EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 December 2019
EMA/155423/2020
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): pramipexole

Procedure No. EMEA/H/C/PSUSA/00002491/201904

Period covered by the PSUR: 06 April 2016 To: 06 April 2019

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Scientific conclusions

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

Based on evidence from the scientific literature, inclusion of information regarding risk factors of dopamine agonist withdrawal syndrome (DAWS) is considered relevant. Presence of impulse control disorders (ICD) has been consistently linked to DAWS in six retrospective chart reviews and one prospective observational study. High daily dose and high cumulative doses of dopamine agonists (DA) has been inconsistently linked to DAWS. Regardless of the inconsistency, the evidence points to an association between DAWS and high daily dose and/or cumulative doses of dopamine agonists. Based on these findings it is considered relevant to include the risk factors ICD, high daily dose and/or cumulative doses of dopamine agonists (DA) in the product information section 4.4.

DAWS has predominantly been reported in patients with Parkinson's disease (PD), although there are reports of it occurring among patients with Restless Legs Syndrome (RLS). The wording about discontinuing pramipexole should therefore not be limited to the PD indication. In consequence 'tapering' should be supplemented by 'discontinuing' in section 4.4 regarding DAWS, to make the wording also applicable for the RLS indication (tapering is not required in the RLS indication).

As DAWS symptoms occur upon dopamine agonist tapering/discontinuation, it is vital to distinguish between undermedication of the underlying medical disorder and DAWS. If the DAWS symptoms are mistakenly attributed to PD the clinician might increase the dose of levodopa, however this will not alleviate the DAWS symptoms. As combination therapy with DA and levodopa are often used, it is considered relevant for healthcare professionals to be informed that withdrawal symptoms do not respond to increasing of the levodopa dose, to aid in the differential diagnosis.

Further, updates of SmPC section 4.2 and PIL section 3 to include information regarding treatment discontinuation and DAWS, are considered relevant.

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 pramipexole the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing pramipexole is unchanged subject to the proposed changes to the product information

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