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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/00000226/202005

Period covered by the PSUR: 17 May 2019 to 17 May 2020

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Scientific conclusions

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

Erythema multiforme: initial signal review by the EMA and PRAC in February 2020 identified four probably related cases without confounding factors including a literature case (Shinya et al) of which three presented a positive dechallenge. Based on this signal review a cumulative review from all sources was requested for the current PSUR.

The cumulative review provided by the MAH in the current PSUR included three cases for which a causal association with apixaban is likely as all three cases report a (partial-event resolving) positive dechallenge on apixaban. In these 3 cases the diagnosis was confirmed by dermatologist or an examination. EM occurred within 4, 8 and 10 days of apixaban treatment start and in one case a drug-induced lymphocyte stimulation test (DLST) was positive for apixaban further supporting the association.

One of these cases was also part of the initial signal evaluation (i.e. literature case by Shinya et al).

Therefore, the MAH should update the PI with the new ADR "erythema multiforme". Based on 1 case of erythema multiforme in out of 11,000 subjects exposed in NVAF clinical trials the frequency very rare should be used for this indication. No case of erythema multiforme were reported for the other two indications (VTEt and VTEp) in clinical trials and the frequency should therefore be not known.

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

Grounds for the variation to the terms of the Marketing Authorisation

On the basis of the scientific conclusions for apixaban the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing apixaban is unchanged subject to the proposed changes to the product information.

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