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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

**PUBLIC SUMMARY OF
POSITIVE OPINION FOR ORPHAN DESIGNATION
OF
L-asparaginase
for the treatment of acute lymphoblastic leukemia**

On 26 January 2005, orphan designation (EU/3/04/258) was granted by the European Commission to medac Gesellschaft fuer klinische Spezialpräparate mbH, Germany, for L-asparaginase (developed using recombinant DNA technology) for the treatment of acute lymphoblastic leukemia.

What is acute lymphoblastic leukemia?

Acute lymphoblastic leukemia 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 leukemia develops, the bone marrow produces large numbers of abnormal blood cells. There are several types of leukemias. Acute lymphoblastic leukemia 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 leukemic 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 leukemia in young children. This disease also affects adults, especially those aged 65 and older. Many people with acute leukemia can be cured. However, despite the available treatments, acute lymphoblastic leukemia remains a serious and life threatening condition in a subgroup of patients.

What are the methods of treatment available?

Treatment for leukemia is complex and depends on a number of factors including the type of leukemia, the extent of the disease and whether the leukemia has been treated before. It also depends on the patient's age, symptoms, and general health. The primary treatment of acute lymphoblastic leukemia 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 (developed using recombinant DNA technology) might be of potential significant benefit for the treatment of acute lymphoblastic leukemia. 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*?

According to the information provided by the sponsor, acute lymphoblastic leukemia was considered to affect about 51,000 persons in the European Union.

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 leukemia 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) and is isolated from the bacteria, *Escherichia coli*. When administrating L-asparaginase to patients with acute lymphoblastic leukemia it destroys L-asparagine present in the blood and the cancer cells are thus deprived of their supply and will die.

What is the stage of development of this medicinal product?

The effects of the medicinal product were evaluated in experimental models.

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

L-asparaginase (developed using recombinant DNA technology) was not marketed anywhere worldwide for acute lymphoblastic leukemia 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 7-8 December 2004 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:

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*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:

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

Language	Active Ingredient	Indication
English	L-asparaginase	Treatment of acute lymphoblastic leukaemia
Czech	L-asparagináza	Treatment of akutní lymfoblastická leukémie
Danish	L-asparaginase	Behandling af akut lymfoblastær leukæmi
Dutch	L-asparaginase	Behandeling van acute lymfoblastaire leukemie
Estonian	L-asparaginaasi	Ägeda lümfoidse leukeemia ravi
Finnish	L-asparaginaasi	Akuutin lymfoblastileukemian hoito
French	L-asparaginase	Traitement de la leucémie lymphoblastique aiguë
German	L-Asparaginase	Behandlung von akuter lymphatischer Leukämie
Greek	L-Ασπαργινάση	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	L-aszparagináz	Treatment of akut lymphoblastos leukémia
Italian	L-asparaginasi	Trattamento della leucemia acuta linfoblastica
Latvian	L-asparagināze	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	L-Asparaginazė	Ūmios limfoblastinės leukozės gydymas
Polish	L-asparaginaza	Leczenie ostrej białaczki limfoblastycznej
Portuguese	L-asparaginase	Tratamento da leucemia linfoblástica aguda
Slovak	L-asparagináza	Liečba akútnej lymfoblastickej leukémie
Slovenian	L-asparaginaza	Zdravljenje akutne limfoblastne levkemije
Spanish	L-Asparaginasa	Tratamiento de la leucemia linfoblástica aguda
Swedish	Krisantaspas	Behandling av akut lymfatisk leukemi
Norwegian	L-asparaginase	Behandling av akutt lymfatisk leukemi
Icelandic	L-Asparagínasi	Meðferð við bráðu eitlifrúmuhvítblæði