



NDA 21-035/S-057
NDA 21-505/S-013

UCB, Inc.
Attention: Kristen Piatak
Regulatory Affairs Manager
1950 Lake Park Drive
Smyrna, GA 30080

Dear Ms. Piatak:

Please refer to your new drug applications (NDAs) dated May 19, 2006, received May 19, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Keppra[®] (levetiracetam) Tablets and Oral Solution.

We acknowledge receipt of your submissions dated September 15, 2006 and March 19, 2007.

These new drug applications provide for the use of Keppra[®] Tablets and Oral Solution as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in adults and children 6 years of age and older with idiopathic generalized epilepsy.

We have completed our review of these applications, as amended and they are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and patient package insert). Marketing the product(s) with FPL that is not identical to the approved labeling text may render the products misbranded and unapproved new drugs.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. In addition, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions "**FPL for approved NDA 21-035/S-057 and NDA 21-505/S-013.**" Approval of these submissions by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for ages 1 month to 2 years and deferring pediatric studies for ages 2 to 6 years for this application.

Pediatric Postmarketing Study Commitment

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in pediatric patients ages 2 to 6 years of age with idiopathic generalized epilepsy.

Final Report Submission: March 2012

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated “**Required Pediatric Study Commitments**”.

Clinical Postmarketing Study Commitment

Please refer to a teleconference between representatives of your firm and the Division on March 16, 2007, in which we noted that although an analysis of the 50% responder rate for absence seizures indicates no change in absence seizure frequency associated with Keppra treatment, examination of new onset absence seizures indicates a tendency toward a greater rate in the levetiracetam treated patients. Therefore, you agreed to provide additional analyses of the risk of absence seizures associated with levetiracetam treatment. This commitment is described below.

2. We note your commitment to further explore this potential association through a thoroughly synthesized analysis of the full placebo-control database. The goal of the analysis will be to compare all patients randomized to placebo with those randomized to levetiracetam. The analysis should include a meta-analysis of absence seizures in all patients who have participated in placebo controlled studies. The analysis should include a subset analysis of two separate populations: 1) patients with a diagnosis that is not strongly associated with absence seizures (e.g. all controlled studies in partial epilepsy) and, 2) those who suffer from syndromes that place the patients at increased risk for absence (Study N166 and N01057). Each analysis should examine all randomized patients (patients with and without absence seizures at baseline) as well as a subset analysis of patients without a prior history of absence seizures. Pediatric and adult subset analyses should also be performed. Analyses should include both descriptive and inferential approaches. If absence seizure information is unavailable in the partial epilepsy studies, you should document that every reasonable attempt was made to derive such information. Included in this effort, you should attempt to examine the adverse event database in terms of rates of newly reported seizure types (i.e. absence in placebo versus levetiracetam groups).

Final Report Submission: by December 2007

Submit all final study reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these

postmarketing study commitments must be prominently labeled “**Postmarketing Study Commitment Protocol**”, “**Postmarketing Study Commitment Final Report**”, or “**Postmarketing Study Commitment Correspondence.**”

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Susan Daugherty, Regulatory Project Manager, at (301) 796-0878.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Labeling

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Russell Katz
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