DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 18644/S-038
NDA 20358/S-045

SUPPLEMENT APPROVAL

GlaxoSmithKline
Attention: Mary E. Martinson
Senior Director, Psychiatry, US Regulatory Affairs
P.O. Box 13398, Five Moore Drive
Research Triangle Park, NC 27709-3398

Dear Ms. Martinson:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received December 3, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Wellbutrin (bupropion HCl) Tablets (NDA 18644) and Wellbutrin SR (bupropion HCl) Sustained-Release Tablets.

We acknowledge receipt of your submissions of December 15, 2009, which constituted a complete response to our action letter of December 1, 2009.

These "Prior Approval" supplemental new drug applications provide for revisions to the product labeling:

- **CLINICAL PHARMACOLOGY: Metabolism** and **PRECAUTIONS: Drug Interactions**- Addition of pharmacokinetic information from a series of studies concerning drug interactions between bupropion and ritonavir and lopinavir/ritonavir.
- **PRECAUTIONS: Drug Interactions**- Addition of ticlopidine and clopidogrel as examples of drugs that are substrates of or inhibitors/inducers of CYP2B6 and thus may interact with bupropion. Addition of statement that bupropion increases the C_{max} and AUC of citalopram by 30% and 40%, respectively.
- **DOSAGE AND ADMINISTRATION** and the **Medication Guide (WELLBUTRIN SR only) -** An update to the statement "Do not chew, divide, or crush tablets" to add "as this may lead to an increased risk of adverse effects, including seizures".
- **MEDICATION GUIDE:** Addition of the statement "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088", as required by FDA Final Rule issued 10-28-2008 Toll Free Number for Reporting Adverse Events on Labeling for Human Drug Products.
- Minor editorial changes to provide consistency between PIs.

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

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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 pending "Changes Being Effected" (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.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

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, email your Regulatory Project Manager, at Juliette.Toure@FDA.HHS.GOV.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20358	SUPPL-45	GLAXOSMITHKLINE	WELLBUTRIN SR
NDA-18644	SUPPL-38	GLAXOSMITHKLINE	WELLBUTRIN (BUPROPION

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/s/

THOMAS P LAUGHREN
05/25/2010