



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

29 January 2016  
EMA/COMP/790054/2015  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

Sodium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl)methyl phosphate for the treatment of acute myeloid leukaemia

On 14 December 2015, orphan designation (EU/3/15/1597) was granted by the European Commission to Otsuka Pharmaceutical Europe Ltd, United Kingdom, for sodium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl)methyl phosphate 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 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 approximately 1.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 77,000 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).

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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 512,900,000 (Eurostat 2015).



## **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 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 the medicine might be of significant benefit for patients with AML because early results from studies show that it might produce a response in patients whose disease has come back after other treatments. 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 consists of an approved leukaemia medicine, decitabine, which has been linked to a substance called deoxyguanosine. When the medicine is injected, decitabine is slowly released from the medicine by enzymes in the body, giving it a prolonged action. The released decitabine becomes incorporated into the DNA (genetic material) of the cell. This blocks the activity of enzymes called DNA methyltransferases (DNMTs), which are responsible for promoting the development and progression of cancer. By blocking DNMTs, decitabine will block the division of the leukaemia cells and lead to their death.

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

The effects of this 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 of the medicine has been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 November 2015 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	Sodium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl)methyl phosphate	Treatment of acute myeloid leukaemia
Bulgarian	Натриев (2R,3S,5R)-5-(4-амино-2-оксо-1,3,5-триазин-1(2H)-ил)-2-(хидроксиметил)тетраhydroфуран-3-ил ((2R,3S,5R)-5-(2-амино-6-оксо-1H-пурин-9(6H)-ил)-3-хидрокситетраhydroфуран-2-ил)метил фосфат	Лечение на остра миелоидна левкемия
Croatian	Natrijev (2R,3S,5R)-5-(4-amino-2-okso-1,3,5-triazin-1(2H)-il)-2-(hidroksimetil)tetrahidrofuran-3-il ((2R,3S,5R)-5-(2-amino-6-okso-1H-purin-9(6H)-il)-3-hidroksitetrahidrofuran-2-il)metilfosfat	Liječenje akutne mijeloidne leukemije
Czech	(2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl) methylfosforečnan sodný	Léčba akutní myeloidní leukémie
Danish	Natrium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl)methylphosphat	Behandling af akut myeloid leukæmi
Dutch	Natrium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazine-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuraan-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purine-9(6H)-yl)-3-hydroxytetrahydrofuraan-2-yl)methyl fosfaat	Behandeling van acute myeloïde leukemie
Estonian	Naatrium (2R, 3S, 5R) -5- (4-amino-2-okso-1,3,5-triasiin-1(2H) -üül) -2- (hüdrosümetüül) tetrahüdrofuraan-3-üül ((2R, 3S, 5R) -5- (2-amino-6-okso-1H-puriin-9 (6H) -üül) -3-hüdrosütetrahüdrofuraan-2-üül) metüülfosfaat	Akuutse müeloidse leukeemia ravi
Finnish	Natrium (2R,3S,5R)-5-(4-amino-2-okso-1,3,5-triatsiini-1(2H)-yyli)-2-(hydroksimetyyli)tetrahydrofuraani-3-yyli ((2R,3S,5R)-5-(2-amino-6-okso-1H-puriini-9(6H)-yyli)-3-hydroksitetrahydrofuraani-2-yyli)metyylifosfaatti	Akuutin myelooisen leukemian hoito
French	(2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazine-1(2H)-yl)-2-(hydroxyméthyl)tétrahydrofurane-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purine-9(6H)-yl)-3-hydroxytétrahydrofurane-2-yl)méthyl phosphate sodique	Traitement de la leucémie aiguë myéloïde
German	Natrium-(2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl-((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl)methylphosphat	Behandlung der akuten myeloischen Leukämie

