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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Plitidepsin for the treatment of primary myelofibrosis

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in June 2011 on request of the sponsor.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 23 February 2011, orphan designation (EU/3/10/837) was granted by the European Commission to Pharma Mar S.A. Sociedad Unipersonal, Spain, for plitidepsin for the treatment of primary myelofibrosis.

What is primary myelofibrosis?

Primary myelofibrosis is a disease of unknown cause in which the bone marrow (the spongy tissue inside the large bones) becomes dense and fibrous, and starts producing abnormal immature blood cells that replace the normal blood cells.

In this disease, some immature blood cells migrate from the bone marrow to other organs, such as the spleen and liver, where they mature. This causes the organs to become enlarged. Patients with primary myelofibrosis can develop several symptoms, including pain in the bones, tiredness, weakness, infections and bleeding.

Primary myelofibrosis is a debilitating disease that is long lasting and may be life threatening because it results in severe anaemia (low red blood cell counts) and infections, and can lead to leukaemia (cancer of the white blood cells).

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

At the time of designation, primary myelofibrosis affected approximately 0.17 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 9,000 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 506,500,000 (Eurostat 2010).

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What treatments are available?

At the time of designation, hydroxyurea and busulfan (which are also used to treat cancer) were authorised in the EU for primary myelofibrosis. In addition, treatments aimed at relieving the symptoms of the disease were used. These included androgens (male hormones), glucocorticoids (a type of steroid) and erythropoietin (a hormone that stimulates the production of red blood cells) to treat anaemia, and surgery to remove the enlarged spleen. In some patients, haematopoietic (blood) stem-cell transplantation was 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 plitidepsin might be of significant benefit for patients with primary myelofibrosis because it works in a different way to existing treatments, and early studies in experimental models show that it may specifically target the bone marrow and improve its function. These assumptions 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?

Plitidepsin is a cytotoxic (cell-killing) substance. In myelofibrosis, it is expected to work mainly by stimulating the production of an enzyme known as p27, whose main activity is to slow down or stop cell division. Around 50% of myelofibrosis patients have reduced amounts of this enzyme. By stimulating the production of p27, plitidepsin is expected to slow down the reproduction and abnormal growth of blood cells in the bone marrow of patients with myelofibrosis, thus slowing down the symptoms of the disease.

What is the stage of development of this medicine?

The effects of plitidepsin have been evaluated in experimental models.

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

At the time of submission, plitidepsin was not authorised anywhere in the EU for primary myelofibrosis or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 November 2010 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Plitidepsin	Treatment of primary myelofibrosis
Bulgarian	Плитидепсин	Лечение на първична миелофиброза
Czech	Plitidepsin	Léčba primární myelofibrózy
Danish	Plitidepsin	Behandling af primær myelofibrose
Dutch	Plitidepsine	Behandeling van primaire myelofibrose
Estonian	Plitidepsiin	Esmase müelofibroosi ravi
Finnish	Plitidepsiini	Primaarisen myelofibroosin hoito
French	Plitidepsine	Traitement de la myélofibrose primitive
German	Plitidepsin	Behandlung der primären Myelofibrose
Greek	Πλιτιδεψίνη	Θεραπεία της πρωτογενούς μυελοσκλήρυνσης
Hungarian	Plitidepszin	Primer mielofibrózis kezelésére
Italian	Plitidepsina	Trattamento della mielofibrosi primitiva
Latvian	Plitidepsīns	Primāras mielofibrozes ārstēšana
Lithuanian	Plitidepsinas	Pirminės mielofibrozės gydymas
Maltese	Plitidepsin	Kura tal-mjelofibrożi primarja
Polish	Plitydepsyna	Leczenie mielofibrozy pierwotnej
Portuguese	Plitidepsina	Tratamento da mielofibrose primária
Romanian	Plitidepsină	Tratamentul mielofibrozei primitive
Slovak	Plitidepsín	Liečba primárnej myelofibrózy
Slovenian	Plitidepsin	Zdravljenje primarne mielofibroze
Spanish	Plitidepsina	Tratamiento de la mielofibrosis primaria
Swedish	Plitidepsin	Behandling av primär myelofibros
Norwegian	Plitidepsin	Behandling av primær myelofibrose
Icelandic	Plítidepsín	Meðferð á beinmergsnetjuhersli

[1] At the time of designation