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EMA/COMP/247606/2005 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sapropterin for the treatment of hyperphenylalaninemia

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in December 2010 on request of the Sponsor.

On 26 August 2005, orphan designation (EU/3/05/308) was granted by the European Commission to Dr Gunter Schaub, Germany, for sapropterin for the treatment of hyperphenylalaninemia.

What is hyperphenylalaninemia?

Hyperphenylalaninemia or phenylketonuria, is an inherited disease caused by a genetic abnormality which results in reduced activity of an enzyme, phenylalanine hydroxylase. This enzyme is responsible for conversion of a certain aminoacid (a building block for proteins) called phenylalanine, into another aminoacid called tyrosine. The result of this enzyme deficiency is an accumulation of high concentrations of phenylalanine in the blood and urine, up to harmful levels. Phenylalanine is toxic at high levels and can lead to severe brain damage. The disease is subdivided into mild, moderate and severe forms, according to the degree of elevation of phenylalanine blood levels.

Hyperphenylalaninemia is chronically debilitating and is characterised by mental retardation if left untreated.

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

At the time of designation, hyperphenylalaninemia affected approximately 1.7 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 78,000 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 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 submission of the application for orphan drug designation, the treatment of hyperphenylalaninemia consisted of lifelong strict dietary protein restriction aiming to reduce phenylalanine intake.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that sapropterin might be of potential significant benefit for the treatment of hyperphenylalaninemia as it might decrease the dietary requirements. The 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?

Sapropterin might help restore the phenylalanine hydroxylase enzyme activity. As a result more phenylalanine might be converted to tyrosine, so that patients may tolerate more phenylalanine and thus higher protein intake. This might decrease the daily dietary requirements.

What is the stage of development of this medicine?

The evaluation of the effects of sapropterin in experimental models is ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with hyperphenylalaninemia were initiated.

Sapropterin was not authorised anywhere worldwide for treatment of hyperphenylalaninemia 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 July 2005 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

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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	Sapropterin	Treatment of hyperphenylalaninemia
Czech	Sapropterin	Léčba hyperfenylalaninémie
Danish	Sapropterin	Behandling af hyperfenylalaninæmi
Dutch	Sapropterine	Behandeling van hyperfenylalaninemie
Estonian	Sapropteriin	Hüperfenüülalanineemia ravi
Finnish	Sapropteriini	Hyperfenyylialaninemian hoito
French	Saproptérine	Traitement de l'hyperphénylalaninémie
German	Sapropterin	Behandlung von Hyperphenylalaninämie
Greek	Σαπροπτερίνη	Θεραπεία της υπερφαινυλαλανιναιμίας
Hungarian	Sapropterin	Hyperphenylalaninaemia kezelése
Italian	Sapropterina	Trattamento dell'iperfenilalaninemia
Latvian	Sapropterīns	Hiperfenilalaninēmijas ārstēšana
Lithuanian	Sapropterinas	Hiperfenilalaninemijos gydymas
Polish	Sapropteryna	Leczenie hiperfenyloalaninemii
Portuguese	Sapropterina	Tratamento da hiperfenilalaninemia
Slovak	Sapropterín	Liečba hyperfenylalaninémie
Slovenian	Sapropterin	Zdravljenje hiperfenilalaninemije
Spanish	Sapropterina	Tratamiento de la hiperfenilalaninemia
Swedish	Sapropterin	Behandling av hyperfenylalaninemi
Norwegian	Sapropterin	Behandling av hyperfenylalaninemi
Icelandic	Sapropterín	Meðferð við fenýlalanínskreyra

[1] At the time of designation