DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020241/S-039
NDA 020764/S-032
NDA 022251/S-001
NDA 022115/S-003

SUPPLEMENT APPROVAL

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 October 2, 2009, received October 2, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lamictal (lamotrigine) tablets, Lamictal (lamotrigine) chewable dispersible tablets, Lamictal ODT (lamotrigine) orally disintegrating tablets, and Lamictal XR (lamotrigine) extended-release tablets.

We acknowledge receipt of your amendments dated May 25, 2011; May 26, 2011; December 22, 2011; August 22, 2012 and December 4, 2012.

This "Changes Being Effected" labeling supplemental new drug application proposes the following changes to two sections in the package insert (PI):

- **ADVERSE REACTIONS: Postmarketing Experience**
  • "Aseptic meningitis" was added under a new subsection "**Nervous System.**"
  • "Lymphadenopathy not associated with hypersensitivity disorder" was added under **Blood and Lymphatic.**

- **OVERDOSAGE**
  • Deletion of the statement recommending gastric lavage under **"Management of Overdosage"**.

We also note that the following changes to the package insert (PI) were approved in the October 24, 2010 Action:

- **ADVERSE REACTIONS: Postmarketing Experience**
  • "Aseptic meningitis" was added under a new subsection "**Nervous System.**"

OVERDOSAGE

• Deletion of the statement recommending gastric lavage under **"Management of Overdosage"**.

APPROVAL & LABELING

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

Concerning the addition of "lymphadenopathy not associated with hypersensitivity disorder", we agree there is sufficient evidence for placement of this adverse reaction in post-marketing, section 6.3 of the label. However, the data you are providing is not sufficient to definitively confirm causality. The significance of this finding, if causality can be confirmed, may require more prominent placement in the label. In order to fully evaluate this, a full review of the adverse event reports on the patients identified in "Appendix B: Tabulation of Best Cases" is necessary. We request that you provide us with full narrative reports of these events (e.g. MedWatch forms).

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 that includes labeling changes 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).

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
Office of Prescription Drug Promotion (OPDP)
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/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).

If you have any questions, call Stephanie N. Parncutt, MHA, Regulatory Project Manager, at (301) 796-4098.

Sincerely,

{See appended electronic signature page}

Eric Bastings, M.D.
Acting Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
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
12/20/2013