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Committee for Orphan Medicinal Products

Recommendation for maintenance of orphan designation at the time of marketing authorisation

Chenodeoxycholic acid sigma-tau (chenodeoxycholic acid) for the treatment of inborn errors in primary bile acid synthesis

On 16 February 2017, the Committee for Orphan Medicinal Products (COMP) concluded its review of the designation EU/3/14/1406 for Chenodeoxycholic acid sigma-tau (chenodeoxycholic acid) as an orphan medicinal product for the treatment of inborn errors in primary bile acid synthesis. The COMP assessed whether, at the time of marketing authorisation, the medicinal product still met the criteria for orphan designation. The Committee looked at the seriousness and prevalence of the condition, and the existence of other methods of treatment. As other methods of treatment are authorised in the European Union (EU), the COMP also considered whether the medicine is of significant benefit to patients with inborn errors in primary bile acid synthesis. The COMP recommended that the orphan designation of the medicine be maintained[1].

Life-threatening or long-term debilitating nature of the condition

The Committee for Medicinal Products for Human Use (CHMP) recommended the authorisation of Chenodeoxycholic acid sigma-tau for: 'treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX)) in infants, children and adolescents aged 1 month to 18 years and adults'.

This falls within the scope of the product's designated orphan indication, which is: 'treatment of inborn errors in primary bile acid synthesis'.

The COMP concluded that there had been no change in the seriousness of these conditions since the orphan designation in 2014. Inborn errors in primary bile acid synthesis remain a group of long-term debilitating and life-threatening diseases because they can cause neurological problems and problems with food absorption and can severely damage the liver, leading to liver disease and liver failure.

[1] The maintenance of the orphan designation at time of marketing authorisation would, except in specific situations, give an orphan medicinal product 10 years of market exclusivity in the EU. This means that in the 10 years after its authorisation similar products with the same therapeutic indication cannot be placed on the market.

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Prevalence of the condition

The sponsor performed a search of the scientific literature and concluded that no publications are available which suggest a change in prevalence of inborn errors in primary bile acid synthesis.

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of inborn errors in primary bile acid synthesis remains below the ceiling for orphan designation, which is 5 people in 10,000. At the time of the review of the orphan designation, the prevalence was still estimated to be not more than 0.2 people in 10,000. This is equivalent to a total of not more than 10,000 people in the EU.

Existence of other methods of treatment

At the time of the review of the orphan designation, two cholic acid products, Orphacol and Kolbam, were authorised in the EU for the treatment of inborn errors in primary bile acid synthesis.

In particular, Kolbam was authorised for the treatment of inborn errors in primary bile acid synthesis due to a deficiency in the enzyme sterol 27-hydroxylase, which is the same disease for which Chenodeoxycholic acid sigma-tau has been authorised. Kolbam was also authorised for 2-methylacyl-CoA racemase deficiency and cholesterol 7α-hydroxylase deficiency.

Orphacol instead was authorised for treatment of inborn errors in primary bile acid synthesis due to deficiencies in different enzymes to Chenodeoxycholic acid sigma-tau: 3β-Hydroxy-Δ5-C27-steroid oxidoreductase deficiency and Δ4-3-oxosteroid-5β-reductase deficiency.

Significant benefit of Chenodeoxycholic acid sigma-tau

The COMP concluded that the claim of a significant benefit of Chenodeoxycholic acid sigma-tau in inborn errors in primary bile acid synthesis is justified because data show that patients with a type of inborn error in primary bile acid synthesis called cerebrotendinous xanthomatosis (CTX) show neurological improvements when treated with this medicine which have not been seen with cholic acid in the treatment of this disease. These data are from the main study of the medicine, the published literature and reports from doctors with experience in treating patients with this disease.

Therefore, although other methods for the treatment of this condition have been authorised in the EU, the COMP concluded that Chenodeoxycholic acid sigma-tau is of significant benefit to patients affected by inborn errors in primary bile acid synthesis.

Conclusions

Based on the data submitted and the scientific discussion within the COMP, the COMP considered that Chenodeoxycholic acid sigma-tau still meets the criteria for designation as an orphan medicinal product and that it should remain in the Community Register of Orphan Medicinal Products.

More information on the COMP assessment can be found in the February 2017 COMP minutes.

Further information on Chenodeoxycholic acid sigma-tau can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.