Review and Evaluation of Clinical Data

NDA 21323 - Lexapro (escitalopram oxalate) Tablets and
NDA 21365 - Lexapro (escitalopram oxalate) Oral Solution

Sponsor:	Forest Laboratories, Inc.
Drug:	Lexapro (escitalopram oxalate)
Material Submitted:	Supplement-44 (Labeling)
DARRTS Supplement Document #	594 for NDA 21323 241 for NDA 21365
Correspondence Date:	03/12/2014
Date Received:	03/12/2014

I. Background

Lexapro (escitalopram oxalate), a selective serotonin reuptake inhibitor (SSRI), was approved for the treatment of major depressive disorder (MDD) on 03/19/2009.

The approval letter dated 03/19/2009 included a postmarketing commitment (PMC), which was a long-term safety study, specifically; an open-label, 24-week safety study with escitalopram in children aged 7-11 years. The letter indicated that the final study report of this safety study should be submitted within 5 years from the approval date - 03/19/2009.

On 03/12/2014, the sponsor, Forest, submitted the final study report of the long-term safety study; and a labeling prior approval supplement which described changes in the pediatric use subsection 8.4 of the Lexapro package insert.

II. Review of Clinical Data

The review of clinical data will focus on 2 questions:

1) whether the sponsor fulfilled their postmarketing commitment

2) whether the language changes in the pediatric use subsection 8.4 of the Lexapro package insert is acceptable based on the safety findings of the study

Review of the Clinical Study Report of the Long-Term Safety Study

Study Number:
SCT-MD-55

Study Title

An Open-label Long-term Study of Escitalopram in Children 7 to 11 Years of Age with Major Depressive Disorder

Name of Investigational Product:

Escitalopram

Indication Studied:

Major Depressive Disorder (MDD)

Subject Studied:

118, male and female outpatients, 7 to 11 years of age, meeting DSM-IV-TR criteria for MDD

Study Design:

Multicenter (16 centers in US), open-label, flexible-dose (escitalopram 10 mg/day or escitalopram 20 mg/day), 24-week study

Study Period:

First Patient, First Visit Date: 28-Oct-2010
Last Patient, Last Visit Date: 31-Jan-2013

Safety Review of the study

Death:

None

Serious adverse events (SAEs):

Two patients (1.7%) reported SAEs (mania and suicidal ideation each in 1 patient)

Discontinuation:

9 patients (7.6%) had AEs that led to discontinuation. The most frequent cause of discontinuation by system organ class was psychiatric disorder (7 patients, 5.9%)

TEAEs:

The most commonly reported TEAEs were gastrointestinal (30.5% of patients) and nervous system disorders (28.8% of patients)

In conclusion, the safety findings are consistent with the safety profile of escitalopram oxalate.

Review of the Proposed Changes in Section 8.4 Pediatric Use

The sponsor proposed the language changes in Section 8.4 Pediatric Use as follows:

8.4 Pediatric Use

(b) (4)

(b) (4) The sSafety and effectiveness of Lexapro (b) (4) have been established in adolescents (12 to 17 years of age) for the treatment of major depressive disorder [*see Clinical Studies (14.1)*]. Although maintenance efficacy in adolescent patients with mMajor dDepressive dDisorder has not been systematically evaluated, maintenance efficacy can be extrapolated from adult data along with comparisons of escitalopram pharmacokinetic parameters in adults and adolescent patients.

The safety and effectiveness of Lexapro have not been established in pediatric (younger than 12 years of age) patients with major depressive disorder. In a 24-week, open-label safety study in 118 children (aged 7 to 11 years) who had major depressive disorder, the safety findings were consistent with the known safety and tolerability profile for Lexapro.

II. Reviewer's Comments and Conclusions

1) The sponsor conducted a long-term safety study described above and they submitted the final study report within 5 years from the approval date. Therefore, the sponsor has fulfilled their PMC.

2) The language changes in the pediatric use subsection 8.4 of the Lexapro package insert is acceptable based on the safety review of the study. Therefore, it is recommended that this supplement be approved.

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October 17, 2014

cc: NDA
M/Mathis, P/David, W/Bender, J/Zhang

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/s/

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10/17/2014

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10/17/2014