



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 [Nle⁴, D-Phe⁷]-alpha-melanocyte stimulating hormone for the treatment of congenital erythropoietic porphyria

On 8 May 2008, orphan designation (EU/3/08/545) was granted by the European Commission to Clinuvel UK Limited, United Kingdom, for [Nle⁴, D-Phe⁷]-alpha-melanocyte stimulating hormone for the treatment of erythropoietic porphyria.

What is congenital erythropoietic porphyria?

Porphyrias are a group of disorders of certain enzymes (proteins that speed up the conversion of certain substances into other substances) responsible for the chemical steps of heme production. Heme is normally present in the body and it is the basic component of haemoglobin, the molecule that carries oxygen in the blood. It is mainly found in the blood, bone marrow, and liver. The signs and symptoms of the disorder vary depending on which chemical step of the heme production that is affected. The porphyrias can be classified according to different criteria, such as the main location of the abnormal enzyme, the leading symptom, and the characteristics of its clinical presentation.

Congenital erythropoietic porphyria is one form of inherited porphyria where the blood forming organs and the skin are affected. In congenital erythropoietic porphyria, there is an in-born lack of one enzyme important for the heme production, and therefore the red blood cells accumulate substances that they normally do not accumulate. These substances damage red blood cells and cause anaemia. These substances are also accumulated in the skin. When skin is exposed to sunlight the accumulated substances react with light and cause severe skin damage, inducing formation of vesicles, ulceration, thinning and disfigurement of the skin.

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

At the time of designation, congenital erythropoietic porphyria affected less than 0.01 in 10,000 people in the European Union (EU)*. This is equivalent to a total of fewer than 500 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?

No satisfactory methods exist that were authorised at the time of application. Strict avoidance of sunlight or strong light altogether is essential to manage the disease, as well as avoidance of mechanical trauma and meticulous skin care.

*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 502,282,000 (Eurostat 2008).

How is this medicine expected to work?

The product, [Nle⁴, D-Phe⁷] alpha-melanocyte stimulating hormone is a synthetic product with similar properties to the naturally occurring alpha-melanocyte stimulating hormone or melanotropin. This hormone is a naturally occurring hormone that stimulates the production of eumelanine in skin cells. Eumelanine, the natural black-brown pigment in the skin, has the capacity to protect cells from irradiation (sun exposure) and its damaging effects on the cellular genetic material. It is thought that the product stimulates eumelanin production in the skin cells and stops cellular damage by inhibiting (blocking) sun light's interaction with the accumulated substances that are found in the skin of patients with congenital erythropoietic porphyria.

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 congenital erythropoietic porphyria were ongoing.

[Nle⁴, D-Phe⁷] alpha-melanocyte stimulating hormone was not authorised anywhere worldwide for congenital erythropoietic porphyria 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 4 March 2008 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
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	[Nle ⁴ , D-Phe ⁷]-alpha-melanocyte stimulating hormone	Treatment of congenital erythropoietic porphyria
Bulgarian	[Nle ⁴ , D-Phe ⁷]- алфа-меланоцитостимулиращ хормон	Лечение на вродена еритропоетична порфирия
Czech	[Nle ⁴ , D-Phe ⁷]-alfa melanocyty stimulující hormon	Léčba vrozené erythropoetické porfyrie
Danish	[Nle ⁴ , D-Phe ⁷]-alfa-melanocytstimulerende hormon	Behandling af kongenit erytropoietisk porfyri
Dutch	[Nle ⁴ , D-Phe ⁷]-alfa-melanocytstimulerend hormoon	Behandeling van congenitale erythropoëtische porphyrie
Estonian	[Nle ⁴ , D-Phe ⁷]-alfa melanotsüüte stimuleeriv hormoon	Kaasasündinud erütropoeetilise porfüüria ravi
Finnish	[Nle ⁴ , D-Phe ⁷]- alfa melanotsyyttejä stimuloiva hormoni	Synnynnäisen erytropoieettisen porfyrian hoito
French	[Nle ⁴ , D-Phe ⁷]-mélanostimuline alpha	Traitement de la porphyrie érythropoïétique congénitale
German	[Nle ⁴ , D-Phe ⁷]-alpha-melanozytenstimulierendes Hormon	Behandlung der kongenitalen erythropoetischen Porphyrie
Greek	[Nle ⁴ , D-Phe ⁷]άλφα-ορμόνη διέγερσης των μελανοκυττάρων	Θεραπεία της συγγενούς ερυθροποιητικής πορφύρας
Hungarian	[Nle ⁴ , D-Phe ⁷]-alfa-melanocyta-stimuláló hormon	Kongenitális erythropoietikus porfíria kezelése
Italian	[Nle ⁴ , D-Phe ⁷]-alfa-melanotropina	Terapia della porfíria eritropoietica congenita
Latvian	[Nle ⁴ , D-Phe ⁷]-alfa melanocītus stimulējošais hormons	Iedzimtas eritropoētiskas porfīrijas ārstēšana
Lithuanian	[Nle ⁴ , D-Phe ⁷]-alfa-melanocytus stimuliuojantis hormonas	Įgimtos eritropoetinės porfīrijos gydymas
Maltese	[Nle ⁴ , D-Phe ⁷]-Ormon li jistimula l-alfa-melanocite	Kura tal-porfirja eritropojetika kongenitali
Polish	[Nle ⁴ , D-Phe ⁷] hormon stymulujący melanocyty alfa	Leczenie wrodzonej porfirii erytropoetycznej
Portuguese	[Nle ⁴ , D-Phe ⁷]-Hormona estimuladora dos melanocitos alfa	Tratamento da porfíria eritropoiética congénita
Romanian	[Nle ⁴ , D-Phe ⁷]-hormon melanocitostimulator alfa	Tratamentul porfiriei eritropoietice congenitale
Slovak	[Nle ⁴ , D-Phe ⁷]-alfa melanocyty stimulujúci hormón	Liečba vrodenej erytropoetickej porfýrie
Slovenian	[Nle ⁴ , D-Phe ⁷]-alfa-melanocyte stimulirajoči hormon	Zdravljenje kongenitalne eritropoetične porfirije
Spanish	[Nle ⁴ , D-Phe ⁷]- hormona estimulante de los melanocitos alfa	Tratamiento de la profiria congénita eritropoyética
Swedish	[Nle ⁴ , D-Phe ⁷]-alfa-melanocytstimulerande hormone	Behandling av medfödd eytropoietisk porfyri

Norwegian	[Nle4, D-Phe7]-alfa-melanocytstimulerende hormon	Behandling av medfødt erythropoietisk porfyri
Icelandic	[Nle4, D-Phe7]-alfa-sortufrumnahvati	Til meðferðar við meðfæddri erýtrópoietic porfýríu