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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): apixaban

Procedure No. EMEA/H/C/PSUSA/00000226/201905

Period covered by the PSUR: from 18 May 2018 to 17 May 2019

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Scientific conclusions

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

Based on a review of the literature, pre-clinical and clinical trial program, and the MAH's safety database, an increase in apixaban exposure of approximately 40-50% would be expected if co-administered with fluconazole. Such an increase would not lead to a need for dose adjustment, as apixaban exposure is predicted to be similar in such an instance to that observed with concomitant administration of diltiazem, a moderate inhibitor of CYP3A4 and a weak inhibitor of P-gp. Therefore, no dose adjustment for apixaban is recommended when administered concomitantly with fluconazole, similar to the recommendations in the SmPC for active substances which are not considered strong inhibitors of both CYP3A4 and P-gp.

However, and in order to inform prescribers, fluconazole is added to the list of inhibitors in section 4.5, which are not considered strong inhibitors of both CYP3A4 and P-gp and whose concomitant administration would result in a moderate increase in apixaban plasma concentration.

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