



NDA 20-711/S-032  
NDA 20-711/S-033

SmithKline Beecham Corporation  
d/b/a GlaxoSmithKline  
5 Moore Drive  
Research Triangle Park, NC 27709

Attention: Mary E. Martinson  
Senior Director, Psychiatry  
U.S. Regulatory Affairs

Dear Ms. Martinson:

Please refer to your supplemental new drug applications dated December 11, 2008 and March 19, 2009, received December 11, 2008 and March 19, 2009, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ZYBAN (bupropion hydrochloride) Sustained-Release tablets.

Reference is also made to our letter dated February 19, 2009, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for bupropion-containing drug products. This information pertains to the risk of suicidality-related events associated with the use of these products.

Supplement S-032, submitted as a “Changes Being Effected” supplemental new drug application, provides the following changes to the package insert label:

1. **CLINICAL PHARMACOLOGY: Renal** and **PRECAUTIONS: Renal Impairment**- Addition of a description of a study comparing the use of bupropion in normal subjects and patients with moderate-to-severe renal impairment.
2. **PRECAUTIONS: Pregnancy**- Deletion of the Bupropion Pregnancy Registry enrollment telephone number since the registry was closed as of November 1, 2007.
3. **OVERDOSAGE**- Addition of QRS prolongation as a reported adverse reaction of overdoses of bupropion under “Human Overdose Experience”. Deletion of the statement recommending gastric lavage under “Overdosage Management”.

Supplement S-033 provides for revisions to the package insert and Medication Guide consistent with our letter dated February 19, 2009.

We also refer to the email correspondence between FDA and GlaxoSmithKline dated May 28, June 5, 11, and 16, 2009, in which agreement was reached on these safety labeling changes in Supplement S-033 and Supplement S-032.

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

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

### **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, “**SPL for approved supplements NDA 20-711/S-032 and S-033.**”

Marketing the product with final printed labeling that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

### **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 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

### **LETTERS TO HEALTH CARE PROFESSIONALS**

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH  
Food and Drug Administration  
Suite 12B05  
5600 Fishers Lane  
Rockville, MD 20857

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## **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, please contact Margarita Tossa, Regulatory Project Manager, at (301)796-4053.

Sincerely,

*{See appended electronic signature page}*

Bob A. Rappaport, M.D.  
Director  
Division of Anesthesia, Analgesia  
and Rheumatology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Enclosure: Package Insert labeling/Medication Guide

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Bob Rappaport  
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