIAD Pharma Ltd
Riverbridge House
Guildford Road
Leatherhead
Surrey KT22 9AD
United Kingdom
Tel. +44 (0)1372 365 900
Fax +44 (0)800 2798 535
E-mail: antoine.buffet@ariad.com

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, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]	Treatment of chronic myeloid leukaemia
Bulgarian	Бензамид, 3-(2-имидазо[1,2-б]пиридазин-3-илетинил)-4-метил-N-[4-[(4-метил-1-пиперазинил)метил]-3-(трифлуорометил)фенил]	Лечение на хронична миелоидна левкемия
Czech	Benzamid, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]	Léčba chronické myeloidní leukémie
Danish	Benzamid, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]	Behandling af kronisk myeloid leukæmi
Dutch	Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]	Behandeling van chronische myeloïde leukemie
Estonian	Bensamiid, 3-(2-imidaso[1,2-b]püridasiin-3-üületünüül)-4-metüül-N-[4-[(4-metüül-1-piperasinüül)metüül]-3-(trifluorometüül)fenüül]	Kroonilise müeloidse leukeemia ravi
Finnish	Bentsamidi 3-(2-imidatso[1,2-b]pyridatsiini-3-yletynyli)-4-metyyli-N-[4-[(4-metyyli-1-piperatsinyli)metyyli]-3-(trifluorometyyli)fenyyli]	Kroonisen myelooisen leukemian hoito
French	Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-yléthynyl)-4-méthyl-N-[4-[(4-méthyl-1-pipérazinyl)méthyl]-3-(trifluorométhyl)phényl]	Traitement de la leucémie myéloïde chronique
German	Benzamid, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]	Behandlung der chronischen myeloischen Leukämie
Greek	Βενζαμίδιο, 3-(2-ιμιδαζο[1,2-β]πυριδαζινο-3-υλεθυνυλο)-4-μεθυλο-N-[4-[(4-μεθυλο-1-πιπεραζινυλο)μεθυλο]-3-(τριφθορομεθυλο)φαινυλ]	Θεραπεία της χρόνιας μυελοειδούς λευχαιμίας
Hungarian	Benzamid, 3-(2-imidazo[1,2-b]piridazin-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperazinil)metil]-3-(trifluorometil)fenil]	Krónikus myeloid leukémia kezelése
Italian	3-(2-imidazo[1,2-b]piridazin-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperazinil)metil]-3-(trifluorometil)fenil]- benzamide	Trattamento della leucemia mieloide cronica
Latvian	3-(2-imidazo[1,2-b]piridazīn-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperazinil)metil]-3-(trifluorometil)fenil] – benzamīds	Hroniskas mieloleikozes ārstēšana
Lithuanian	Benzamidas, 3-(2-imidazo[1,2-b]piridazin-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperazinil)metil]-3-(trifluorometil)fenil]-	Lėtinės mielocitinės leukemijos gydymas

Language	Active ingredient	Indication
Maltese	Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]	Kura tal-lewkimja mjelojda kronika
Polish	Benzamid, 3-(2-imidazo[1,2-b]pyridazin-3-yletynyl)-4-metylo-N-[4-[(4-metylo-1-piperazynyl)metyl]-3-(trifluorometyl)fenyl]	Leczenie przewlekłej białaczki szpikowej
Portuguese	Benzamina, 3-(2-imidazo[1,2-b]piridazina-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperazinil)metil]-3-(trifluorometil)fenil]	Tratamento da leucemia mielóide crónica
Romanian	Benzamidă, 3-(2-imidazo[1,2-b]piridazin-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperazinil)metil]-3-(trifluorometil)fenil]	Tratamentul leucemiei mieloidice cronice
Slovak	Benzamid, 3-(2-imidazo[1,2-b]pyridazín-3-yletynyl)-4-metyl-N-[4-[(4-metyl-1-piperazinyl)metyl]-3-(trifluórmetyl)fenyl]	Liečba chronickej myeloidnej leukémie
Slovenian	Benzamid, 3-(2-imidazo[1,2-b]piridazin-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperazinil)metil]-3-(trifluorometil)fenil]	Zdravljenje kronične mieloične levkemije
Spanish	Benzamida, 3-(2-imidazo[1,2-b]piridacina-3-iletinil)-4-metil-N-[4-[(4-metil-1-piperacinil)metil]-3-(trifluorometil)fenil]	Tratamiento de la leucemia mieloides crónica
Swedish	Benzamid, 3-(2-imidazo[1,2-b]pyridazín-3-yletynyl)-4-metyl-N-[4-[(4-metyl-1-piperazinyl)metyl]-3-(trifluorometyl)fenyl]	Behandling av kronisk myelogen leukemi
Norwegian	Benzamíð, 3-(2-ímidazó[1,2-b]pýrídízín-3-ýletýnýl)-4-metýl-N-[4-[(4-metýl-1-piperazínýl)metýl]-3-(tríflúórómetýl)fenýl]	Meðferð við langvinnu kyrningahvítblæði
Icelandic	Benzamide, 3-(2-imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]	Treatment of chronic myeloid leukaemia