EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 September 2015
EMA/627629/2015 Corr. 1[1]
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[2]

Kolbam

cholic acid

On 24 September 2015, the Committee for Medicinal Products for Human Use (CHMP) adopted a revised opinion, recommending the granting of a marketing authorisation under exceptional circumstances[3] for the medicinal product Kolbam, intended for the treatment of inborn errors in primary bile acid synthesis due to deficiencies of the following liver enzymes: sterol 27-hydroxylase (presenting as cerebrotendinous xanthomatosis, CTX), 2- (or α-) methylacyl-CoA racemase (AMACR) or cholesterol 7α-hydroxylase (CYP7A1). Kolbam was designated as an orphan medicinal product on 9 December 2011. The applicant for this medicinal product is Retrophin Europe Limited.

The revised CHMP opinion comes after the annulment on 11 June 2015 of the marketing authorisation for Kolbam in the EU following a judgment of the General Court[4]. Based on this judgment, on 7 September 2015, the European Commission requested the CHMP to review its previous scientific opinion for Kolbam adopted on 23 January 2014.

Kolbam will be available as 50 and 250 mg capsules. The active substance of Kolbam is cholic acid, a bile acid preparation (A05AA03). Orally administered cholic acid acts to replace the missing endogenous primary bile acids both in terms of their physiological functions and their metabolic regulation.

The benefits with Kolbam are its ability to inhibit the production of cholestatic and hepatotoxic bile acid metabolites by down-regulating cholesterol 7α-hydroxylase, the rate limiting enzyme in bile acid synthesis in patients with inborn errors in primary bile acid synthesis due to deficiencies of the following liver enzymes: sterol 27-hydroxylase (presenting as cerebrotendinous xanthomatosis, CTX), 2- (or α-) methylacyl-CoA racemase (AMACR) or cholesterol 7α-hydroxylase (CYP7A1).

[1] This SmOP was updated on 08 October 2015 to reflect that Kolbam has been granted a marketing authorisation under exceptional circumstances
[2] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion
[3] In exceptional circumstances, an authorisation may be granted subject to certain specific obligations, to be reviewed annually. This happens when the applicant can show that they are unable to provide comprehensive data on the efficacy and safety of the medicinal product, due to the rarity of the condition it is intended for, limited scientific knowledge in the area concerned, or ethical considerations involved in the collection of such data.
[4] See judgment of the General Court.

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Adverse events that have been reported with oral cholic acid therapy are diarrhoea, reflux, nausea, malaise, jaundice and skin lesion. The majority of events observed in treated patients were mild or moderate in intensity, and the events were transitory and generally did not interfere with the therapy.

The full indication is: "treatment of inborn errors in primary bile acid synthesis due to sterol 27-hydroxylase (presenting as cerebrotendinous xanthomatosis, CTX) deficiency, 2- (or α-) methylacyl-CoA racemase (AMACR) deficiency or cholesterol 7α-hydroxylase (CYP7A1) deficiency in infants, children and adolescents aged 1 month to 18 years and adults." It is proposed that Kolbam be initiated and monitored by physicians, including paediatricians, experienced in the management of the specific deficiencies.

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.