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Committee for Medicinal Products for Human Use

Conbriza

bazedoxifene

Procedure No.: EMEA/H/C/000913/PSU/030

Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation

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Scientific conclusions

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

Palpitations - cumulative review

A review of the safety database for cases reporting the MedDRA term palpitations from 17 April 2009 through 16 October 2012 identified 20 medically confirmed cases, representing 3.4% of the total 590 cases received cumulatively. There were no non-medically confirmed cases of palpitations received.

The 20 cases were all spontaneously reported from Japan and all involved female patients. Palpitations were assessed as serious in one case and as non-serious in the remaining nineteen cases. In five cases, the reporting health professionals assessed palpitations as unrelated to bazedoxifene. In another case, bazedoxifene was continued and palpitations resolved. Two other cases reporting palpitations and dyspnoea in patients of unspecified ages did not provide sufficient information for proper assessment.

Six cases of palpitations were considered possibly related by the reporting health professional; another six cases were reported by the health care professionals to be probably related to bazedoxifene. Most of the cases provided limited information on timely relationship, dechallenge and concomitant medication and should therefore rather be classified as possibly related. Only in two cases a timely correlation seems to be plausible; events started with the beginning of bazedoxifene therapy and patients recovered when therapy with bazedoxifene was withdrawn. The cases are not well documented and it is unclear if they provide sufficient evidence for a correlation between palpitations and bazedoxifene. Nevertheless, as there are at least twelve cases considered possibly related to bazedoxifene the SmPC should be updated to include palpitations.

Rash / pruritus – cumulative review

The MAH has undertaken a review of all cases of skin and subcutaneous reactions received since the international birth date (IBD). Of the 137 relevant adverse events (AEs), the most frequently recorded MedDRA terms were rash (21) and pruritus (20). Fifty-seven (57) cases contained events within the categories erythemas, pruritus, and rashes, eruptions and exanthems. Fifty-four (54) cases originated from Japan and the remaining three cases were from Spain. Four cases included skin-related AEs considered serious, recorded as pruritus (2), pruritus generalized (2), rash (1), and rash generalized (1). Bazedoxifene therapy was permanently or temporarily discontinued in 46 cases, continued unchanged in five cases, and action taken with bazedoxifene was not reported in six cases. One case in which bazedoxifene therapy continued indicated resolution of the pruritus event with treatment.

Of the 57 cases, 38 cases lacked information for a meaningful assessment. One case with limited information described a positive rechallenge. Eight of the 57 cases contained information suggesting additional possible contributing factors for the skin events. In the eleven remaining cases, the role of bazedoxifene could not be excluded due to temporal association with the skin-related AEs or absence of additional contributing factors; three of the eleven cases reported positive rechallenge. In addition, there were 5 cases including pruritus rash or rash macular reported in the non-medically confirmed adverse event. A possible correlation between bazedoxifene and rash/pruritus cannot be excluded in these cases. Rash and pruritus should therefore be included in the SmPC.

Therefore, in view of available data regarding palpitations and rash/pruritus, the PRAC considered that the following changes to the product information were warranted:

Update of section 4.8 of the SmPC to add the adverse reactions palpitations, rash and pruritus with frequency unknown, under the appropriate SOC. The Package Leaflet has been updated accordingly. In addition, section 6 of the Package Leaflet has been updated to add the contact details for the local representative in Croatia, which is acceptable.

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 Conbriza the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing the active substance bazedoxifene is favourable subject to the proposed changes to the product information.

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