Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication), the scientific conclusions of CHMP are as follows:

The article by Klouwer et al. (2019) reported an increased risk of hepatotoxicity for patients with ZSD and pre-existing hepatic impairment. Additional information with regard to hepatotoxicity in patients with pre-existing hepatic impairment was retrieved from the cases provided by the MAH and a EudraVigilance search.

Since the safety information for the approved use is rather limited, the results and conclusion in the article by Klouwer et al, regarding an increased hepatotoxicity risk for patients with ZSD with pre-existing liver impairment and the available information in relevant cases of hepatotoxicity reported for different uses of Cholic acid (1 fatal case of acute hepatic failure, 2 cases of hepatic failure, one fatal and the other reporting recovery, 3 fatal cases of liver disorders), all in patients with pre-existing liver disease, should be taken into consideration for the EU product information. As a result, an update of the product information is deemed necessary. The update provides information on an increased risk of hepatotoxicity in patients with pre-existing liver disease, treated with cholic acid. It further outlines that patients with hepatic impairment should be closely monitored and stopping rules should apply when treated with Kolbam.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication) is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.