11 August 2015
EMA/COMP/432053/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)acetamide, tetrahydrochloride for the treatment of acute myeloid leukaemia

On 28 July 2015, orphan designation (EU/3/15/1517) was granted by the European Commission to Pierre Fabre Médicament, France, for 2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)acetamide, tetrahydrochloride 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 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).

*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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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, with data from early studies showing that patients whose disease had come back responded to treatment with this medicine when given in combination with cytarabine (another medicine authorised for this condition). 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?

This medicine is a 'topoisomerase inhibitor', which means that it blocks the activity of enzymes inside cells called topoisomerases. Topoisomerases are important for cells to divide, therefore blocking their activity in cancer cells is expected to stop their growth. This medicine also contains a chain (known as a 'polyamine chain') that helps the medicine enter cancer cells.

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 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 18 June 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:

Pierre Fabre Médicament
45, Place Abel Gance
92100 Boulogne
France
Tel. +33 1 49 10 83 77
Fax +33 1 49 10 02 16
E-mail: nathalie.gyselinck@pierre-fabre.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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)acetamide, tetrahydrochloride	Treatment of acute myeloid leukaemia
Bulgarian	2-((3-((4-((3-аминопропил)амино)бутил)амино)пропил)амино)-N-((5S,5aS,8aR,9R)-9-(4-хидрокси-3,5-диметоксифенил)-8-оксо-5,5a,6,8,8a,9-хексахидрофуро[3',4':6,7]нафто[2,3-d][1,3]диоксол-5-ил)ацетамид, тетрахидрохлорид	Лечение на остра миелоидна левкемия
Croatian	2-((3-((4-((3-aminopropil)amino)butil)amino) propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroksi-3,5-dimetoksifenil)-8-okso-5,5a,6,8,8a,9-heksahidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioksol-5-il)acetamidtetraklorid	Liječenje akutne mijeloične leukemije
Czech	Tetrahydrochlorid 2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimetoxyfenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]nafto[2,3-d][1,3]dioxol-5-yl)acetamid	Léčba akutní myeloidní leukémie
Danish	2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)acetamid, tetrahydroklorid	Behandling af akut myeloid leukæmi
Dutch	2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyfenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]nafto[2,3-d][1,3]dioxol-5-yl)acetamide, tetrahydrochloride	Behandeling van acute myeloïde leukemie
Estonian	2-((3-((4-((3-aminopropüül)amino)butüül)amino)propüül)amino)-N-((5S,5aS,8aR,9R)-9-(4-hüdroksü-3,5-dimetoksüfenüül)-8-okso-5,5a,6,8,8a,9-heksahüdrofuro[3',4':6,7]nafto[2,3-d][1,3]dioksool-5-üül)atsetamiid, tetravesinikkloriid	Akuutse müeloidse leukeemia ravi

[1] At the time of designation

Language	Active ingredient	Indication
Finnish	2-((3-((4-((3-aminopropyyli)amino)butyyli)amino)propyyli)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroksi-3,5-dimetoksifenyyli)-8-okso-5,5a,6,8,8a,9-heksahydrofuro[3',4':6,7]nafto[2,3-d][1,3]dioksol-5-yyli)asetamidi, tetrahydrokloridi	Akuutin myelooisen leukemian hoito
French	Tétrachlorhydrate de 2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-diméthoxyphényl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)acetamide	Traitement de la leucémie aiguë myéloïde
German	2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)acetamidtetrahydrochlorid	Behandlung der akuten myeloischen Leukämie
Greek	2-((3-((4-((3-αμινοπροπυλ)αμινο)βουτυλ)αμινο)προπυλ)αμινο)-N-((5S,5aS,8aR,9R)-9-(4-υδροξυ-3,5-διμεθοξυφαινυλ)-8-οξο-5,5a,6,8,8a,9-εξαϋδροφουρο[3',4':6,7]ναφθο[2,3-d][1,3]διοξολ-5-yl)ακεταμίδιο, τετραϋδροχλωρικό	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	2-((3-((4-((3-aminopropil)amino)butil)amino)propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroxi-3,5-dimetoxifenil)-8-oxo-5,5a,6,8,8a,9-hexahidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioxol-5-il)acetamid tetrahidroklorid	Akut myeloid leukaemia kezelése
Italian	2-((3-((4-((3-amminopropil)amino)butil)amino)propil(amino)-N-((5S,5aS,8aR,9r)-9-(4-idrossi-3,5-dimetossifenil)-8-osso-5,5a,6,8,8a,9-esaidrofuro[3',4':6,7]nafto[2,3-d][1,3]diossol-5-il)acetamide, tetraidrocloruro	Trattamento della leucemia mieloide acuta
Latvian	2-((3-((4-((3-aminopropil)amino)butil)amino)propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroksi-3,5-dimetoksifenil)-8-okso-5,5a,6,8,8a,9-heksahidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioksol-5-il)acetamīds, tetrahidrohlorīds	Akūtas mieloleikozes ārstēšana
Lithuanian	2-((3-((4-((3-aminopropil)amino)butil)amino)propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroksi-3,5-dimetoksifenil)-8-okso-5,5a,6,8,8a,9-heksahidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioksol-5-il)acetamidas, tetrahidrochloridas	Ūmios mieloleukozės gydymas

