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

London, 25 September 2008
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SUMMARY OF POSITIVE OPINION*
for
KUVAN

International Nonproprietary Name (INN): ***sapropterin dihydrochloride***

On 25 September 2008 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion,** recommending to grant a marketing authorisation for the medicinal product Kuvan, 100 mg, soluble tablets intended for the treatment of hyperphenylalaninemia (HPA). Kuvan was designated as an orphan medicinal product on 8 June 2004. The applicant for this medicinal product is Merck KGaA.
The active substance of Kuvan is sapropterin dihydrochloride, a "various alimentary tract and metabolism" medicinal product (ATC code: A16AX07). It is a synthetic version of the naturally occurring tetrahydrobiopterin (6R-BH4), which is a cofactor of hydroxylases for phenylalanine, tyrosine and tryptophan. It is proposed as an oral treatment for hyperphenylalaninaemia (HPA) in patients with phenylketonuria (PKU) or BH4 deficiency.

The benefits with Kuvan are its ability demonstrated in two placebo-controlled studies, to reduce phenylalanine levels in patients with phenylketonuria (PKU) who have been shown to be responsive to BH4 treatment. The most common side effects are headache and rhinorrhoea.

A pharmacovigilance plan for Kuvan, as for all medicinal products, will be implemented as part of the marketing authorisation.

The approved indication is:"Kuvan is indicated for the treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients of 4 years of age and over with phenylketonuria (PKU) who have been shown to be responsive to such treatment. Kuvan is also indicated for the treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients with tetrahydrobiopterin (BH4) deficiency, who have been shown to be responsive to such treatment". Treatment with Kuvan must be initiated and supervised by a physician experienced in the treatment of PKU and BH4 deficiency.
Detailed recommendations for the use of this product will be described in the Summary of Product Characteristics (SPC) which will be published in the European Public Assessment Report (EPAR) and will be available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers that there is a favourable benefit to risk balance for *Kuvan* and therefore recommends the granting of the marketing authorisation.

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* Summaries of positive opinion are published without prejudice to the Commission Decision, which will normally be issued within 67 days from adoption of the Opinion.

** Applicants may request a re-examination of any CHMP opinion, provided they notify the EMEA in writing of their intention to request a re-examination within 15 days of receipt of the opinion.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 85 45
E-mail: mail@emea.europa.eu http://www.emea.europa.eu