

27 May 2016  
EMA/COMP/254160/2016  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol methanesulfonate for the treatment of acute myeloid leukaemia

On 28 April 2016, orphan designation (EU/3/16/1640) was granted by the European Commission to Celgene Europe Limited, United Kingdom, for 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol methanesulfonate 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, where blood cells are produced) produces large numbers of abnormal, immature white blood cells. These abnormal cells quickly build up in large numbers in the bone marrow and are found in the blood.

AML is a long-term debilitating and life-threatening disease because these abnormal immature cells take the place of the normal blood cells, causing bleeding episodes, blood clots and a reduced ability to fight infections.

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

At the time of designation, AML affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 people\*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the 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. At

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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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

the time of designation, the main treatments for AML were chemotherapy (medicines to treat cancer) and haematopoietic (blood) stem-cell transplantation (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow).

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with AML. The medicine works in a novel way against cancer cells and early data indicate improved response with the medicine in patients whose disease does not respond to other treatments or has come back. In addition, ongoing clinical trials also show the medicine comparing favourably with standard treatment. 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?**

The medicine works by blocking the action of abnormal (mutated) forms of an enzyme called isocitrate dehydrogenase 2 (IDH2). IDH2 plays an important role in generating energy for cells. Mutated IDH2 enzymes have been associated with cancers such as AML and are found in some AML cancer cells. By blocking the action of these enzymes, the medicine is expected to help slow down the disease.

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

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

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

At the time of submission, the medicine was not authorised anywhere in the EU for AML. Orphan designation had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 23 March 2016 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 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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   | 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol methanesulfonate                   | Treatment of acute myeloid leukaemia       |
| Bulgarian | 2-метил-1-[(4-[6-(трифлуорометил)пиридин-2-ил]-6-{[2-(трифлуорометил)пиридин-4-ил]амино}-1,3,5-триазин-2-ил)амино]пропан-2-ол метансулфонат                         | Лечение на остра миелоидна левкемия        |
| Croatian  | 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{[2-(trifluorometil)piridin-4-il]amino}-1,3,5-triazin-2-il)amino]propan-2-ol metansulfonat                         | Liječenje akutne mijeloične leukemije      |
| Czech     | 2-methyl-1-[(4-[6-(trifluormethyl)pyridin-2-yl]-6-{[2-(trifluormethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol methansulfonát                       | Léčba akutní myeloidní leukémie            |
| Danish    | 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol methansulfonat                     | Behandling af akut myeloid leukæmi         |
| Dutch     | 2-methyl-1-[(4-[6-(trifluormethyl)pyridine-2-yl]-6-{[2-(trifluormethyl)pyridine-4-yl]amino}-1,3,5-triazine-2-yl)amino]propaan-2-ol methaansulfonaat                 | Behandeling van acute myeloïde leukemie    |
| Estonian  | 2-metüül-1-[(4-[6-(trifluorometüül)püridiin-2-üül]-6-{[2-(trifluorometüül)püridiin-4-üül]amino}-1,3,5-triasiin-2-üül)amino]propaan-2-ool metaansulfonaat            | Akuutse müeloidse leukeemia ravi           |
| Finnish   | 2-metyyli-1-[(4-[6-(trifluorometyyli)pyridiini-2-yyli]-6-{[2-(trifluorometyyli)pyridiini-4-yyli]amino}-1,3,5-triatsiini-2-yyli)amino]propan-2-olimetaanisulfonaatti | Akuutin myelooisen leukemian hoito         |
| French    | 2-méthyl-1-[(4-[6-(trifluorométhyl)pyridine-2-yl]-6-{[2-(trifluorométhyl)pyridine-4-yl]amino}-1,3,5-triazine-2-yl)amino]propane-2-ol méthanesulfonate               | Traitement de la leucémie aiguë myéloïde   |
| German    | 2-Methyl-1-[(4-[6-(trifluormethyl)pyridin-2-yl]-6-{[2-(trifluormethyl)pyridin-4-yl]amino}-1,3,5-triazin-2-yl)amino]propan-2-ol methanesulfonat                      | Behandlung der akuten myeloischen Leukämie |
| Greek     | Μεθανοσουλφονική 2-μεθυλ-1-[(4-[6-(τριφθορομεθυλ)πυριδιν-2-υλ]-6-{[2-(τριφθορομεθυλ)πυριδιν-4-υλ]αμινο}-1,3,5-τριαζιν-2-υλ)αμινο]προπαν-2-όλη                       | Θεραπεία της οξείας μυελοειδούς λευχαιμίας |
| Hungarian | 2-metil-1-[(4-[6-(trifluórmetyl)piridin-2-il]-6-{[2-(trifluórmetyl)piridin-4-il]amino}-1,3,5-triazin-2-il)amino]propán-2-ol metánszulfonát                          | Akut myeloid leukaemia kezelése            |
| Italian   | 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{[2-(trifluorometil)piridin-4-il]amino}-1,3,5-triazin-2-il)amino]propan-2-olo metansolfonato                       | Trattamento della leucemia mieloide acuta  |

