DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDA 090906/S-002

PRIOR APPROVAL SUPPLEMENT
APPROVAL – NEW STRENGTH

Alvogen Pine Brook LLC
U.S. Agent for Lotus Pharmaceutical Co., Ltd.
10 Bloomfield Avenue, Building B
Pine Brook, NJ 07058
Attention: Patricia Jaworski
Vice President, Regulatory Affairs

Dear Madam:

This is in reference to your supplemental abbreviated new drug application (sANDA) dated May 31, 2012, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for Roweepra (Levetiracetam Tablets USP), 500 mg.

Reference is also made to the complete response letter issued by this office on February 18, 2014, and to your amendments dated May 14, 2014; and January 4, January 9, and August 17, 2015.

The supplemental application, submitted as a "Prior Approval Supplement," provides for:

- Addition of new strengths, 250 mg, 750 mg, and 1000 mg for Roweepra (Levetiracetam Tablets USP).
- Alternate drug substance manufacturer at [redacted] (b) (4).

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the sANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Roweepra (Levetiracetam Tablets USP), 250 mg, 750 mg, and 1000 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Keppra Tablets, 250 mg, 750 mg, and 1000 mg of UCB Inc. (UCB). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

The RLD upon which you have based your ANDA, UCB's Keppra Tablets, 250 mg, 750 mg, and 1000 mg, is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent No. 8,802,142 (the '142 patent), is scheduled to expire (with pediatric exclusivity added) on December 7, 2031.

Your ANDA contains a paragraph IV certification to the patent[1] under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Roweepra (Levetiracetam Tablets USP), 250 mg, 750 mg, and 1000 mg under this ANDA. You have notified the agency that Lotus Pharmaceutical Co., Ltd. (Lotus) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that no action for infringement was brought against Lotus within the statutory 45-day period.

With respect to 180-day generic drug exclusivity, we note that Lotus was the first ANDA applicant for Levetiracetam Tablets USP, 250 mg and 750 mg, to submit a substantially complete ANDA with a paragraph IV certification to the '142 patent. Therefore, with this approval, Lotus is eligible for 180 days of generic drug exclusivity for Levetiracetam Tablets USP, 250 mg and 750 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act will begin to run from the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv).[2] Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

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[1] We note that the '142 patent was submitted to the agency after submission of your supplement for the 250 mg, 750 mg, and 1000 mg strengths. Litigation, if any, with respect to this patent would not create a statutory stay of approval.

[2] Because another ANDA for Levetiracetam Tablets USP, 250 mg and 750 mg, was filed before the date of enactment of the *Medicare Prescription Drug, Improvement and Modernization Act* (MMA) (Public Law 108-173) on December 8, 2003, references to the 180-day exclusivity provisions are to the section of the FD&C Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your sANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

Carol A. Holquist, RPh
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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Carol Holquist

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