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

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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF aplidine for the treatment of multiple myeloma

On 16 November 2004, orphan designation (EU/3/04/245) was granted by the European Commission to PharmaMar SA Sociedad Unipersonal, Spain, for aplidine for the treatment of multiple myeloma.

What is multiple myeloma?

Multiple myeloma is a cancer of a type of white blood cells called plasma cells. Plasma cells are found in 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. Platelets make the blood clot, and white blood cells fight infection. In multiple myeloma an excessive number of plasma cells are produced. Normally, the division of cells takes place in a controlled manner but with multiple myeloma, the process gets out of control and abnormal plasma cells multiply, producing many myeloma cells. These fill up the bone marrow and interfere with production of the normal white cells, red cells and platelets. This leads to a number of possible complications, which include anaemia, bone pain and fractures, raised levels of calcium in the blood and kidney disease. Multiple myeloma is life-threatening.

What are the methods of treatment available?

The main treatment of multiple myeloma is chemotherapy (using drugs to kill cancer cells) usually combined with steroids (a group of chemical substances, belonging to a larger class of molecules, the so-called hormones, which have an effect on the activity of certain organs). Other types of treatment for multiple myeloma are radiotherapy (using high-dose x-rays or other high-energy rays to kill cancer cells) and immunotherapy (using drugs that stimulate the body's own immune system to kill cancer cells). Radiotherapy (using high-dose x-rays or other high-energy rays to kill cancer cells) can be useful to treat painful areas and weakened bones. Several products were authorised for the condition in the Community at the time of submission of the application for orphan drug designation.

Aplidine could be of potential significant benefit for the treatment of multiple myeloma 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 the orphan status.

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

According to the information provided by the sponsor, multiple myeloma was considered to affect about 69,000 persons in the European Union.

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How is this medicinal product expected to act?
Aplidine is a medicinal product originally isolated from a marine organism called *Aplidium albicans*. The mechanism of action of aplidine is under investigation but it is assumed that it might block the growth of the multiple myeloma cells and might help in the destruction of these cells.

What is the stage of development of this medicinal product?
The effects of aplidine were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with multiple myeloma were ongoing.

Aplidine was not authorised anywhere worldwide for treatment of multiple myeloma, at the time of submission. Orphan designation of aplidine was granted in the European Union for acute lymphoblastic leukemia.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 7 October 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.

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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.

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

Language	Active Ingredient	Indication
English	Aplidine	Treatment of multiple myeloma
Czech	Aplidine	Léčba mnohočetného myelomu
Danish	Aplidine	Behandling af multipelt myelom
Dutch	Aplidine	Behandeling van multipel myeloom
Estonian	Aplidiin	Hulgimüeloomi ravi
Finnish	Aplidine	Multippeli myelooman hoito
French	Aplidine	Traitement du myélome multiple
German	Aplidine	Behandlung des multiplen Myeloms
Greek	Απλιδίνη	Θεραπευτική αγωγή πολλαπλού μυελώματος
Hungarian	Aplidine	Myeloma multiplex kezelése
Italian	Aplidine	Trattamento del mieloma multiplo
Latvian	Aplidine	Multiplās mielomas ārstēšana
Lithuanian	Aplidinas	Dauginės mielomos gydymas
Maltese	Aplidine	Treatment of multiple myeloma
Polish	Aplidyna	Leczenie szpiczaka mnogiego
Portuguese	Aplidine	Tratamento do mieloma múltiplo
Slovak	Aplidine	Liečba mnohopočetného myelómu
Slovenian	Aplidin	Zdravljenje multiplega mieloma
Spanish	Aplidine	Tratamiento del mieloma múltiple
Swedish	Aplidine	Behandling av multipelt myelom
Norwegian	Aplidin	Behandling av myelomatose
Icelandic	Aplidín	Meðferð við mergæxlageri