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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): denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer)

Procedure No. EMEA/H/C/PSUSA/00000954/201809

Period covered by the PSUR: 26/09/2017 To: 26/09/2018

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer), the scientific conclusions of CHMP are as follows:

The PRAC considers that due to the fact that fatal cases of hypocalcaemia have been reported for Prolia also during this reporting interval, and there was a timely typical association with Prolia administration, the wording 'including fatal cases' should be added to the current text regarding hypocalcaemia in section 4.4 of the SmPC.

Further, post-marketing experience including multiple cases with positive re-challenge supports the conclusion that denosumab may be causally associated with the development of lichenoid drug reactions, and this new ADR should be added in section 4.8 of the SmPC and the Package Leaflet.

In addition, as post-marketing experience including multiple cases with positive re-challenge, as well as non-clinical evidence of involvement of the RANK / RANKL signalling pathway in the hair growth cycle support a conclusion that denosumab may be causally associated with the development of alopecia, this new ADR should be added in section 4.8 of the SmPC and the Package Leaflet.

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 denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer) 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.