11 October 2012
EMA/640279/2012
Committee for Medicinal Products for Human Use (CHMP)

Zyprexa Velotab

(olanzapine)

Procedure No. EMEA/H/C/000287/FUM 030

CHMP assessment report for paediatric use studies submitted according to Article 45 of the Regulation (EC) No 1901/2006

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

Disclaimer: The assessment report was drafted before the launch of the European Medicines Agency's new corporate identity in December 2009. This report therefore has a different appearance to documents currently produced by the Agency.

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Assessment of paediatric studies according to Art 45 of the Regulation (EC) No 1901/2006 (the Paediatric Regulation)
Active substance: Olanzapine (Zyprexa/Zyprexa Velotab)
MAH: Eli Lilly Nederland B.V.

Olanzapine studies in Children and Adolescents

Introduction:

As required by the Paediatric Regulation (article 45 of the Regulation 1901/2006, as amended), information on three additional olanzapine studies that have included altogether 36 children and adolescents were provided in December 2008 by the MAH. The submission consisted of an Abriaviated Clinical Study Report for study F1D-MC-HGKL, Synopsis of Study F1D-MC-HGCT and a Publication of Study F1D-UT-HGFP.

Clinical studies with children and adolescents:

1. Long Term Open-Label Trial of Olanzapine in Children with Childhood Onset Schizophrenia. [F1D-MC-HGCT]

The objective was to establish long-term safety of olanzapine in a dose range of 2.5 mg every other day to 20 mg/day in a population of children and adolescents, 8 to 19 years of age (n=6), who derived significant clinical benefit with olanzapine during study F1D-MC-HGCS or F1D-MC-HGCR. This was a multicenter, open-label inpatient or outpatient study. After a 2- to 9-day screening and treatment phase, patients could enter an indefinite long-term olanzapine therapy phase. The duration of treatment experienced by patients in this study ranged from a minimum of 3 weeks to a maximum of 40 weeks on olanzapine.

No serious adverse events or deaths occurred in this study. Five of 6 patients experienced non-serious side effects from the drug.

2. Open-Label Study of Olanzapine in Children with Pervasive Developmental Disorder (PDD) [F1D-UT-HGFP]

The objective of this open label study was to investigate the safety and efficacy of olanzapine in the treatment of PDD in 25 children, especially with respect to problems in social relationships and communication. The study consisted of two periods: a screening and washout period of about 2 weeks (period I) and a 12-week open-label therapy period (period II).

The study results have been published in J Clin Psychopharmacol 2002;22:455–460 According to the publication the present study evaluated systematically the safety of olanzapine in children. The most important adverse events were weight gain, loss of strength (asthenia), and increased appetite. Three children developed an extrapyramidal syndrome that disappeared after the dose was lowered. Thus, olanzapine would appear to be a relatively safe medication for children. However, the weight gain might interfere with treatment.

3. Efficacy and Safety of Olanzapine in Patients with Borderline Personality Disorder (BPD): A Randomized, Flexible-Dose, Double-Blind Comparison with Placebo. [F1D-MC-HGKL]

This was a multicenter, randomized, 12-week, double-blind, placebo-controlled study, with a 12-week, open-label extension. All patients received olanzapine during the open label period. Patients with BPD were randomized to 1 of 2 treatment groups: olanzapine 2.5 to 20 mg/day or placebo.
Of the patients who were <18yrs of age, 5 enrolled double-blind period, and 4 entered open-label period

This study originally planned to enroll a subpopulation of adolescent BPD patients. Due to concerns expressed by ethical review boards about the appropriateness of including adolescents in this trial, the study protocol was amended to exclude this subpopulation. Therefore, all reported analyses are limited to the adult data. Among adolescents in the olanzapine treatment group, the following AEs were reported: weight increased, asthma, headache, rhinitis allergic, and back pain. All were considered to

be of mild severity. There were no serious or potentially clinically significant laboratory findings among adolescent patients in either treatment group.

Conclusion:

Since olanzapine is not indicated for use in adolescents no efficacy aspect was discussed. None of these patients experienced serious, unexpected, possibly causally related adverse events. Based on the review of the submitted documents, studies concerning olanzapine in adolescents and children do not give any reason for further SPC changes at the moment. The studies have included 36 children and adolescents with s**chizophrenia (6 patients), pervasive developmental disorder (25 patients) and borderline personality disorder** (5 patients). Drug-related adverse events were of similar quality as reported in adults, although based on the submitted studies, the safety of olanzapine in children and adolescents cannot be fully evaluated. Olanzapine does not have a treatment indication in these age groups currently.