EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Nelarabine for the treatment of acute lymphoblastic leukaemia

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Rev.1: transfer of sponsorship	6 March 2007
Rev.2: information about Marketing Authorisation	29 July 2008
Rev.3: transfer of sponsorship	18 May 2015
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 16 June 2005, orphan designation (EU/3/05/293) was granted by the European Commission to GlaxoSmithKline Research & Development Limited, United Kingdom, for nelarabine for the treatment of acute lymphoblastic leukaemia.

The sponsorship was transferred to Glaxo Group Limited, United Kingdom, in August 2006 and subsequently to Novartis Europharm Limited, United Kingdom, in April 2015.

What is acute lymphoblastic leukaemia?

Acute lymphoblastic 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” that 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. Acute lymphoblastic leukaemia is a cancer of certain white blood cells called lymphocytes. In this disease the lymphocytes multiply too quickly and live too long, so there are too many of them circulating in the blood. These leukaemic lymphocytes look normal, but they are not fully developed and do not work properly. Over a period of time these abnormal cells replace the normal white cells, red cells and platelets in the bone marrow. It is the most common type of leukaemia in young children. This disease also affects adults, especially those aged 65 and older. Many people with acute leukaemia can be cured. However, despite the available treatments,

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acute lymphoblastic leukaemia remains a serious and life threatening condition in a subgroup of patients.

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

At the time of designation, acute lymphoblastic leukaemia affected approximately 1.1 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).

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 patient's age, symptoms, and general health. The primary treatment of acute lymphoblastic leukaemia is chemotherapy (using drugs to kill cancer cells) followed or combined with radiotherapy (using high-energy x-rays or other types of high-energy rays to kill cancer cells). Bone marrow transplantation is also available.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that nelarabine might be of potential significant benefit for the treatment of acute lymphoblastic leukaemia mainly because it might improve the long-term outcome of the patients. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain orphan status.

How is this medicine expected to work?

Enzymes are proteins produced by the human body that speed up the conversion of certain substances into other substances. Once in the blood, an enzyme naturally present in the body, converts nelarabine in a substance called arabinofuranosylguanine (ara-G). Ara-G is incorporated in the human genetic material (DNA) of the cancer cell and might lead to induce the so-called programmed cell death (apoptosis), which is an important process for the natural death of cells. Thus, it is believed that nelarabine could trigger cancer cell death in patients with acute lymphoblastic leukaemia.

What is the stage of development of this medicine?

The effects of nelarabine were evaluated in experimental models.

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

Nelarabine was not marketed anywhere worldwide for acute lymphoblastic leukaemia, at the time of submission.

Orphan designation of acute lymphoblastic leukaemia was granted in the United States for treatment of acute lymphoblastic leukaemia and lymphoblastic lymphoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 May 2005 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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 466,600,000 (Eurostat 2005).

Update: Nelarabine (Atriance) has been authorised in the EU since 22 August 2007 for the treatment of patients with T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens. Due to the small patient populations in these disease settings, the information to support these indications is based on limited data.

More information on Atriance can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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:

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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	Nelarabine	Treatment of acute lymphoblastic leukaemia
Bulgarian	Неларабин	Лечение на остра лимфобластна левкемия
Croatian	Nelarabina	Liječenje akutne limfoblastične leukemije
Czech	Nelarabin	Léčba akutní lymfoblastické leukémie
Danish	Nelarabin	Behandling af akut lymfoblastær leukæmi
Dutch	Nelarabine	Behandeling van acute lymfoblastaire leukemie
Estonian	Nelarabiin	Ägeda lümfoidse leukeemia ravi
Finnish	Nelarabiini	Akuutin lymfoblastileukaemian hoito
French	Nélarabine	Traitement de la leucémie lymphoblastique aiguë
German	Nelarabin	Behandlung der akuten lymphoblastischen Leukämie
Greek	Νελαραβίνη	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	Nelarabine	Akut lymphoblastos leukémia kezelése
Italian	Nelarabina	Trattamento della leucemia acuta linfoblastica
Latvian	Nelarabīns	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	Nelarabinas	Ūmios limfoblastinės leukozės gydymas
Polish	Nelarabina	Leczenie ostrej bialaczki limfoblastycznej
Portuguese	Nelarabina	Tratamento da leucemia linfoblástica aguda
Romanian	Nelarabina	Tratamentul leucemiei limfoblastice acute
Slovak	Nelarabín	Liečba akútnej lymfoblastickej leukémie
Slovenian	Nelarabin	Zdravljenje akutne limfoblastne levkemije
Spanish	Nelarabina	Tratamiento de la leucemia linfoblástica aguda
Swedish	Nelarabin	Behandling av akut lymfatisk leukemi
Norwegian	Nelarabin	Behandling av akutt lymfoblastisk leukemi
Icelandic	Nelarabíin	Meðferð við bráðu eitlifrumuhvítblæði

[1] At the time of transfer of sponsorship