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

Language	Active ingredient	Indication
Greek	(2R,3S,5R)-5-(4-αμινό-2-οξο-1,3,5-τριαζίν-1(2H)-υλ)-2-(υδροξυμεθυλ)τετραϋδροφουραν-3-υλικό ((2R,3S,5R)-5-(2-αμινό-6-οξο-1H-πουρίν-9(6H)-υλ)-3-υδροξυτετραϋδροφουραν-2-υλ)μεθυλφωσφορικό νάτριο	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	(2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-il)-2-(hidroximetil)tetrahidrofurán-3-il((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-il)-3-hidroxi-tetrahidrofurán-2-il)metilfoszfát nátrium	Akut myeloid leukaemia kezelése
Italian	(2R,3S,5R)-5-(4-ammino-2-oxo-1,3,5-triazina-1(2H)-il)-2-(idrossimetil)tetraidrofurano-3-il ((2R,3S,5R)-5-(2-ammino-6-oxo-1H-purina-9(6H)-il)-3-idrossitetraidrofurano-2-il)metil fosfato di sodio	Trattamento della leucemia mieloide acuta
Latvian	Nātrija (2R,3S,5R)-5-(4-amino-2-oksi-1,3,5-triazin-1(2H)-il)-2-(hidroksimetil)tetrahidrofurān-3-il ((2R,3S,5R)-5-(2-amino-6-oksi-1H-purīn-9(6H)-il)-3-hidroksitetrahidrofurān-2-il)metilfosfāts	Akūtas mieloleikozes ārstēšana
Lithuanian	Natrio (2R,3S,5R)-5-(4-amino-2-okso-1,3,5-triazinas-1(2H)-il)-2-(hidroksimetil)tetrahidrofuran-3-il ((2R,3S,5R)-5-(2-amino-6-okso-1H-purin-9(6H)-il)-3-hidroksitetrahidrofuran-2-il)metil fosfatas	Ūmios mieloleukozės gydymas
Maltese	Sodium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxytetrahydrofuran-2-yl)methyl phosphate	Kura tal-lewkimja mjeloidja akuta
Polish	(2R,3S,5R)-5-[4-amino-2-okso-1,3,5-triazyno-1(2H)-yl]-2-(hydroksymetylo)tetrahydrofuran-3-ylo-{{(2R,3S,5R)-5-[2-amino-6-okso-1H-puryń-9(6H)-ylo]-3-hydroksytetrahydrofuran-2-ylo}}metylofosforan sodu	Leczenie ostrej białaczki szpikowej
Portuguese	Fosfato de (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-il)-2-(hidroximetil)tetra-hidrofuran-3-il ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-il)-3-hidroxitetra-hidrofuran-2-il)metil sódio	Tratamento da leucémia mielóide aguda
Romanian	(2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-il)-2-(hidroximetil)tetrahidrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-il)-3-hidroxitetrahidrofuran-2-il)metil fosfat de sodiu	Tratamentul leucemiei mieloidice acute
Slovak	(2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazín-1(2H)-yl)-2-(hydroxymetyl)tetrahydrofurán-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purín-9(6H)-yl)-3-hydroxytetrahydrofurán-2-yl)metyl fosforečnan sodný	Liečba akútnej myeloidkej leukémie
Slovenian	Natrijev (2R,3S,5R)-5-(4-amino-2-okso-1,3,5-triazin-1(2H)-il)-2-(hidroksimetil)tetrahidrofuran-3-il ((2R,3S,5R)-5-(2-amino-6-okso-1H-purin-9(6H)-il)-3-hidroksitetrahidrofuran-2-il)metil fosfat	Zdravljenje akutne mieloične levkemije

Language	Active ingredient	Indication
Spanish	Sodio (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazina-1(2H)-il)-2-(hidroximetil)tetrahidrofurano-3-il ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purina-9(6H)-il)-3-hidroxitetrahidrofurano-2-il)metil fosfato	Tratamiento de la leucemia mieloide aguda
Swedish	Natrium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroximetyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9(6H)-yl)-3-hydroxitetrahydrofuran-2-yl)metylfosfat	Behandling av akut myeloisk leukemi
Norwegian	Natrium (2R,3S,5R)-5-(4-amino-2-okso-1,3,5-triazin-1(2H)-yl)-2-(hydroksymetyl)tetrahydrofuran-3-yl ((2R,3S,5R)-5-(2-amino-6-okso-1H-purin-9(6H)-yl)-3-hydroksytetrahydrofuran-2-yl)metylfosfat	Behandling av akutt myelogen leukemi
Icelandic	Natríum (2R,3S,5R)-5-(4-amínó-2-oxó-1,3,5-tríasín-1(2H)-ýl)-2-(hýdroxýmetyl)tetrahýdrófúran-3-ýl ((2R,3S,5R)-5-(2-amínó-6-oxó-1H-púrín-9(6H)-ýl)-3-hýdroxýtetrahýdrófúran-2-ýl)metyl fosfat	Meðferð við bráðu kyrningahvítblæði

Withdrawing