4 March 2013
EMA/COMP/456792/2008 Rev.3
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pegylated L-asparaginase for the for the treatment of acute lymphoblastic leukaemia

On 22 September 2008, orphan designation (EU/3/08/569) was granted by the European Commission to Enzon (UK) Limited, United Kingdom, for pegylated L-asparaginase for the treatment of acute lymphoblastic leukaemia.

The sponsorship was transferred to Defiante Farmacêutica, S.A., Portugal, in September 2010 and subsequently to Sigma-tau Rare Diseases S.A., Portugal, in November 2012.

What is acute lymphoblastic leukaemia?

Acute lymphoblastic leukaemia (ALL) is a cancer of the white blood cells called lymphocytes. In this disease, the lymphocytes multiply too quickly and live for 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 and red blood cells and platelets in the bone marrow (the spongy tissue inside the large bones in the body that produces blood cells). ALL is the most common type of leukaemia in young children but the disease also affects adults, especially those aged 65 and older. Many people with acute leukaemia can be cured. However, despite the available treatments, ALL remains a serious and life-threatening condition in some patients.

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

At the time of designation, ALL affected approximately 0.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 35,000 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).

[*]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 502,800,000 (Eurostat 2008).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What treatments are available?

Treatment for ALL 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. The main treatment is chemotherapy (medicines used to kill cancer cells) followed by or combined with radiotherapy (using radiation to kill cancer cells). Bone marrow transplantation is also used.

The sponsor has provided sufficient information to show that pegylated L-asparaginase might be of potential significant benefit for the treatment of ALL because it is a new formulation of L-asparaginase that is given less often than conventional forms of the medicine. It is also expected to increase the medicine's tolerability by decreasing the response of the immune system to the L-asparaginase. These assumptions will have 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 consists of L-asparaginase that has been 'pegylated' (coated with a chemical called polyethylene glycol or PEG). This reduces the rate at which it is cleared from the body and reduces the interaction between L-asparaginase and the immune system.

L-asparaginase is an enzyme that breaks down the substance L-asparagine in the blood. L-asparagine is produced by the normal cells in the human body. Certain cancer cells, such as the cancerous cells in ALL, cannot make L-asparagine, so they need take it up from the blood in order to grow. By reducing the levels of L-asparagine in the blood, the cancerous ALL cells are deprived of their supply of L-asparagine and die.

What is the stage of development of this medicine?

The effects of pegylated L-asparaginase have been evaluated in experimental models.

According to the information submitted by the sponsor at the time of submission of the application for orphan designation, no clinical trials in patients with the designated pegylated L-asparaginase had been started.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 July 2008 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:

Sigma-tau Rare Diseases S.A.
Rua dos Ferreiros, 260
9000-082 Funchal
Portugal
Telephone: +351 291 20 30 70
Telefax: +351 291 20 30 79

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	Pegylated L-asparaginase	Treatment of acute lymphoblastic leukaemia
Bulgarian	Пегилирана L-аспарагиназа	Лечение на остра лимфобластна левкемия
Czech	Pegylovaná L-asparagináza	Léčba akutní lymfoblastické leukémie
Danish	Pegyleret L-asparaginase	Behandling af akut lymfoblastær leukæmi
Dutch	Gepegyleerde L-asparaginase	Behandeling van acute lymfoblastaire leukemie
Estonian	Pegüleeritud L-asparaginaas	Ägeda lümfoblastilise leukeemia ravi
Finnish	Pegyloitu L-asparaginaasi	Akuutin lymfoblastileukemian hoito
French	L-asparaginase pégylée	Traitement de la leucémie lymphoblastique aiguë
German	PEGylierte L-Asparaginase	Behandlung der akuten lymphatischen Leukämie
Greek	Πεγκυλιωμένη L-ασπαραγινάση	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	PEG L-aszparagináz	Akut lymphoblastos leukaemia kezelése
Italian	L-asparaginasi pegilata	Trattamento della leucemia linfoblastica acuta
Latvian	Pegilēta L-asparagināze	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	Pegiliuota L-asparaginazė	Ūmios limfoblastinės leukemijos gydymas
Maltese	Pegylated L-asparaginase	Kura tal-lewkimja limfoblastika akuta
Polish	PEG- L-asparaginaza	Leczenie ostrej białaczki limfoblastycznej
Portuguese	L-asparaginase PEGguilada	Tratamento da leucémia linfoblástica aguda
Romanian	L-asparaginază pegilată	Tratamentul leucemiei limfoblastice acute
Slovak	Pegylovaná L-asparagináza	Liečba akútnej lymfoblastickej leukémie
Slovenian	Pegilirana L-asparaginaza	Zdravljenje akutne limfoblastne levkemije
Spanish	L-asparraginasa pegilada	Tratamiento de la leucemia linfoblástica aguda
Swedish	Pegylerat L-asparaginas	Behandling av akut lymfatisk leukemi
Norwegian	Pegylert L-asparaginase	Behandling av akutt lymfoblastisk leukemi
Icelandic	Pegýleraður L-asparagínasi	Meðferð við bráðu eitilfrumuhvítblæði

[1] At the time of designation