9 June 2016
EMA/789888/2016
Committee for Medicinal Products for Human Use (CHMP)

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

Ketoconazole HRA

Active substance(s): ketoconazole (centrally authorised product only)

Procedure no.: EMEA/H/C/PSUSA/00010316/201511

Period covered by the PSUR: 20 May 2015-19 November 2015

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for ketoconazole (centrally authorised product only), the scientific conclusions of CHMP are as follows:

Ketoconazole is a potent inhibitor of CYP3A4 enzyme. Pharmacokinetics of medicines that are substrates of CYP3A4 can be affected when administered concomitantly with ketoconazole, potentially leading to clinically significant serious ADRs and/or the need for dose adjustment of these medicinal products. The PRAC considers that, in view of the available data the interaction of ketoconazole with crizotinib, ibrutinib and the direct-acting antiviral (DAAV) combination of ombitasvir-paritaprevir-ritonavir should be added to the product information. A contraindication with the direct-acting antiviral (DAAV) combination of ombitasvir-paritaprevir-ritonavir should also be included in the product information.

Therefore, in view of the data presented in the reviewed PSUR(s), the PRAC considered that changes to the product information of medicinal products containing ketoconazole were warranted.

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 ketoconazole (centrally authorised product only) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing ketoconazole (centrally authorised product only) 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.