EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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: ranolazine

Procedure No. EMEA/H/C/PSUSA/00002611/201501

Period covered by the PSUR: 27 January 2013 – 26 January 2015

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Scientific conclusions

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

Scientific conclusions and grounds for variation to the terms of the marketing authorisations

The cumulative review of hyponatremia/SIADH cases provided by the MAH identified a total of 29 cases (16 spontaneous reports and 13 SAEs from clinical studies) which contained at least one MedDRA Preferred Term from the broad Standardised MedDRA Query (SMQ) Hyponatraemia/syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH). It was noted that hyponatremia has been observed with similar frequency in the ranolazine (0.09%) and placebo (0.12%) groups in a placebo controlled study. In this study the frequency of hyponatraemia in the ranolazine group was rare. Considering all reported cases, there is a strong causality relation between the use of ranolazine and the occurrence of severe *hyponatremia*. In most of these cases the MAH stated that the concomitant medications (e.g. diuretics, sartans, angiotensin-converting-enzyme inhibitors) provide an alternative aetiology for hyponatremia; however, the patients developed hyponatremia either after adding ranolazine to their existing medications or had temporal relation to ranolazine initiation or had positive re-challenge or the causality with the existing medication could be excluded. Considering the reported serious adverse events (SAEs) with 10 positive de-challenges and the temporal relationship of these events to ranolazine, the adverse drug reaction hyponatremia is considered to be an important identified risk that should be listed in section 4.8 of the SmPC (System Organ Class (SOC) Metabolism and nutrition disorders, frequency rare).

Therefore, in view of available data regarding hyponatremia, the PRAC considered that changes to the product information were warranted.

In addition, in view of the current safety profile of Ranexa the PRAC considered that the PSUR cycle should be extended from 2 years to 3 years.

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

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