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EMA/COMP/378/2004 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Aplidine for the treatment of acute lymphoblastic leukaemia

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in June 2011 on request of the sponsor.

On 9 July 2003, orphan designation (EU/3/03/151) was granted by the European Commission to Pharma Mar SA Sociedad Unipersonal, Spain, for aplidine 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.

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

At the time of designation, acute lymphoblastic leukaemia affected approximately 0.4 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 15,000 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. Treatments that had been authorised at the time of submission of the application for orphan drug designation included different chemotherapeutic agents (drugs to kill cancer cells). Bone marrow transplantation is also available.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that aplidine might be of potential significant benefit for the treatment of acute lymphoblastic leukaemia, because it may act in a different way than other available medicines. 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?

Aplidine is a medicinal product originally isolated from a marine organism called *Aplidium albicans* and currently obtained by total synthesis. It is a compound formed by molecules called peptides that can combine and form proteins. The mechanism of action of aplidine is under investigation but might block the growth of the leukaemia cells and might help in the destruction of these cells.

What is the stage of development of this medicine?

The effects of aplidine were evaluated in experimental models. At the time of submission of the application for orphan designation, no clinical trials in patients with acute lymphoblastic leukaemia were initiated.

Aplidine was not marketed anywhere worldwide for acute lymphoblastic leukaemia or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 June 2003 recommending the granting of this designation.

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[*]Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 385,000,000 (Eurostat 2002) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

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	Aplidine	Treatment of acute lymphoblastic leukaemia
Danish	Aplidine	Behandling af akut lymfoblastisk leukæmi
Dutch	Aplidine	Behandeling van acute lymfoblastenleukemie
Finnish	Aplidine	Akuutin lymfaattisen leukemian hoito
French	Aplidine	Traitement de la leucémie lymphoblastique aiguë
German	Aplidine	Benhandlung der acuten lymphoblastischen Leukäemie
Greek	Aplidine	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Italian	Aplidine	Trattamento della leucemia linfoblastica acuta
Portuguese	Aplidine	Tratamento da leucemia linfoblástica aguda
Spanish	Aplidine	Tratamiento de la leucemia linfoblástica aguda
Swedish	Aplidine	Behandling av akut lymfoblastleukemi

[1] At the time of designation