



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pegylated recombinant *Erwinia chrysanthemi* L-asparaginase for the treatment of acute lymphoblastic leukaemia

On 5 August 2011, orphan designation (EU/3/11/889) was granted by the European Commission to Alize Pharma II, France, for pegylated recombinant *Erwinia chrysanthemi* L-asparaginase for the treatment of acute lymphoblastic leukaemia.

The sponsorship was transferred to EUSA Pharma SAS, France, in March 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 abnormal lymphocytes are not fully developed and do not work properly. Over a period of time, they replace the normal white blood cells, red blood cells and platelets in the bone marrow (the spongy tissue inside the large bones in the body, where blood cells are produced).

ALL is the most common type of leukaemia in young children, but the disease also affects adults, especially those aged 65 years and older. Many people with ALL can be cured. However, despite the available treatments, ALL remains a serious and life-threatening disease in some patients.

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

At the time of designation, acute lymphoblastic leukaemia affected less than 1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of less than 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).

*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 506,300,000 (Eurostat 2011).



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. At the time of designation, the main treatment for ALL was chemotherapy (medicines to treat cancer) followed by or combined with radiotherapy (treatment with radiation). Haematopoietic (blood) stem cell transplantation was also used. This is a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow.

The sponsor has provided sufficient information to show that pegylated recombinant *Erwinia chrysanthemi* L-asparaginase might be of significant benefit for the treatment of ALL because its prolonged effect is expected to result in less frequent dosing for patients. In addition, it is expected to result in fewer immune reactions compared with unpegylated L-asparaginase medicines. This assumption 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?

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.

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 to 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.

The medicine is made using 'recombinant DNA technology': the L-asparaginase is made by the bacterium *Escherichia coli* that has received a gene that makes it able to produce it in large quantities.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with this medicine in patients with ALL had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for ALL. Orphan designation of this medicine had been granted in the United States of America for ALL.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 May 2011 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Pegylated recombinant <i>Erwinia chrysanthemi</i> L-asparaginase	Treatment of acute lymphoblastic leukaemia
Bulgarian	Пегилирана рекомбинантна L-аспарагиназа от <i>Erwinia chrysanthemi</i>	Лечение на остра лимфобластна левкемия
Czech	Rekombitně vyrobená pegylovaná L-asparaginasa z <i>Erwinia chrysanthemi</i>	Léčba akutní lymfoblastické leukémie
Danish	Pegylet rekombinant <i>Erwinia chrysanthemi</i> L-asparaginase	Behandling af akut lymfoblastær leukæmi
Dutch	Gepegyleerde recombinante <i>Erwinia chrysanthemi</i> L-asparaginase	Behandeling van acute lymfoblastaire leukemie
Estonian	Pegüleeritud rekombinantne <i>Erwinia chrysanthemi</i> L-asparaginaas	Ägeda lümfoblastilise leukeemia ravi
Finnish	Peguloitu rekombinantti <i>Erwinia chrysanthemi</i> L-asparaginaasi	Akuutin lymfoblastileukemian hoito
French	L-asparaginase pégylée recombinante d' <i>Erwinia chrysanthemi</i>	Traitement de la leucémie lymphoblastique aiguë
German	Pegylierte rekombinante <i>Erwinia chrysanthemi</i> -L-Asparaginase	Behandlung der akuten lymphatischen Leukämie
Greek	Πεγκυλιωμένη ανασυνδυασμένη ασπαραγινάση από <i>Erwinia chrysanthemi</i>	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	Pegilált rekombináns <i>Erwinia chrysanthemi</i> L-aszparagináz	Akut lymphoblastos leukaemia kezelése
Italian	L-asparaginasi pegilata ricombinante da <i>Erwinia chrysanthemi</i>	Trattamento della leucemia linfoblastica acuta
Latvian	Pegilāta rekombinanta <i>Erwinia chrysanthemi</i> L-asparagināze	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	Pegiliuota rekombinantinė <i>Erwinia chrysanthemi</i> L-asparaginazė	Ūmios limfoblastinės leukemijos gydymas
Maltese	L-asparaginase rikombinanti pegilat minn <i>Erwinia chrysanthemi</i>	Kura tal-lewkimja limfoblastika akuta
Polish	Pegylowana rekombinowana L-asparaginaza <i>Erwinia chrysanthemi</i>	Leczenie ostrej białaczki limfoblastycznej
Portuguese	L-asparaginase recombinante peguilada da <i>Erwinia chrysanthemi</i>	Tratamento da leucémia linfoblástica aguda
Romanian	L-asparaginază recombinantă pegilată din <i>Erwinia chrysanthemi</i>	Tratamentul leucemiei limfoblastice acute
Slovak	Pegylovaná rekombinantná Lasparagináza z <i>Erwinia chrysanthemi</i>	Liečba akútnej lymfoblastickej leukémie
Slovenian	Pegilirana rekombinantna <i>Erwinia chrysanthemi</i> L-asparaginaza	Zdravljenje akutne limfoblastne levkemije
Spanish	L-asparaginasa recombinante pegilada de <i>Erwinia chrysanthemi</i>	Tratamiento de la leucemia linfoblástica aguda

¹ At the time of designation

Language	Active ingredient	Indication
Swedish	Pegylerat rekombinant <i>Erwinia chrysanthemi</i> L-asparaginas	Behandling av akut lymfatisk leukemi
Norwegian	Pegylert rekombinant <i>Erwinia chrysanthemi</i> L-asparaginase	Behandling av akutt lymfoblastisk leukemi
Icelandic	Pegýleraður raðbrigða L-asparagínasi úr <i>Erwinia chrysanthemi</i>	Meðferð við bráðu eitilfrumuhvítblæði