18 December 2013
EMA/157197/2014
Committee for Medicinal Products for Human Use (CHMP)

Sifrol

International non-proprietary name: pramipexole

Procedure No. EMEA/H/C/PSUSA/00002491/201304

Period covered by the PSUR: 7 April 2010 – 6 April 2013

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

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Scientific conclusions

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

Based on evidence from clinical trials data showing an increased reporting rate of cases of delirium in patients receiving pramipexole treatment as compared to placebo as well as in light of post-marketing reports of cases of mania and delirium, the PRAC concluded that a causal relationship of these events with the use of pramipexole could not be excluded. The PRAC acknowledged the difficulties in diagnosing and recognizing mania and delirium in patients due to the fluctuating nature of these conditions, the significant overlap of symptomatology between different conditions, and complexity in differential diagnosis of psychiatric diseases. Hence, the cumulative number of 191 cases reported post-marketing, of which the majority had been confirmed by healthcare professionals, was considered substantial, even though the PRAC acknowledged that some of the cases would have been likely attributed to other causes. Furthermore, biomedical understanding of these mental illnesses, in particular for delirium for which an association with a surplus of dopamine as well as with use of dopamine agonists has been suggested in the scientific literature, were considered further supportive of a possible causal association.

In conclusion, since there was at least a reasonable suspicion of mania and delirium to be adverse reactions to pramipexole treatment, and taking into account the seriousness of these conditions and that early diagnosis is crucial, the PRAC considered that changes to the product information were warranted to inform healthcare professionals and patients accordingly.

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

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