19 September 2013
EMA/740413/2013
Committee for Medicinal Products for Human Use (CHMP)

Thymanax

International non-proprietary name: agomelatine

Procedure No. EMEA/H/C/000916/PSUV/0017

Period covered by the PSUR: 20 February 2012 – 19 February 2013

Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation

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Scientific conclusions

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

Data from PSUR 6 did not change the benefit-risk profile of the product.

In the data presented efficacy has not been shown in patients > 75 years and that the recommendation was made agomelatine should not be used in this population. Respective changes in section 4.2 of the SmPC were recommended.

Based on an assessment of the main results of 13 new clinical studies, enrolling approximately 5000 patients with major depressive disorder, the overall efficacy of agomelatine based on outcomes on the HAM-D scale was considered modest, but generally in line with findings from previously assessed studies that formed the basis for the EU approval in 2009.

Hepatotoxicity remained the main safety concern. Data from this PSUR confirmed previous knowledge in this area. To clarify the recommendations in the SmPC, the PRAC considered that section 4.3 of the SmPC should be updated to include a contraindication in patients with transaminases exceeding 3 X upper limit of normal. Further to this, section 4.4 and 4.8 of the SmPC should be updated to include information on cases of hepatic failure reported with fatal outcome or liver transplantation in patients with hepatic risk factors. Otherwise, the risk minimisation measures were considered to be sufficient. The MAH was in the process of performing a survey to evaluate the effectiveness of these risk minimisation measures, the results of which were to be discussed in the following PSUR.

Skin reactions and suicide were still considered to be important potential risks of the product.

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

Grounds recommending the variation to the terms of the Marketing Authorisations

On the basis of the scientific conclusions for Thymanax the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing the active substance agomelatine is favourable subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisations should be varied.