DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021515/S-026/S-027
NDA 022108/S-005/S-006

SUPPLEMENT APPROVAL

Valeant Pharmaceuticals North America
Attention: James H. Medley, Ph.D.
Vice President, Regulatory Affairs
700 US Rt. 202/206 N
Bridgewater, NJ 08807

Dear Dr. Medley:

Please refer to your Supplemental New Drug Applications (sNDA) dated May 26, 2011 (021515/S-026 & 022108/S-005), and July 8, 2011 (021515/S-027 & 022108/S-006) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Wellbutrin XL (bupropion hydrochloride) 150 mg and 300 mg Extended-Release Tablets (NDA 021515) and Aplenzin (bupropion hydrobromide) 174 mg, 348 mg, and 522 mg Extended-Release Tablets (NDA 022108).

We additionally acknowledge receipt of your amendment dated June 30, 2011.

Reference is also made to Agency correspondences dated April 20, 2011, June 18, 2011, and June 24, 2011, requesting revisions to the Wellbutrin XL and Aplenzin labelings.

These supplemental new drug applications provide for the following changes to product labeling:

NDAs 21515/S-026 & 22108/S-005 submitted as a "CBE" supplements

- Under **Precautions**, the addition of the following new subsection;
  7.7 **Drug-Laboratory Test Interactions**
  False-positive urine immunoassay screening tests for amphetamines have been reported in patients taking bupropion. This is due to lack of specificity of some screening tests. False-positive test results may result even following discontinuation of bupropion therapy. Confirmatory tests, such as gas chromatography/mass spectrometry, will distinguish bupropion from amphetamines.

- Corollary changes to the **Medication Guide** regarding false positive test results for amphetamines.

NDAs 21515/S-027 & 22108/S-006 submitted as a "Prior Approval" supplements

- Revisions to **CLINICAL PHARMACOLOGY: Metabolism** and **PRECAUTIONS: Drug Interactions** – Information regarding drug-drug interactions between bupropion and drugs that inhibit or induce CYP2B6, such as ritonavir or efavirenz. In addition, information about potential interactions between bupropion and drugs which require metabolic activation by CYP2D6 in order to be effective (e.g., tamoxifen).

We have completed our review of these supplemental applications. 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 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), 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).

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 Juliette Touré, PharmD, Senior 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:
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/

MITCHELL V Mathis
07/26/2011
For Dr. Laughren