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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name: gadoversetamide

Procedure No. EMEA/H/C/PSUSA/00001508/201501

Period covered by the PSUR: 1 February 2014 – 31 January 2015

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Scientific conclusions

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

Sclerotic bodies on skin biopsy have been associated with Nephrogenic Systemic Fibrosis (NSF). Two recently published articles have reported the development of gadolinium associated skin plaques, with sclerotic bodies and focal calcification on histology in patients without other features of Nephrogenic Systemic Fibrosis. These gadolinium associated skin plaques were apparent within a timeframe of approximately 4 years following multiple administrations of gadolinium containing contrast agents, including gadodiamide a non-ionic linear GdCA.

In response to the Request for Supplementary Information the MAH has confirmed that they have not received specifically with their product any cases of gadolinium associated skin plaques with fibrosis and sclerotic bodies in patients who do not otherwise have a diagnosis of Nephrogenic Systemic Fibrosis. A review of published pre-clinical studies provided by the MAH has shown in relation to the tested marketed gadolinium GdCAs that the highest gadolinium skin concentration were seen with administration of the non-ionic linear GdCAs, with the highest levels seen post administration of Omniscan. Macroscopic and microscopic NSF-like skin lesions were seen in the animals with the highest gadolinium skin concentrations. There is clear potential for underreporting or under recognition of gadolinium associated skin plaques in patients who have not presented with other signs or symptoms of NSF and therefore it is recommended that the product information for Optimark is updated to reflect these recent published cases. For transparency, the PRAC recommends that the amendment to the product information should factually reflect what has been reported in the literature.

In conclusion in view of the available data relevant to gadolinium associated skin plaques the PRAC considered that changes to the Optimark product information are warranted.

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 gadoversetamide the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing gadoversetamide is favourable subject to the proposed changes to the product information

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