



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

14 December 2017  
EMA/20821/2018  
Committee for Medicinal Products for Human Use (CHMP)

## Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): methylthioninium chloride

Procedure No. EMEA/H/C/PSUSA/00002029/201705

Period covered by the PSUR: 06/05/2016 - 05/05/2017



## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR(s) for methylthioninium chloride, the scientific conclusions of CHMP are as follows:

Eight cases of serotonin syndrome have been reported by the MAH, including cases described in literature. Methylthioninium chloride is recognised to be associated with severe central nervous system toxicity and has been shown to act as a monoamine oxidase inhibitor that can give rise to serotonin toxicity. The available evidence supported the possibility of a causal relationship and inclusion of the adverse reaction in the Product Information. A specific warning on this adverse reaction was considered of relevance to the prescriber.

Two literature cases of photosensitivity have been reported by the MAH in this reporting interval. In addition, further to a cumulative review performed by the MAH, 10 cases of photosensitivity associated with off-label use of methylthioninium chloride have been identified, including photosensitising-induced epithelial desquamation in several infants receiving phototherapy. This has been attributed to the interaction of methylene blue with light leading to the breakdown of lysosomal membranes. Considering the close temporal relationship and the plausible mechanism, the causal relationship between methylthioninium chloride and photosensitivity was considered possible. A specific warning regarding concomitant phototherapy or use of the product under certain light conditions was considered of relevance to the prescriber.

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 methylthioninium chloride the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing methylthioninium chloride 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.