Language	Active ingredient	Indication
Maltese	2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)acetamide, tetrahydrochloride	Kura tal-lewkimja mjelojda akuta
Polish	tetrachlorowodorek 2-((3-((4-((3-aminopropylo)amino)butylo)amino)propylo)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroksy-3,5-dimetoksyfenyl)-8-okso-5,5a,6,8,8a,9 heksahydrofuro[3',4':6,7]nafto[2,3-d][1,3]dioksol-5-yl)acetamidu	Leczenie ostrej białaczki szpikowej
Portuguese	2-((3-((4-((3-aminopropil)amino)butil)amino)propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroxi-3,5-dimetoxifenil)-8-oxo-5,5a,6,8,8a,9-hexahidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioxol-5-yl)acetamida, tetracloridrato	Tratamento da leucémia mielóide aguda
Romanian	Tetraclorhidrat de 2-((3-((4-((3-aminopropil)amino)butil)amino)propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroxi-3,5-dimetoxifenil)-8-oxo-5,5a,6,8,8a,9-hexahidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioxol-5-il)acetamidă	Tratamentul leucemiei mieloide acute
Slovak	tetrahydrochlorid 2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimetoxyfenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]nafto[2,3-d][1,3]dioxol-5-yl)acetamidu	Liečba akútnej myeloickej leukémie
Slovenian	2-((3-((4-((3-aminopropil)amino)butil)amino)propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroksi-3,5-dimetoksifenil)-8-okso-5,5a,6,8,8a,9-heksahidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioksol-5-il)acetamid, tetrahidroklorid	Zdravljenje akutne mieloične levkemije
Spanish	2-((3-((4-((3-aminopropil)amino)butil)amino)propil)amino)-N-((5S,5aS,8aR,9R)-9-(4-hidroxi-3,5-dimetoxifenil)-8-oxo-5,5a,6,8,8a,9-hexa hidrofuro[3',4':6,7]nafto[2,3-d][1,3]dioxol-5-il)acetamida, tetrahidrocloruro	Tratamiento de la leucemia mieloide aguda
Swedish	2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro [3 ', 4': 6,7] naphthol[2,3-d] [1,3] dioxol-5-yl) acetamid, tetrahydroklorid	Behandling av akut myeloisk leukemi

Language	Active ingredient	Indication
Norwegian	2-((3-((4-((3-aminopropyl)amino)butyl)amino)propyl)amino)-N-((5S,5aS,8aR,9R)-9-(4-hydroksy-3,5-dimetoksyfenyl)-8-oxo-5,5a,6,8,8a,9-heksahydrofuro[3',4':6,7]nafthol[2,3-d][1,3]dioksol-5-yl)acetamid, tetrahydroklorid	Behandling av akutt myelogen leukemi
Icelandic	2-((3-((4-((3-amínópropýl)amínó)bútýl)amínó)própýl)amínó)-N-((5S,5aS,8aR,9R)-9-(4-hýdroxý-3,5- dímethoxýfenýl)-8-oxó-5,5a,6,8,8a,9-hexahýdrófúró[3‘,4‘:6,7]naftól[2,3-d][1,3]díoxól-5-yl)acetamíð,tetrahýdróklóríð	Meðferð við bráðu kyrningahvítblæði