

22 June 2010
EMA/COMP/91045/2010
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-Methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one for the treatment of acute myeloid leukaemia

On 10 June 2010, orphan designation (EU/3/10/742) was granted by the European Commission to Aprea AB, Sweden, for 2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one (also known as APR-246) 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) 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 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 the time of designation, the main treatments for AML 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 bone marrow from a matched donor).

*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 506,500,000 (Eurostat 2010).

The sponsor has provided sufficient information to show that 2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one might be of significant benefit for patients with AML because it works in a different way to existing treatments and early studies show that it might improve the treatment of patients with this condition, particularly those 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?

Some AML patients have modified forms of a protein called p53 in their cancer cells. The p53 protein is involved in causing cell death, and cancer cells carrying a modified form of the p53 protein are less able to respond to standard treatments. The exact way that 2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one works in AML is not known, but it is thought to restore the normal function of the p53 protein. As a result, this medicine is expected to restore the ability of p53 to cause death of cancer cells, slowing down the progression of AML. It may also restore the ability of cancer cells to respond to other treatments.

What is the stage of development of this medicine?

The effects of 2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with 2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one that included patients with AML were ongoing.

At the time of submission, 2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one 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 3 February 2010 recommending the granting of this designation.

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:

Aprea AB
Karolinska Institutet Science Park
SE-171 65 Solna
Sweden
Telephone: +46 8 508 845 01
Telefax: +46 8 524 870 22
E-mail: charlotta.liljebris@aprea.com

Patient associations' contact points

Leukaemia CARE

One Birch Court,
Blackpole East,
Worcester,
Worcestershire WR3 8SG
24 hour CARE line 0800 169 6680 (UK residents only)
Telephone: +44 1905 755977 / +44 845 521 3456
Telefax: +44 1905 755166
Email: info@leukaemiacare.org.uk

Ligue Nationale Contre le Cancer

14 Rue Corvisart
75013 Paris
FRANCE
Telephone: +33 (0)1 53 55 24 00
Telefax: +33 (0)1 43 36 91 10
E-mail: lique@lique-cancer.net

European Cancer Patient Coalition

ECPC Office
Am Rothenanger 1b
85521 Riemerling
GERMANY
Telephone: +49 89 628 36 807
Telefax: +49 89 628 36 808
E-mail: info@ecpc-online.org

Translations of the active ingredient and indication in all official EU languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one	Treatment of acute myeloid leukaemia
Bulgarian	2-метоксиметил-2-хидроксиметил-1-азабицикло[2,2,2]октан-3-он	Лечение на остра миелоидна левкемия
Czech	2-methoxymethyl-2-hydroxymethyl-1-azabicyklo[2,2,2]oktan-3-on	Léčba akutní myeloidní leukémie
Danish	2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-on	Behandling af akut myeloid leukæmi
Dutch	2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-on	Behandeling van acute myeloïde leukemie
Estonian	2-metoksimetüül-2-hüdroksimetüül-1-asabitsüklo[2,2,2]oktaan-3-on	Akuutse müeloidse leukeemia ravi
Finnish	2-metoksimetyyli-2-hydroksimetyyli-1-azabisyklo[2.2.2]oktan-3-oni	Akuutin myelooisen leukemian hoito
French	2-méthoxyméthyle-2-hydroxyméthyle-1-azabicyclo[2,2,2]octane-3-one	Traitement de la leucémie aiguë myéloïde
German	2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2.2.2]octan-3-on	Behandlung der akuten myeloischen Leukämie
Greek	2- μεθοξυμεθυλο-2-υδροξυμεθυλο-1-αζαδικοκκλο[2,2,2]οκταν-3-όνη	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	2-metoximetil-2-hidroximetil-1-azabiklo[2,2,2]oktán-3-on	Akut myeloid leukaemia kezelése
Italian	2-metossimetil-2-idrossimetil-1-azabiciclo[2.2.2]ottan-3-one	Trattamento della leucemia mieloide acuta
Latvian	2-metoksimetil-2-hidroksimetil-1-azabiklo[2,2,2]oktāns-3-ons	Akūtas mieloleikozes ārstēšana
Lithuanian	2-metoksimetil-2-hidroksimetil-1-azabiklo[2,2,2]oktan-3-onas	Ūmios mieloleukozės gydymas
Maltese	2-methoxymethyl-2-hydroxymethyl-1-azabicyclo[2,2,2]octan-3-one	Kura tal-lewkimja mjelojda akuta
Polish	2-metoksymetylo-2-hydroksymetylo-1-azabicyklo[2,2,2]oktan-3-on	Leczenie ostrej białaczki szpikowej
Portuguese	2-metoximetil-2-hidroximetil-1-azabiciclo[2.2.2]-3-octanona	Tratamento da leucémia mielóide aguda
Romanian	2-metoximetil-2-hidroximetil-1-azabiciclo[2,2,2]octan-3-ona	Tratamentul leucemiei mieloide acute
Slovak	2-metoxymetyl-2-hydroxymetyl-1-azabicyklo[2,2,2]oktán-3-ón	Liečba akútnej myeloickej leukémie
Slovenian	2-metoksimetil-2-hidroksimetil-1-azabiklo[2,2,2]oktan-3-on	Zdravljenje akutne mieloične levkemije
Spanish	2-metoximetil-2-hidroximetil-1-azabiciclo[2,2,2]octan-3-ona	Tratamiento de la leucemia mieloide aguda

¹ At the time of designation

Language	Active ingredient	Indication
Swedish	2-metoximetyl-2-hydroximetyl-1-azabicyklo[2,2,2]oktan-3-on	Behandling av akut myeloisk leukemi
Norwegian	2-metoksymetyl-2-hydroksymetyl-1-azabisyklo[2.2.2]oktan-3-on	Behandling av akutt myelogen leukemi
Icelandic	2-metoxýmetyl-2-hýdroxýmetyl-1-azabísýkló[2.2.2]oktan-3-ón	Meðferð við bráðu kyrningahvítblæði