EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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): edotreotide

Procedure No. EMEA/H/C/PSUSA/00010552/201906

Period covered by the PSUR: 7 December 2018 to 7 June 2019

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Scientific conclusions

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

In the previous interval, the MAH for edotreotide kit for radiopharmaceutical preparation had received cumulatively 4 non-serious reports of injection site pain, including 3 during the reporting interval, one of which was considered highly associated with the radiopharmaceutical. Of note the SmPC advises that after radiolabelling, the solution obtained also contains, as excipient, hydrochloric acid from the generator eluate.

In the current reporting interval, the number of cases has increased to 10. Of the 6 additional non-serious cases, 3 cases describe burning and tingling pain extending from the arm to the neck and lasting 20 seconds, which is considered highly probably related to edotreotide. The pH in all 3 cases was 3.5. In a further case, the patient experienced stabbing pain extending from the hand to the shoulder during the injection and this was reported to be due to the low pH of the solution. Causality in these cases is probable. Of note, none of these cases appear to have a previous history of psychiatric disorder as a confounding factor. Considering the data, an association with injection site pain is plausible given the acidic nature of the solution. It is therefore recommended that *Injection site pain* is labelled in 4.8 of the SmPC of the kit for radiopharmaceutical preparation under SOC *General disorders and administration site conditions* with frequency *Not known*, with a corresponding update to the PL.

Of note, edotreotide solution for injection contains no hydrochloric acid. The final pH is between 4 and 8. No cases of injection site pain have been identified with these medicines and no Product Information changes are recommended.

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 edotreotide the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing edotreotide is unchanged subject to the proposed changes to the product information for edotreotide kit for radiopharmaceutical preparation.

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.