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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): pentosan polysulfate sodium (for centrally authorised product)

Procedure No. EMEA/H/C/PSUSA/00010614/201812

Period covered by the PSUR: 02/06/2018 to 01/12/2018

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

Annex IV

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Taking into account the PRAC Assessment Report on the PSUR(s) for pentosan polysulfate sodium (for centrally authorised product), the scientific conclusions of CHMP are as follows:

In literature, pigmentary maculopathy has been reported rarely, with pentosan polysulfate sodium, especially after long-term use. Visual symptoms might include complaints of reading difficulty and prolonged adjustment to low or reduced light environments. After extensive investigations, which included molecular testing for hereditary retinal disease, the authors of the study found these cases to resemble no other known retinal disease. Additionally, from the EudraVigilance database, at least one case describes similar findings on macula. There are a further 10 cases under SOC “eye disorders”, including visual impairment, blindness, retinopathy or optic neuritis.

Pending further investigation, it remains unclear whether drug cessation will halt or alter the course of the retinal disease.

Although majority of the reports available in literature describe a minimum exposure to PPS of 12 years and a higher dosage than recommended in the SmPC, 1 case occurred with the recommended daily dose of 300 mg (Pierce et al). Moreover, 3 cases retrieved from Vigilyse included also the recommended dosage of 300 mg/day. Regarding the time of exposure to PPS, Foote et al article includes 1 patient exposed during 27 months and a case from Vigilyse describes an exposure of less than 2 years. Therefore, based on the available data it cannot be concluded that the pathophysiologic changes cannot be detected earlier (perhaps in an asymptomatic, reversible stage), even with the recommended daily dosage of 300 mg.

In the light of this information, the PRAC recommended an update of the product information to warn about this risk and recommend regular ophthalmic examinations for early detection of pigmentary maculopathy, particularly in patients taking pentosan polysulfate sodium long-term.

Additionally, the PRAC recommended the distribution of a DHPC, since even if rare, it is a potentially irreversible, serious condition, which might not be easily recognized by the urology community.

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 pentosan polysulfate sodium (for centrally authorised product) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing pentosan polysulfate sodium (for centrally authorised product) 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.