18 August 2016
EMA/612150/2016
Procedure Management and Committees Support Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Brintellix

vortioxetine

Procedure no: EMEA/H/C/002717/P46/003.2

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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1. Introduction

This report covers the following post-authorisation commitments undertaken by the MAH:

To evaluate the suicide related events (questions 1 and 2) and the cases of sedation from vortioxetine use (question 3).

Submission date:	24 May 2016
Start of procedure:	20 June 2016
CHMP Rapporteur's preliminary assessment report circulated on:	25 July 2016
CHMP Rapporteur's updated assessment report circulated on:	n/a
CHMP opinion:	18 August 2016

2. Assessment of the post-authorisation measure PAM

Questions 1 & 2: the suicide related events

In the extension period of the study, there were 5 patients reporting suicidal ideation only.

In addition, one patient reported both suicidal ideation and suicidal behaviour.

All patients who reported suicidal ideation or suicidal behaviour during the extension period had suicidal ideation prior to treatment with study drug.

Furthermore, one patient attempted to suicide. He took an overdose of "78 tablets of Tylenol®" 33 days after the first dose of the study drug.

Question 3: sedation as side effect

In the extension period one patient out of 41 patients reported an adverse effect of sedation. This event occurred 67 days after the first dose of study drug. The patient completed the study as planned.

3. Rapporteur's overall conclusion

The Applicant has answered both questions regarding the suicidal ideation and attempt, as well as that about sedation as a side effect in the extension study.

In the SPC, information about suicide/suicidal thoughts or clinical worsening is already present in the section 4.4 , with the double idea that depression is associated with an increased risk of suicidal thoughts, self-harm and suicide, and that patients with a history of suicide-related events or whose exhibiting a significant degree of suicidal ideation prior to commencement of treatment are at greater risk of suicidal thoughts and attempts, and should receive careful monitoring during the treatment.

The information already present in the SPC is considered sufficient to cover the risk of suicidal thoughts/risk of attempts during the treatment with vortioxetine.

Sedation as an adverse drug effect is not mentioned in the SPC. In a review published in 2014, Citrome I. reported no case of sedation associated with vortioxetine. The most common adverse events were nausea, constipation, and vomiting (Citrome I. Vortioxetine for major depressive disorder: a systematic review of the efficacy and safety profile for this newly approved antidepressant – DARE, 2014). In another publication, vortioxetine is considered to be at low risk for sedation (Keks NA et al. Vortioxetine: a multimodal antidepressant or another selective serotonin reuptake inhibitor? Australas Psychiatry 2015; 23(3): 210-213 - Abstract).

The Applicant should follow the cases of sedation and/or sleep disturbances. Such symptoms are well described after use of other antidepressants, SSRI's for example (Meyler's side effects of psychiatric drugs. Elsevier, 2009).

☒ PAM fulfilled (all commitments fulfilled) - No further action required