25 July 2019
EMA/466411/2019
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): umeclidinium bromide / vilanterol

Procedure No. EMEA/H/C/PSUSA/00010264/201812

Period covered by the PSUR: 18/12/2017 - 17/12/2018

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSURs for umeclidinium bromide / vilanterol, the scientific conclusions of CHMP are as follows:

Following a post-approval regulatory requests in the last PSUR (EMEA/H/C/PSUSA/00010264/201712), the MAH provided a review of the adverse drug reaction (ADR) 'dizziness'. The MAH identified 203 cases of dizziness, 191 were reported as non-serious, and 12 reported as serious. Fifty-eight cases report positive de-challenge. Seven of these 58 cases contained relevant medical history that can cause dizziness. Of the remaining 51 cases, 22 cases reported time to onset (TTO) of 0-2 days, and six of these cases reported no concomitant medications. Of the 203 cases, five cases reported positive re-challenge and two further cases described events that reoccurred the same day after each dose. The MAH reported the details of these 7 cases with positive re-challenge. Though the TTO is not clear in all the cases, 4 cases occurred within 1 day. The PRAC considered that the short TTO reported in the 48% of the cases (0 – 1 day) is suggestive of a possible causal relation between the administration of UMEC/VI and the event. The undesirable effect 'dizziness' is known and included with an uncommon frequency in the PI of aclidinium, suggesting a possible class effect for anticholinergics. Based on the above and also taking into account that serious cases have been reported, a product information (PI) update with regard to the adverse reaction 'dizziness' is warranted. Update of section 4.8 of the SmPC to add 'dizziness' with a frequency not known is recommended. The package leaflet should be updated accordingly.

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

Grounds for the variation to the terms of the marketing authorisations

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

The CHMP recommends that the terms of the marketing authorisations should be varied.