10 November 2016
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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): umeclidinium bromide

Procedure No. EMEA/H/C/PSUSA/00010263/201604

Period covered by the PSUR: 16 October 2015 – 15 April 2016

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Scientific conclusions

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

“Urinary retention” is a known class effect of anticholinergic drugs and a warning is already included in the SmPC recommending the use of umeclidinium bromide (UMEC) with caution in patients with urinary retention.

“Bladder outflow obstruction and Urinary retention” are potential risks in the current RMP.

In this PSUR for UMEC, 3 serious cases of urinary retention were retrieved in the interval period (3 cumulatively), 1 non serious case of urinary flow decreased (1 cumulatively), 5 non serious cases of dysuria (7 cumulatively).

Based on the results of the cumulative evaluations for UMEC and considering the pharmacological plausibility of anticholinergic effect on urinary function, there is sufficiently evidence to warrant an update of the Product Information with “**urinary retention, and dysuria"** as ADRs associated to UMEC.

From a cumulative review provided by the MAH 23 adverse events in the Glaucoma SMQ (broad) from 20 spontaneous case reports and 1 post marketing surveillance case report were observed.

A total of 7 serious AE was reported (angle closure glaucoma, n=2; blindness, n=1; eye pain, n=1 and vision blurred, n=3). Of these, 2 serious case reports (1 of narrow angle glaucoma and 1 of vision blurred) contained sufficient information for a causal relationship with UMEC.

Three further cases of glaucoma (one of them from consumer) and 1 further case of angle closure glaucoma, all submitted after the DLP of this PSUR, were retrieved from EV database.

Taking into account that : i) glaucoma is a class effect of antimuscarinic drugs; ii) glaucoma is a potential risk in the RMP; iii) a warning stating that umeclidinium bromide (UMEC) should be used with caution in patients with narrow angle glaucoma already exist in the current Product Information (PI); iv) the PI of UMEC/VI has been updated to include the undesirable effect glaucoma, the PRAC considers that there is sufficient evidence of association with UMEC in monotherapy to update the PI to include the ADR **"glaucoma".** In addition, it is noted that in 3 well documented cases, “**vision blurred”** occurred with a close temporal association (≤ 4 days) with start of treatment with UMEC. Therefore, the PRAC concluded that the PI should be updated also to reflect these undesirable effects.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considers that changes to the product information of medicinal products containing umeclidinium bromide are 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 umeclidinium bromide the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing umeclidinium bromide 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.