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

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in March 2009 on request of the Sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of

H-Tyrosine-Glycine-Phenylalanine-Glycine-Glycine-OH for the treatment of chronic idiopathic myelofibrosis

On 20 October 2003, orphan designation (EU/3/03/167) was granted by the European Commission to Abiogen Pharma S.p.A, Italy, for H-Tyrosine-Glycine-Phenylalanine-Glycine-Glycine-OH for the treatment of chronic idiopathic myelofibrosis.

What is chronic idiopathic myelofibrosis?
Chronic idiopathic myelofibrosis is a disease in which cancer cells are found in the blood and 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. White blood cells fight infection. Platelets make the blood clot. When myelofibrosis develops, the bone marrow produces large number of abnormal blood cells. In chronic idiopathic myelofibrosis the abnormal population of cells produce substances that alter the growth media of bone marrow and makes bone marrow very dense and rigid. As the abnormal bone marrow environment is no more adequate for the cells, some migrate to other sites where proliferation and maturation take place.
Chronic idiopathic myelofibrosis is life threatening, in particular due to the decreased life expectancy of patients.

What is the estimated number of patients affected by the condition*?
At the time of designation, chronic idiopathic myelofibrosis affected approximately 1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 39,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?
Currently only hydroxyurea is authorised in the Community for the treatment of the condition. Other drugs are used for the treatment of symptoms of the disease such as androgen, glucocorticoids or erythropoietin for anaemia; splenectomy (surgical removal of the spleen) is performed in case of excessive enlargement of the spleen (splenomegaly); and bone marrow transplantation in some patients.

*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 about 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.

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H-Tyrosine-Glycine-Phenylalanine-Glycine-Glycine-OH might be of potential significant benefit for the treatment of chronic idiopathic myelofibrosis because it can act in a different way than other available treatments. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?
Polypeptides are substances made of sequences of units called amino acids. H-Tyrosine-Glycine-Phenylalanine-Glycine-Glycine-OH is the smallest amino acid sequence of a bigger polypeptide with the property to stimulate the cell growth (mitogenesis) and the maturation of young cells into adult cells (differentiation). H-Tyrosine-Glycine-Phenylalanine-Glycine-Glycine-OH is expected to exercise these activities in the cells that are affected in chronic idiopathic myelofibrosis and might thereby stimulate their proliferation and development in bone marrow. This could then lead to an increased number of mature cells in the blood.

What is the stage of development of this medicine?
At the time of submission of the application for orphan designation, clinical trials in patients with chronic idiopathic myelofibrosis were ongoing.

H-Tyrosine-Glycine-Phenylalanine-Glycine-Glycine-OH was not marketed anywhere worldwide for chronic idiopathic myelofibrosis 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 10 September 2003 a positive opinion recommending the grant of the above-mentioned 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 Community) 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.

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Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	H-Tyrosine-Glycine-Phenylalanine-Glycine-Glycine-OH	Treatment of chronic idiopathic myelofibrosis
Danish	H-tyrosin-glycin-fenylalanin-glycin-glycin-OH	Behandling af kronisk idiopatisk myelofibrose
Dutch	H-Tyrosine-Glycine-Fenylalanine-Glycine-Glycine-OH	Behandeling van chronische idiopathische myelofibrose
Finnish	H-tyrosiini-glysiini-fenylalaniini-glysiini-glysiini-OH	Kroonisen idiopaattisen myelofibroosin hoito
French	H-Tyrosine-Glycine-Phénylalanine-Glycine-Glycine-OH	Traitement de la splénomégalie myéloïde chronique idiopathique
German	H-Thyrosin-Glycin-Phenylalanin-Glycin-Glycin-OH	Behandlung von chronischer idiopathischer Myelofibrose
Greek	H-Τυροσίνη-Γλυκίνη-Φαινυλαλανίνη-Γλυκίνη-Γλυκίνη-OH	Θεραπεία της χρόνιας ιδιοπαθούς μυελοσκλήρυνσης
Italian	H-Tirosina-Glicina-Fenilalanina-Glicina-Glicina-OH	Trattamento della mielofibrosi idiopatica cronica
Portuguese	H-Tirosina-Glicina-Fenilalanina-Glicina-Glicina-OH	Tratamento da mielofibrose idiopática crónica
Spanish	H-Tirosina-Glicina-Fenilalanina-Glicina-Glicina-OH	Tratamiento de la mielofibrosis idiopática crónica
Swedish	H-tyrosin-glycin-fenylalanin-glycin-glycin-OH	Behandling av kronisk idiopatisk myelofibros