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SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name: tadalafil

Procedure No. EMEA/H/C/PSUSA/00002841/201410

Period covered by the PSUR: 16 April 2014 – 15 October 2014

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Scientific conclusions

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

Following the update of the product information of riociguat, in which the concomitant administration of riociguat with phosphodiesterase type 5 PDE5 inhibitors (such as sildenafil, tadalafil, and vardenafil) was contraindicated because of an increased risk of hypotension, the MAH considered based upon a review of available data sources that an update to the tadalafil Core Data Sheet (CDS) was warranted.

Both riociguat and tadalafil act on the NO-sGC-cGMP pathway, this may amplify nitric oxide (NO) activity and potentially result in synergistic systemic vasodilatation. Nitrates also act on this pathway. Class labelling for PDE5 inhibitors and for riociguat include a contraindication for the concomitant use of nitrates. In addition, the safety of riociguat in combination with the PDE5 inhibitor sildenafil was examined in a phase IIB double-blind, placebo-controlled safety study, PATENT-PLUS, in which there was a high rate of study discontinuation secondary to hypotension, and there were 3 deaths, 1 of which was assessed as possibly related to the combination of sildenafil and riociguat.

Therefore, in view of available data regarding concomitant administration of tadalafil with riociguat, the PRAC has considered that changes to the product information were warranted.

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

Grounds recommending the variation to the terms of the Marketing Authorisation

On the basis of the scientific conclusions for tadalafil the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing tadalafil is favourable subject to the proposed changes to the product information

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