



## Committee for Orphan Medicinal Products

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

### N-(5-tert-butylisoxazol-3-yl)-N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl}urea di-hydrochloride salt for the treatment of acute myeloid leukaemia

On 23 March 2009, orphan designation (EU/3/09/622) was granted by the European Commission to Ambit Europe Limited, United Kingdom, for N-(5-tert-Butylisoxazol-3-yl)-N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl}urea di-hydrochloride salt 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 bone) 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 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. The primary treatments of AML are 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 N-(5-tert-Butylisoxazol-3-yl)-N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl}urea di-hydrochloride salt might be of significant benefit for the treatment of AML, mainly because it works in a different way to other medicines and may be used in combination with other treatments. This assumption 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?**

This medicine is a chemically produced substance that is expected to work by blocking a protein called receptor tyrosine kinase. This protein can be found on the surface of the cancerous cells in AML, and is involved in stimulating the cell to grow and divide uncontrollably. The medicine blocks the receptor tyrosine kinase of the type FLT3. By blocking this receptor, the medicine is expected to control the division of the cancerous cells and slow down the development of the disease.

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

The effects of N-(5-tert-Butylisoxazol-3-yl)-N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl}urea di-hydrochloride salt have been evaluated in experimental models.

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

At the time of submission, this medicine was not authorised anywhere in the EU for treatment of 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 9 February 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 marketing authorisation.

**For more information:**

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

<b>Language</b>	<b>Active ingredient</b>	<b>Indication</b>
English	N-(5-tert-Butylisoxazol-3-yl)-N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl}urea dihydrochloride salt	Treatment of acute myeloid leukaemia
Bulgarian	Дихидрохлоридна сол на N-(5-терц-бутилизоксазол-3-ил)- N'-{4-[7-(2-(морфолин-4-ил)етокси)имидазо[2,1-b][1,3]бензотиазол-2-ил]фенил} урея	Лечение на остра миелоидна левкемия
Czech	N-(5-tert-butylisoxazol-3-yl)- N'-{4-[7-(2-(morfolin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]fenyl} močovina, dihydrochlorid-sůl	Léčba akutní myeloidní leukémie
Danish	N-(5-tert-butylisoxazol-3-yl)- N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl} urinstofdihydrochlorid-salt	Behandling af akut myeloid leukæmi
Dutch	N-(5-tert-butylisoxazol-3-yl)- N'-{4-[7-(2-(morfoline-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]fenyl} ureum-dihydrochloride-zout	Behandeling van acute myeloïde leukemie
Estonian	N-(5-tert-Butüülisoksasool-3-üül)- N'-{4-[7-(2-(morfoliini-4-üüll)etoksü)imidaso[2,1-b][1,3]bensotiasool-2-üüll]fenüül} karbamiid dihidrokloriid sool	Akutuise müeloidse leukeemia ravi
Finnish	N-(5-tert-butyyli-isoksatsoli-3-yyli)-N'-{4-[7-(2-(morfoliini-4-yyli)etoksi)imidatso[2,1-b][1,3]bentsotiatsoli-2-yyli]fenyyli} ureadihydrokloridisuola	Akuutin myelooisen leukemian hoito
French	Dihydrochlorure de N-(5-tert-butylisoxazol-3-yl)- N'-{4-[7-(2-(morpholin-4-yl)éthoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phényl} urée	Traitement de la leucémie aiguë myéloïde
German	N-(5-tert-Butylisoxazol-3-yl)- N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl} harnstoffdihydrochlorid-Salz	Behandlung der akuten myeloischen Leukämie
Greek	Διδροχλωρικό άλας N'-(5-tert-βουτυλισοξαζολ-3-υλο)- N'-{4-[7-(2-(μορφολιν-4-υλο)αιθοξυ)ιμιδαζο[2,1-b][1,3]βενζοθειαζολ-2-υλο]φαινυλο} ουρίας	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	N-(5-terc-butylisoxazol-3-il)- N'-{4-[7-(2-(morpholin-4-il)etoxi)imidazo[2,1-b][1,3]benzotiazol-2-il]fenil} urea di-hidroklorid só	Akut myeloid leukaemia kezelése
Italian	N-(5-tert-butylisossazol-3-il)- N'-{4-[7-(2-(morfolin-4-yl)etossi)imidazo[2,1-b][1,3]benzotiazol-2-il]fenil} urea dicloridrato	Trattamento della leucemia mieloide acuta

