25 May 2023
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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): vortioxetine

Procedure No. EMEA/H/C/PSUSA/00010052/202209

Period covered by the PSUR: 29 September 2020 To: 29 September 2022

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for vortioxetine, the scientific

conclusions of CHMP are as follows:

In view of available data on **dyspepsia** from clinical trials and spontaneous reports, including in several cases a close temporal relationship, 43 cases reporting a positive de-challenge and 1 case reporting a positive re-challenge, the PRAC considers a causal relationship between vortioxetine and dyspepsia is at least a reasonable possibility.

In view of available data on **movement disorders (akathisia**, **bruxism**, ~~**dystonia, including Meige syndrome,**~~ **trismus**, **restless leg syndrome**, **tremor)** from clinical trials, the literature and spontaneous reports, including in several cases a close temporal relationship, a positive de-challenge (akathisia: n=18, bruxism: n=18, trismus: n=7, restless leg syndrome: n= 26, tremor: n=93) and re-challenge (1 case for bruxism, trismus and tremor), the PRAC considers a causal relationship between vortioxetine and movement disorders is at least a reasonable possibility.

In view of available data on **sexual dysfunction** from clinical trials, the literature and spontaneous reports, including in several cases a close temporal relationship, 79 cases reporting a positive de-challenge, the PRAC considers a causal relationship between vortioxetine and sexual dysfunction is at least a reasonable possibility.

In view of available data on **withdrawal reactions** from the literature and spontaneous reports, including several cases reported in the current PSUR period with a plausible time to onset, some cases where symptoms resolved after resuming treatment with vortioxetine (positive "de-challenge") and 2 cases where consecutive treatment interruptions caused withdrawal reactions (positive "re-challenge"), and in view of a plausible mechanism of action, the PRAC Rapporteur considers a causal relationship between vortioxetine and withdrawal reactions is at least a reasonable possibility.

In view of available data on **vision blurred** from spontaneous reports, including in several cases a close temporal relationship, 46 cases reporting a positive de-challenge and 1 case reporting a positive re-challenge, and in view of a plausible mechanism of action, the PRAC Rapporteur considers a causal relationship between vortioxetine and vision blurred is at least a reasonable possibility.

In view of available data on **galactorrhoea** from spontaneous reports, including in several cases a close temporal relationship, and 3 cases reporting a positive de-challenge from the current PSUR period, and in view of a plausible mechanism of action, the PRAC Rapporteur considers a causal relationship between vortioxetine and galactorrhoea is at least a reasonable possibility.

The PRAC Rapporteur concluded that the product information of products containing vortioxetine should be amended accordingly.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for vortioxetine the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing vortioxetine 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.