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APPLICATION NUMBER:

22-251

OTHER ACTION LETTER(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

COMPLETE RESPONSE

NDA 22-251

SmithKline Beecham Corporation
d/b/a GlaxoSmithKline
Attention: Eric Benson, Senior Director, US Regulatory Affairs
Five Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709

Dear Mr. Benson:

Please refer to your new drug application (NDA) dated November 28, 2007, received November 28, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lamictal ODT (lamotrigine) Orally Disintegrating Tablets, 25mg, 50mg, 100mg, and 200mg.

This new drug application provides for a new immediate release formulation of lamotrigine.

We acknowledge receipt of your additional submissions to NDA 22-251 dated January 31, 2008, March 28, 2008, April 29, 2008, May 1, 2008, June 23, 2008, September 9, 2008, September 23, 2008, and September 25, 2008.

We also acknowledge receipt of your amendment dated December 18, 2008, which was not reviewed for this action. We ask that you incorporate it by specific reference as part of your response to this letter.

We have completed the review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, included our recommendations to address these issues.

DEFICIENCIES

1. New draft labeling must be submitted. Submit draft labeling that incorporates revisions proposed by you in a December 12, 2008 electronic communication and further discussed with you during a December 18, 2008 telephone meeting, as well as all previous revisions as reflected in the most recently approved package insert. We note that your December 12, 2008 proposed labeling included revisions to the Lamictal ODT labeling and Medication Guide.

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 include annotations with the supplement number for previously-approved labeling changes.

2. The draft carton and container labeling must be revised. Submit the draft carton and container labeling revised as follows (although we acknowledge that you have provided these labels via electronic communication on December 19, 2008):

   Add the following bolded statement or appropriate alternative to the carton and container labels per 21 CFR 208.24(d): "**ATTENTION PHARMACIST: Each patient is required to receive the enclosed Medication Guide**".

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to require the submission of a REMS if FDA has determined that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

In accordance with section 505-1(a) of the FDCA, we have determined that a REMS is necessary for Lamictal ODT to ensure that the benefits of the drug outweigh the risks of suicidal thoughts and behavior with antiepileptic drugs (AEDs), including lamotrigine.

Your proposed REMS must contain the following:

Medication Guide: As one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Lamictal ODT poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Lamictal ODT. FDA has determined that Lamictal ODT is a product that has serious risk (relative to benefits) of which patients should be made aware because information concerning the risk could affect patients' decisions to use, or continue to use Lamictal ODT. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Lamictal ODT.

Timetable for Assessment: The proposed REMS must include a timetable for assessment of the REMS that shall be no less frequent than by 18 months, 3 years, and in the 7th year after the REMS is initially approved. We recommend that you specify the interval that each assessment will cover and the planned date of submission to the FDA of the assessment. We recommend that assessments be submitted within 60 days of the close of the interval.

We acknowledge that your December 18, 2008, amendment includes your proposed REMS. However, because these documents have not been reviewed this cycle, we ask that you incorporate them by specific reference as part of your response to this letter.

The REMS, once approved, will create enforceable obligations.

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA Guidance for Industry *Formal Meetings With Sponsors and Applicants for PDUFA Products*, February, 2000 (http://www.fda.gov/cder/guidance/2125fnl.htm).

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Jacqueline H. Ware, Pharm.D., Supervisory Regulatory Project Manager, at (301) 796-1160.

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

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

12/24/2008 09:15:34 AM