Latvian	N-(5-tert-butilizoksazol-3-il)-N'-{4-[7-(2-(morfolīn-4-il)etoksi)imidazo[2,1-b][1,3]benzotiazol-2-il]fenil}urīnvielas dihidrochlorīda sāls	Akūtas mieloleikozes ārstēšana
Lithuanian	N-(5-tert-butilisoksazol-3-il)- N'-{4-[7-(2-(morfolin-4-il)etoksi)imidazo[2,1-b][1,3]benzotiazol-2-il]fenil}karbamido dihidrochlorido druska	Ūmios mieloleukozės gydymas
Maltese	N-(5-tert-Butylisoxazol-3-yl)- N'-{4-[7-(2-(morpholin-4-yl)ethoxy)imidazo[2,1-b][1,3]benzothiazol-2-yl]phenyl}urea dihydrochloride salt	Kura tal-lewkimja mjelojda akuta
Polish	Dichlorowodorek N'-(5-tert-butyloizoksazol-3-ilo)- N'-{4-[7-(2-(morfolin-4-ylo)etoksy)imidazo[2,1-b][1,3]benzotiazol-2-ilo]fenylo}mocznika	Leczenie ostrej białaczki szpikowej
Portuguese	Di-cloridrato de N-(5-ter-butilisoxazol-3-il)-N'-{4-[7-(2-(morfolin-4-il)etoxi)imidazol [2,1-b][1,3]benzotiazol-2-il]fenil}ureia	Tratamento da leucémia mielóide aguda
Romanian	Sare dihidrocloridică de N-(5-terț-butilizoxazol-3-il)- N'-{4-[7-(2-(morfolin-4-il)etoxi)imidazo[2,1-b][1,3]benzotiazol-2-il]fenil}uree	Tratamentul leucemiei mieloidice acute
Slovak	Dichlorid N-(5-terc-butylixazol-3-yl)-N'-{4-[7-(2-(morfolin-4-yl)etoxy)imidazo[2,1-b][1,3]benzotiazol-2-yl]fenyl}močoviny	Liečba akútnej myeloickej leukémie
Slovenian	N-(5-tert-Butilizoksazol-3-yl)-N'-{4-[7-(2-(morfolin-4-yl)etoksi)imidazo[2,1-b][1,3]benzotiazol-2-yl]fenil}urea dihidrokloridna-sol	Zdravljenje akutne mieloične levkemije
Spanish	N-(5-tert-butilisoxazol-3-il)-N'-{4-[7-(2-(morfolin-4-il)etoxi)imidazo[2,1-b][1,3]benzotiazol-2-il]fenil}urea, dihidrocloruro	Tratamiento de la leucemia mieloidice aguda
Swedish	N-(5-tert-butylisoxazol-3-yl)- N'-{4-[7-(2-(morfolin-4-yl)etoxi)imidazo[2,1-b][1,3]benzotiazol-2-yl]fenyl}ureadihydrokloridsalt	Behandling av akut myeloisk leukemi
Norwegian	N-(5-tert-butylisoksazol-3-yl)-N'-{4-[7-(2-(morfolin-4-yl)etoksy)imidazo[2,1-b][1,3]benzotiazol-2-yl]fenyl}urea-dihydrokloridsalt	Behandling av akutt myelogen leukemi
Icelandic	N-(5-tert-bútýlísóxasól-3-ýl)- N'-{4-[7-(2-(morfólín-4-yl)etoxý)ímidasó[2,1-b][1,3]bensótíásól-2-ýl]fenýl}úreutvíhýdróklóríðsalt	Meðferð við bráðu kyrningahvítblæði