25 April 2014
EMA/COMP/127723/2008 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

5'-O-(trans-9"-octadecenoyl)-1-ß-D-arabinofuranosyl cytosine for the treatment of acute myeloid leukaemia

First publication	10 July 2008
Rev.1: sponsor's change of address	29 July 2008
Rev.2: sponsor's name and address change	25 April 2014

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 14 September 2007, orphan designation (EU/3/07/476) was granted by the European Commission to Clavis Pharma ASA, Norway, for 5'-O-(trans-9"-octadecenoyl)-1-ß-D-arabinofuranosyl cytosine for the treatment of acute myeloid leukaemia.

In April 2014, Clavis Pharma ASA changed name to Aqualis ASA.

What is acute myeloid leukaemia?

Acute myeloid leukaemia is a disease in which cancer cells are found in the blood and the bone marrow. The bone marrow is the spongy tissue inside the large bones in the body. Normally, the bone marrow makes cells called "blasts", which mature into several different types of blood cells that have specific functions in the body. These include red cells, white cells and platelets. Red blood cells carry oxygen and other materials to all tissues of the body. White blood cells fight infection. Platelets make the blood clot. When leukaemia develops, the bone marrow produces large numbers of abnormal blood cells. There are several types of leukaemias. In myeloid leukaemia, blasts that should develop into a type of white blood cells called granulocytes are affected. The blasts do not mature, and become too many. These blast cells are then found in the blood; they also accumulate in the bone marrow where they take the place of the other types of normal blood cells, causing anaemia, easy bruising, and frequent infections. Myeloid leukaemia can be acute, when it develops quickly with many blasts. Acute myeloid leukaemia is life-threatening.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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

At the time of designation, acute myeloid leukaemia affected approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 100,000 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 leukaemia is complex, and depends on a number of factors including the type of leukaemia, the extent of the disease and whether the leukaemia has been treated before. It also depends on the age, the symptoms, and the general health of the patient. The primary treatment of acute myeloid leukaemia is chemotherapy (using drugs to kill cancer cells). Several products were authorised for the condition in the Community at the time of submission of the application for orphan drug designation. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that 5'-O-(trans-9"-octadecenoyl)-1-ß-D-arabinofuranosyl cytosine might be of potential significant benefit for the treatment of acute myeloid leukaemia because it might possibly be used when other treatments have failed. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

5'-O-(trans-9"-octadecenoyl)-1-ß-D-arabinofuranosyl cytosine is a product similar to cytidine, which in turn is a building block of the fundamental genetic material of cells (DNA and RNA). 5'-O-(trans-9"-octadecenoyl)-1-ß-D-arabinofuranosyl cytosine blocks the synthesis of DNA and RNA. By doing this the drug stops the production of genetic material necessary for cell growth and division. Thus, the drug inhibits the growth cells and specially tumour cells which grow and duplicate very actively.

What is the stage of development of this medicine?

The effects of 5'-O-(trans-9"-octadecenoyl)-1-ß-D-arabinofuranosyl cytosine were evaluated in experimental models.

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

5'-O-(trans-9"-octadecenoyl)-1-ß-D-arabinofuranosyl cytosine was not authorised anywhere worldwide for acute myeloid leukaemia or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 25 July 2007 recommending the granting of this designation.

*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.
At the time of designation, this represented a population of 500,300,000 (Eurostat 2007).

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:

Aqualis ASA
Sjølyst Plass 2
0278 Oslo
Norway
Tel. +47 23 01 49 90
E-mail: mail@aqualis.no

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	5'-O-(trans-9''-octadecenoyl)-1-β-D-arabinofuranosyl cytosine.	Treatment of acute myeloid leukaemia
Bulgarian	5'-O-(транс-9''-октадеценоил)-1- β -D-арабинофуранозил цитозин	Лечение на остра миелоидна левкемия
Czech	5'-O-(trans-9''-oktadecenoyl)-1-beta-D-arabinofuranosylcytosin	Léčba akutní myeloidní leukémie
Danish	5'-O-(trans-9''-octadecanoyl)-1-β-D-arabinofuranosylcytosin	Behandling af akut myeloid leukæmi
Dutch	5'-O-(trans-9''-octadecenoyl)-1-β-D-arabinofuranosyl cytosine.	Behandeling van acute myeloïde leukemie
Estonian	5'-O-(trans-9''-octadetsenoüül)-1-beta-D-arabinofuranosüül tsütosiin	Akuutse müeloidse leukeemia ravi
Finnish	5'-O-(trans-9''-oktadekenoyyli)-1-beeta-D-arabinofuranosyylisytosiini	Akuutin myelooisen leukemian hoito
French	5'-O-(trans-9''-octadécènoyl)-1-bêta-D-arabinofuranosyl cytosine	Traitement de la leucémie aiguë myéloïde
German	5'-O-(trans-9''-Octadecenoyl)-1-β-D-arabinofuranosyl-cytosin	Behandlung der akuten myeloischen Leukämie
Greek	5'-O-(trans-9''-δεκαοκτενοϋλ)-1-β-D-αραβινοφουρανοσυλ κυτοσίνη	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	5'-O-(transz-9''-oktadecenoil)-1-β-D-arabinofuranozil-citozin	Akut myeloid leukaemia kezelése
Italian	5'-O-(trans-9-octadecenoil)-1-beta-D-arabinofurasonil citosina	Trattamento della leucemia mieloide acuta
Latvian	5'-O-(trans-9"-oktadecenoil)-1-beta-D-arabinofuranozilcitozīns	Akūtas mieloleikozes ārstēšana
Lithuanian	5'-O-(trans-9''-oktadecenoil)-1-β-D-arabinofuranozil citozinas	Ūmios mieloleukozės gydymas
Maltese	5'-O-(trans-9''-octadecenoyl)-1-β-D-arabinofuranosyl cytosine	Kura tal-lewkimja mjelojda akuta
Polish	5'-O-(trans-9''-oktadecenoilo)-1-beta-D-arabinofuranozylocytozyna	Leczenie ostrej białaczki szpikowej
Portuguese	5'-O-(trans-9"-octadecenoíl)-1-beta-D-arabinofuranosil citosina	Tratamento da leucemia mielóide aguda
Romanian	5'-O-(trans-9''-octadecenoil)-1-beta-D-arabinofuranozil citozina	Tratamentul leucemiei mieloide acute
Slovak	5'-O-(trans-9´´-oktadecenoyl)-1-beta-D-arabinofuranozylcytozín	Liečba akútnej myeloickej leukémie
Slovenian	5'-O-(trans-9''-oktadecenoil)-1-beta-D-arabinofuranozil citozin	Zdravljenje akutne mieloične levkemije

[1] At the time of designation

Language	Active Ingredient	Indication
Spanish	5'-O-(trans-9''-octadecenoil)1-beta-D-arabinofuranosil citosina	Tratamiento de la leucemia mieloide aguda
Swedish	5'-O-(trans-9''-oktadecenoyl)-1-beta-D-arabinofuranosyl-cytosin	Behandling av akut myeloisk leukemi
Norwegian	5'-O-(trans-9''-oktadesenoyl)-1-β-D-arabinofuranosyl cytosin	Behandling av akutt myelogen leukemi
Icelandic	5'-O-(trans-9''-oktadekenóýl)-1-beta-D-arabínófúranósýl sýtósín	Meðferð við bráðu kyrningahvítblæði