27 June 2019
EMA/492014/2019
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): methotrexate

Procedure No. EMEA/H/C/PSUSA/00002014/201810

Period covered by the PSUR: 01 July 2017 - 31 October 2018

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Scientific conclusions

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

With regard to the interaction of methotrexate and nitrous oxide, cases of neurotoxicity following intrathecal administration were reported. Section 4.5 of the SmPC for products with at least one indication in oncology should be updated to revise existing wording for the interaction of methotrexate with nitrous oxide.

Cases of injection-site necrosis have been identified and assessed as causally related to methotrexate-containing pre-filled syrignes and pre-filled pens. The MAHs of methotrexate-containing pre-filled syringes and pre-filled pens are requested to update section 4.8 of the SmPC to include injection site necrosis. The PIL should be updated accordingly.

The Section 2 of the Package leaflet of products with at least one indication in oncology should be updated to reflect that contraindication in pregnancy only relates to non-oncologic indications.

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 methotrexate the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing methotrexate is unchanged subject to the proposed changes to the product information.

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