16 May 2011
EMA/COMP/129879/2008 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Amonafide L-malate for the treatment of acute myeloid leukaemia

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in March 2011 on request of the sponsor.

On 22 October 2007, orphan designation (EU/3/07/483) was granted by the European Commission to INC Research UK Ltd, United Kingdom, for amonafide L-malate for the treatment of acute myeloid leukaemia.

The sponsorship was transferred to Antisoma Research Limited, United Kingdom, in January 2009.

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 cell 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.

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

At the time of designation, acute myeloid leukaemia affected approximately 1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 50,000 people, and is below the

*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 498,000,000 (Eurostat 2006).

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threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and 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 amonafide L-malate might be of potential significant benefit for the treatment of acute myeloid leukaemia because of its mechanism of action which is different from current treatments. 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?

Amonafide L-malate is a compound made up of amonafide free base and L-malic acid. Amonafide L-malate binds to and inhibits (blocks) molecular complexes involved in the replication of DNA, the genetic material in the cells. This is a central step in the proliferation of tumour cells and thus amonafide L-malate inhibits the growth of tumour cells.

What is the stage of development of this medicine?

The effects of amonafide L-malate 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.

Amonafide L-malate was not authorised anywhere worldwide for the treatment of acute myeloid leukaemia, at the time of submission. Orphan designation of amonafide had been granted in the United States for the treatment of acute myeloid leukaemia.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 September 2007 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:

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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	Amonafide L-malate	Treatment of acute myeloid leukaemia
Bulgarian	Амонафид L-малат	Лечение на остра миелоидна левкемия
Czech	Amonafid L-malát	Léčba akutní myeloidní leukémie
Danish	Amonafid L-malat	Behandling af akut myeloid leukæmi
Dutch	Amonafide L-malaat	Behandeling van acute myeloïde leukemie
Estonian	Amonafiid L-malaat	Akuutse müeloidse leukeemia ravi
Finnish	Amonafidi L-malaatti	Akuutin myelooisen leukemian hoito
French	Malate-L d'amonafide	Traitement de la leucémie aiguë myéloïde
German	Amonafid L-Malat	Behandlung der akuten myeloischen Leukämie
Greek	L- μηλική αμοναφίδη	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	Amonafid L- maleát	Akut myeloid leukaemia kezelése
Italian	Amonafide L-malato	Trattamento della leucemia mieloide acuta
Latvian	Amonafīda L-malāts	Akūtas mieloleikozes ārstēšana
Lithuanian	Amonafido L-malatas	Ūmios mieloleukozės gydymas
Maltese	Amonafide-L-malate	Kura tal-lewkimja mjelojda akuta
Polish	Jabłczan L-amonafidu	Leczenie ostrej białaczki szpikowej
Portuguese	L-malato de amonafida	Tratamento da leucemia mielóide aguda
Romanian	Amonafidă L-malat	Tratamentul leucemiei mieloide acute
Slovak	Amonafid L-malát	Liečba akútnej myeloickej leukémie
Slovenian	Amonafid L-malat	Zdravljenje akutne mieloične levkemije
Spanish	Malato de L amonafida	Tratamiento de la leucemia mieloide aguda
Swedish	Amonafid L-malat	Behandling av akut myeloisk leukemi
Norwegian	Amonafid-L-malat	Behandling av akutt myelogen leukemi
Icelandic	Amónafíð-L-malat	Meðferð við bráðu kyrningahvítblæði

[1] At the time of designation