DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205836
NDA 205837
NDA 205838

NDA APPROVAL

UCB, Inc.
1950 Lake Park Drive
Smyrna, GA 30080

Attention: Deborah Hogerman
Vice President, Regulatory Affairs

Dear Ms. Hogerman:

Please refer to your New Drug Applications (NDAs) dated November 19, 2014, received November 20, 2014, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for:

Name of Drug Product: BRIVIACT (brivaracetam); 10, 25, 50, 75, and 100 mg oral tablets; injection (50 mg/5 mL); and oral solution (10 mg/mL)

Our Reference Number: NDA 205836 (oral tablets)
NDA 205837 (injection 50 mg/5 mL)
NDA 205838 (oral solution 10 mg/mL)

We also refer to our approval letter dated February 18, 2016, which contained the following error: incorrect listing under "The most common side effects of BRIVIACT" in the Medication Guide.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain February 18, 2016, the date of the original approval letter.

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

These new drug applications provide for the use of BRIVIACT as adjunctive therapy in the treatment of partial onset seizures in patients 16 years of age and older with epilepsy.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels and the carton and immediate container labels submitted on November 19, 2014, for the tablet and injection formulations and February 2, 2016, for the oral solution formulation, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008). Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "Final Printed Carton and Container Labels for approved NDA # 205836, 205837, 205838." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for BRIVIACT was not referred to an FDA advisory committee because the safety profile is acceptable for the treatment of partial-onset seizures in patients with epilepsy and because the clinical trial design is similar to previously approved products in the class.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the

product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for neonates from birth to less than one month of age because necessary studies are impossible or highly impracticable due to a small number of available subjects.

We are deferring submission of your pediatric studies for subjects from one month to less than 16 years of age because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(C) of the FDCA. These required studies are listed below.

3042-1 A pharmacokinetic analysis to determine a dosing regimen in children from 4 years to less than 16 years of age that provides drug exposure that is similar to the exposure that is effective in adult patients with partial onset seizures. This analysis will require pharmacokinetic data from studies of both adult and pediatric patients. These studies have already been performed.

Final Analysis Plan Submission:	10/2016
Final Report Submission:	06/2020

3042-2 A pharmacokinetic and safety analysis in children from 1 month to less than 16 years of age to determine whether the bioavailability of the intravenous and oral formulations is similar and to determine an acceptable safety margin of the intravenous formulation when administered at doses that are found acceptable for oral administration. The study should include routine safety monitoring including careful cardiac monitoring before, during, and after infusion. Subjects should be balanced among age cohorts.

Final Protocol Submission:	08/2016
Study/Trial Completion:	01/2020
Final Report Submission:	06/2020

3042-3 A prospective, randomized, controlled, double-blinded, efficacy and safety study of brivaracetam for the adjunctive treatment of partial onset seizures in children from 1 month to less than 4 years of age. The primary efficacy endpoint during the controlled phase will examine seizure frequency based upon video/electroencephalographic data. The placebo and drug treatment groups will be compared by inferential statistical methods to identify a treatment effect.

Routine safety endpoints should be monitored. Behavioral and cognitive endpoints should be included. Subjects should be balanced among age cohorts.

Final Protocol Submission:	05/2017
Study/Trial Completion:	02/2022
Final Report Submission:	08/2022

3042-4 Long-term safety study of brivaracetam in the adjunctive treatment of partial onset seizures in children from 1 month to less than 16 years of age. Routine safety measures should be monitored. Behavioral and cognitive endpoints should be included. A total of at least 200 patients must be enrolled. Subjects should be balanced among age cohorts.

Final Protocol Submission:	03/2011 (completed)
Study/Trial Completion:	02/2022
Final Report Submission:	08/2022

Submit the protocol(s) to your corresponding appropriate IND(s) with a cross-reference letter to the appropriate NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS" in large font, bolded type at the beginning of the cover letter of the submission.

REQUESTED PHARMACOVIGILANCE

We request that you perform postmarketing surveillance and enhanced pharmacovigilance for interstitial nephritis. All confirmed or possible cases of interstitial nephritis must be reported to us in an expedited fashion. We also request that you provide annual reports providing a cumulative and synthesized analysis of all postmarketing cases of renal failure, interstitial nephritis, and other reported alterations in renal function. This should include an analysis of causality, a list of recent and concomitant medications with start and stop dates, information on recent infections, associated symptoms (e.g., rash, fever), pertinent laboratory values including serum creatinine, creatinine clearance, pertinent serum electrolytes, serum pH, eosinophil count, urinalysis, microscopic urine findings (e.g., eosinophils, lymphocytes, white or red cell casts), biopsy reports, and any other important information about the event(s). For each patient that you identify, please provide information as to whether diseases of autoimmune inflammation (e.g., sarcoidosis, Sjögren's syndrome, systemic lupus erythematosus) have been ruled out.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert, Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

PDUFA V APPLICANT INTERVIEW

FDA has contracted with Eastern Research Group, Inc. (ERG) to conduct an independent interim and final assessment of the Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs under PDUFA V ("the Program"). The PDUFA V Commitment Letter states that these assessments will include interviews with applicants following FDA action on applications reviewed in the Program. For this purpose, first-cycle actions include approvals, complete responses, and withdrawals after filing. The purpose of the interview is to better understand applicant experiences with the Program and its ability to improve transparency and communication during FDA review.

ERG will contact you to schedule a PDUFA V applicant interview and provide specifics about the interview process. Your responses during the interview will be confidential with respect to the FDA review team. ERG has signed a non-disclosure agreement and will not disclose any identifying information to anyone outside their project team. They will report only anonymized results and findings in the interim and final assessments. Members of the FDA review team will be interviewed by ERG separately. While your participation in the interview is voluntary, your feedback will be helpful to these assessments.

If you have any questions, contact Cathleen Michaloski, Sr. Regulatory Project Manager, by email Cathleen.michaloski@fda.hhs.gov or by phone (301) 796-1123.

Sincerely,

{See appended electronic signature page}

Ellis F. Unger, M.D.
Director
Office of Drug Evaluation I
Office of New Drugs
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

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

/s/

ELLIS F UNGER
02/18/2016