DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022115/S-006

NDA APPROVAL

GlaxoSmithKline
Attention: Elizabeth McConnell, PharmD
Associate Director, Neurology, US Regulatory Affairs
PO Box 13398
Five Moore Drive
Research Triangle Park, NC 27709

Dear Dr. McConnell:

Please refer to your Supplemental New Drug Application (sNDA) dated March 31, 2010, received March 31, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lamictal XR (lamotrigine) Extended-Release tablets.

We also refer to our approval letter dated April 25, 2011 which contained the following error: The last bullet of the section of the MedGuide entitled "What Should I Tell My Healthcare Provider Before Taking Lamictal XR" contained the following sentence: *Breastfeeding while taking LAMICTAL XR is not recommended.* This sentence is being removed from the updated approved label.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain April 25, 2011, the date of the original approval letter.

We also acknowledge receipt of your amendments dated May 27, 2010; July 30, 2010; October 28, 2010; November 18, 2010; November 19, 2010; February 8, 2011; February 14, 2011; February 25, 2011; March 18, 2011; your risk evaluation and mitigation strategy (REMS) assessment dated April 19, 2010(2); April 21, 2011 and April 25, 2011.

This "Prior Approval" supplemental new drug application proposes monotherapy in patients 13 years of age and older with partial seizures who are receiving therapy with a single antiepileptic drug (AED). This supplemental new drug application also provides for elimination of the approved REMS.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

We note that your April 25, 2011, submission includes final printed labeling (FPL) for your package insert and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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 and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

Pediatrics
We are granting a waiver of the requirements under PREA for Lamictal conversion to monotherapy in pediatric patients ages 1 month to less then 13 years for the same reason as the waiver granted for the immediate release formulation of Lamictal, which is described in our April 14, 2010 letter. The reason for granting the waiver is because necessary studies are impossible or highly impracticable because:

- conducting a placebo-controlled trial would not be feasible due to ethical considerations, and
- historical control studies are not possible due to the lack of suitable historical data.

We are waiving the pediatric study requirement for ages birth up to 1 month because the necessary studies are impossible or highly impracticable, as there are too few children in this age group with the disease to study.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Lamictal XR (lamotrigine) Extended-Release tablets was originally approved on May 29, 2009, and the most recent REMS modification was approved on April 14, 2010. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

On April 19, 2011, you propose that FDA no longer require a REMS for Lamictal XR (lamotrigine) Extended-Release tablets.

We have determined that it is no longer necessary to include the Medication Guide as an element of the approved REMS, and that a REMS is no longer necessary to ensure that the benefits of Lamictal XR (lamotrigine) Extended-Release tablets outweigh its risks. Therefore, we agree with your proposal and a REMS for Lamictal XR (lamotrigine) Extended-Release tablets is no longer required.

We remind you that the Medication Guide will continue to be part of the approved labeling in accordance with 21 CFR 208.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), 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).

If you have any questions, contact Stephanie N. Keefe, Regulatory Project Manager, at (301) 796-4098.

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: Content of Labeling

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

/s/

ERIC P BASTINGS on behalf of RUSSELL G KATZ
04/25/2011