EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Keppra

levetiracetam

Procedure no. EMEA/H/C/000277/PSUV/0140

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

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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

Post-marketing data including two cases with positive de- and rechallenge, collected during the PSUR reporting period, revealed an interaction between levetiracetam and macrogol-containing laxatives, whereby the efficacy of levetiracetam was reduced when both drugs were administered at the same time. As this interaction may result in loss of seizure control and hospitalisation, the PRAC recommended the update of SmPC section 4.5 of levetiracetam to inform healthcare professionals accordingly. Furthermore, based on the review of clinical, pre-clinical, post-marketing and literature data, the PRAC concluded that agranulocytosis should be considered a rare adverse reaction to levetiracetam. While there were no cases detected in clinical trials, several post marketing spontaneous reports of agranulocytosis had been reported as suggestive of a causal association due to a compatible temporal relationship of drug exposure and occurrence of the events. The PRAC therefore recommended to update SmPC section 4.8 accordingly. Finally, the PRAC considered that it was important to include in SmPC section 4.6 cumulative information on the exposure to levetiracetam of pregnant women and the fact that a teratogenic effect of levetiracetam cannot be excluded as well as information on the increased risk of congenital malformations with antiepileptic polytherapy as compared to levetiracetam monotherapy, as this information will help healthcare professionals to make sound decisions on the antiepileptic treatment of pregnant women with epilepsy. Minor updates to the Package Leaflet were made as well.

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

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