EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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): brimonidine (centrally authorised product only)

Procedure No. EMEA/H/C/PSUSA/00010093/201608

Period covered by the PSUR: 22 February 2016 to 31 August 2016

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Scientific conclusions

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

Bradycardia as a systemic alpha-2 adrenergic effect of Mirvaso is highly plausible, if absorbed systemically in sufficient amount. Cumulatively, 6 cases of bradycardia-related terms were reported, and although confounding factors exist in some cases, overall the evidence is considered to be suggestive of an association between Mirvaso and bradycardia, particularly when applied to inflamed skin. This is also supported by the previously identified adverse event of hypotension, as alpha-2 adrenergic stimulation would be expected to cause both effects. Therefore, the PRAC considered that section 4.8 of the SmPC should be updated to add the adverse reaction 'bradycardia' with a frequency 'rare'.

Dizziness is a common symptom of the already listed adverse event 'hypotension'. Cumulatively 37 post-marketing reports of the preferred term dizziness have been received and of the cumulative total of 18 cases discussed in this PSUR under 'haemodynamic effect' as suggestive of an alpha-2 adrenergic effect of brimonidine, 9 cases included an event of dizziness. The PRAC considers that the evidence is suggestive of a causal association between brimonidine gel and dizziness, therefore the PRAC concluded that section 4.8 of the SmPC should be updated to add the adverse reaction 'dizziness' with a frequency 'uncommon'.

Of the 18 cases discussed by the MAH as suggestive of an alpha-2 adrenergic effect of brimonidine, 6 occurred after Mirvaso was applied following recent laser therapy, and 1 case of bradycardia was associated with application to sun-burned skin. It is biologically plausible that increased systemic absorption via inflamed skin could increase the risk of systemic haemodynamic effects; therefore although a relationship cannot be definitely proven, the available evidence supports an association between recent laser therapy and the occurrence of haemodynamic adverse events on application of Mirvaso. Therefore, the PRAC considered that section 4.4 of the SmPC should be updated to add a warning on the risk of haemodynamic effects following laser therapy.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing brimonidine 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 brimonidine (centrally authorised product only) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing brimonidine (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.