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

| Language   | Active ingredient  | Indication                                 |
|------------|--|--|
| Latvian    | 2-metil-1-[(4-[6-(trifluormetil)piridīn-2-il]-6-{ [2-(trifluormetil)piridīn-4-il]amino} -1,3,5-triazīn-2-il)amino]propān-2-ola metānsulfonāts        | Akūtas mieloleikozes ārstēšana             |
| Lithuanian | 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{ [2-(trifluorometil)piridin-4-il]amino} -1,3,5-triazin-2-il)amino]propan-2-ol metansulfonatas      | Ūmios mieloleukozės gydymas                |
| Maltese    | 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{ [2-(trifluoromethyl)pyridin-4-yl]amino} -1,3,5-triazin-2-yl)amino]propan-2-ol methanesulfonate  | Kura tal-lewkimja mjelojda akuta           |
| Polish     | Metanosulfonian 2-metylo-1-[(4-[6-(trifluorometylo)pirydyn-2-yl]-6-{ [2-(trifluorometylo)pirydyn-4-yl]amino} -1,3,5-triazyno-2-yl)amino]propan-2-olu | Leczenie ostrej białaczki szpikowej        |
| Portuguese | Metanossulfonato de 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{ [2-(trifluorometil)piridin-4-il]amino} -1,3,5-triazin-2-il)amino]propan-2-ol  | Tratamento da leucémia mielóide aguda      |
| Romanian   | Metansulfonat de 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{ [2-(trifluorometil)piridin-4-il]amino} -1,3,5-triazin-2-il)amino]propan-2-ol     | Tratamentul leucemiei mieloidice acute     |
| Slovak     | 2-metyl-1-[(4-[6-(trifluórmetyl)pyridín-2-yl]-6-{ [2-(trifluórmetyl)pyridín-4-yl]amino} -1,3,5-triazín-2-yl)amino]propan-2-ol metansulfonát          | Liečba akútnej myeloickej leukémie         |
| Slovenian  | 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{ [2-(trifluorometil)piridin-4-il]amino} -1,3,5-triazin-2-il)amino]propan-2-ol metansulfonat        | Zdravljenje akutne mieloične levkemije     |
| Spanish    | Metanosulfonato de 2-metil-1-[(4-[6-(trifluorometil)piridin-2-il]-6-{ [2-(trifluorometil)piridin-4-il]amino} -1,3,5-triazin-2-il)amino]propan-2-ol   | Tratamiento de la leucemia mieloides aguda |
| Swedish    | 2-metyl-1-[(4-[6-(trifluorometyl)pyridin-2-yl]-6-{ [2-(trifluorometyl)pyridin-4-yl]amino} -1,3,5-triazin-2-yl)amino]propan-2-ol metansulfonat        | Behandling av akut myeloisk leukemi        |
| Norwegian  | 2-metyl-1-[(4-[6-(trifluorometyl)pyridin-2-yl]-6-{ [2-(trifluorometyl)pyridin-4-yl]amino} -1,3,5-triazin-2-yl)amino]propan-2-ol-metansulfonat        | Behandling av akutt myelogen leukemi       |
| Icelandic  | 2-metyl-1-[(4-[6-(tríflúrómetýl)þýridín-2-ýl]-6-{ [2-(tríflúrómetýl)þýridín-4-ýl]amínó} -1,3,5-tríazín-2-ýl)amínó]própan-2-ól metansúlfónat          | Meðferð við bráðu kynningahvítblæði        |