



European Medicines Agency  
Pre-authorisation Evaluation of Medicines for Human Use

**Document Date:** London, 29 July 2008  
**Doc.Ref.:** EMEA/COMP/359204/2006

## **COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS**

### **PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF L-asparaginase encapsulated in erythrocytes for the treatment of acute lymphoblastic leukaemia**

On 27 October 2006, orphan designation (EU/3/06/409) was granted by the European Commission to Erytech Pharma S.A., France, for L-asparaginase encapsulated in erythrocytes for the treatment of acute lymphoblastic leukaemia.

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

#### **What are the methods of treatment available?**

Treatment for leukaemia is complex and depends on a number of factors including the type of leukemia, 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 L-asparaginase encapsulated in erythrocytes might be of potential significant benefit for the treatment of acute lymphoblastic leukaemia. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain orphan status.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, acute lymphoblastic leukaemia was considered to affect approximately 0.5 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 23,000 persons in total.

**How is this medicinal product expected to act?**

L-asparagine is a substance produced by the normal cells in the human body. Certain cancer cells, such as the lymphoblastic leukaemia cells, are unable to produce L-asparagine and therefore take it from the blood since they need it for their rapid growth. L-asparaginase is an enzyme (a protein that speed up the conversion of certain substances into other substances). When administrating L-asparaginase to patients with acute lymphoblastic leukaemia it destroys L-asparagine present in the blood and the cancer cells are thus deprived of their supply and will die. The L-asparaginase is wrapped (encapsulated) in red blood cells (human erythrocytes) as they have offer the cellular compartment for the enzymatic reaction.

**What is the stage of development of this medicinal product?**

The evaluation of the effects of L-asparaginase encapsulated in erythrocytes in experimental models is ongoing.

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

L-asparaginase encapsulated in erythrocytes was not marketed anywhere worldwide for acute lymphoblastic leukaemia or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 6 September 2006 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

**For more information:**

Sponsor's contact details:

Erytech Pharma S.A.

60, avenue Rockefeller

69008 Lyon

France

Telephone: +33 4 78 74 44 38

Telefax: +33 4 78 75 56 29

E-mail: [science@erytech.com](mailto:science@erytech.com)

---

\* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients' associations contact points:

**Leukaemia Care**

2 Shrubbery Avenue

Worcester

WR1 1QH

United Kingdom

0800 169 6680 (freephone for UK residents)

Telephone: +44 19 05 33 00 03 / +44 84 57 67 32 03

Telefax: +44 19 05 33 00 90

E-mail: [enquiries@leukaemiaCARE.org.uk](mailto:enquiries@leukaemiaCARE.org.uk)

**Ligue Nationale Contre le Cancer**

13 Av. de la Grande Armee

75116 Paris

France

Telephone: +33 1 45 00 00 17

Telefax: +33 1 45 00 63 06

E-mail: [ligue@ligue-cancer.net](mailto:ligue@ligue-cancer.net)

**Aplastischen Anämie e. V.**

Am Lettenholz 41

83646 Bad Tölz

Germany

Telephone: +49 80 41 80 65 06

Telefax : +49 80 41 80 65 07

E-mail: [info@aplastische-anaemie.de](mailto:info@aplastische-anaemie.de)

**Translations of the active ingredient and indication in all EU languages  
and Norwegian and Icelandic**

<b>Language</b>	<b>Active Ingredient</b>	<b>Indication</b>
English	L-Asparaginase encapsulated in erythrocytes	Treatment of acute lymphoblastic leukaemia
Czech	L-asparagináza uzavřená v erythrocytech	Léčba akutní lymfoblastické leukémie
Danish	L-asparaginase indkapslet i erythrocytter	Behandling af akut lymfoblastær leukæmi
Dutch	L-asparaginase, ingekapseld in erythrocyten	Behandeling van acute lymfoblastaire leukemie
Estonian	Punaverelibledesse kapseldatud L-asparaginaas	Ägeda lümfoblastilise leukeemia ravi
Finnish	Punasoluihin kapseloitu L-asparaginaasi	Akuutin lymfoblastileukemian hoito
French	L-Asparaginase encapsulée dans des érythrocytes	Traitement de la leucémie lymphoblastique aiguë
German	In Erythrozyten verkapselte L-Asparaginase	Behandlung der akuten lymphatischen Leukämie
Greek	L-ασπαραγινάση ενθυλακωμένη σε ερυθρά αιμοσφαίρια	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	Erythrocytába kapszulázott L-aszparagináz	Akut lymphoblastos leukaemia kezelése
Italian	L-asparaginasi incapsulata in eritrociti	Trattamento della leucemia linfoblastica acuta
Latvian	Eritrocītos iekapsulēta L-asparagināze	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	L-Asparaginazė, absorbuota eritrocituose	Ūmios limfoblastinės leukemijos gydymas
Polish	L-asparaginaza zawarta w erythrocytach	Leczenie ostrej białaczki limfoblastycznej
Portuguese	L-asparaginase encapsulada em eritrócitos	Tratamento da leucemia linfoblástica aguda
Slovak	L-asparagináza uzavretá v erythrocytoch	Liečba akútnej lymfoblastickej leukémie
Slovenian	L-asparaginaza inkapsulirana v eritrocitih	Zdravljenje akutne limfoblastne levkemije
Spanish	L-asparaginasa encapsulada en eritrocitos	Tratamiento de la leucemia linfoblástica aguda
Swedish	L-asparaginas inkapslad i erythrocyter	Behandling av akut lymfatisk leukemi
Norwegian	L-asparaginase innkapslet i røde blodlegemer	Behandling av akutt lymfoblastisk leukemi
Icelandic	L-asparagínasi hjúpaður inn í rauðum blóðkornum	Meðferð við bráðu eitlifrumuhvítblæði