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 5,6,7,8 tetrahydrobiopterin for the treatment of hyperphenylalaninemia.

On 2 October 2003, orphan designation (EU/3/03/163) was granted by the European Commission to Prof. Dr. A. A. Roscher, Germany, for 5,6,7,8 tetrahydrobiopterin for the treatment of hyperphenylalaninemia.
The sponsorship was transferred to Orphanetics Pharma Entwicklungs GmbH, Austria, in December 2005.

What is hyperphenylalaninemia?

Hyperphenylalaninemia or phenylketonuria, is a congenital disease (due to a genetic abnormality) and is caused by a reduced activity of an enzyme, phenylalanine hydroxylase. This enzyme is responsible to convert a certain aminoacid (a building block for a protein) called phenylalanine, into another aminoacid called tyrosine. The result is an accumulation of phenylalanine in the blood (and urine), which 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 these blood levels.
Hyperphenylalaninemia is a chronically debilitating and is characterised by mental retardation if left untreated.

What are the methods of treatment available?

At the time of submission of the application for orphan drug designation, the treatment of hyperphenylalaninemia consisted of lifelong dietary protein restriction, in other terms a low phenylalanine diet.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that the medicinal product might be of potential significant benefit for the treatment of hyperphenylalaninemia, particularly in terms of improved tolerance to phenylalanine dietary intake. The 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, hyperphenylalaninemia was considered to affect about 64,000 persons in the European Union.

How is this medicinal product expected to act?

Tetrahydrobiopterin might help to restore the phenylalanine hydroxylase enzyme activity. As a result more phenylalanine might be converted to tyrosine, hence decreasing the toxic level.

What is the stage of development of this medicinal product?

The evaluation of the effects of 5,6,7,8 tetrahydrobiopterin in experimental models is ongoing.

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

The medicinal product was not marketed anywhere worldwide for hyperphenylalaninemia 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 30 July 2003 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.

For more information:

Sponsor's contact details:
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*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 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.

Patients' associations contact points:

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Translations of the active ingredient and indication in all EU languages

LANGUAGE	Active Ingredient	Indication
English	5,6,7,8-Tetrahydrobiopterin	Treatment of hyperphenylalaninemia
Danish	5,6,7,8-Tetrahydrobiopterin	Behandling af hyperfenylalaninæmi
Dutch	5,6,7,8-Tetrahydrobiopterine	Behandeling van hyperfenylalaninemie
Finnish	5,6,7,8-tetrahydrobiopteriini	Hyperfenylalaninemian hoito
French	5,6,7,8-Tétrahydrobioptérine	Traitement de l'hyperphénylalaninémie
German	5,6,7,8-Tetrahydrobiopterin	Therapie der Hyperphenylalaninämie
Greek	5,6,7,8-Τετραϋδροβιοπτερίνη	Θεραπεία της υπερφαινυλαλανιναιμίας
Italian	5,6,7,8-Tetraidrobiopterina	Trattamento dell'iperfenilalaninemia
Portuguese	5,6,7,8-Tetrahidrobiopterina	Tratamento da hiperfenilalaninémia
Spanish	5,6,7,8-Tetrahidrobiopterina	Tratamiento de la hiperfenilalaninemia
Swedish	5,6,7,8-Tetrahydrobiopterin	Behandling av hyperfenylalaninemi