DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20972/S-46
NDA 21360/S-35

SUPPLEMENT APPROVAL

Bristol-Myers Squibb, Company
Attention: Katherine Takaki, PhD
Director, Global Regulatory and Safety Sciences
5 Research Parkway, Mailstop 2CW-507
Wallingford, CT 06492

Dear Dr. Takaki:

Please refer to your Supplemental New Drug Applications (sNDA) dated November 26, 2013, received November 26, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for SUSTIVA® (efavirenz), capsules 200 mg and 50 mg and SUSTIVA® (efavirenz) tablets, 600 mg.

We acknowledge receipt of your amendments dated January 10, 2014, May 9, 2014, May 12, 2014, and May 23, 2014.

These "Prior Approval" supplemental new drug applications propose the following:

- Removal of the CONTRAINDICATIONS, Contraindicated Drugs section
- Addition of efavirenz induction effect on CYP3A and CY2B6 information to the WARNINGS AND PRECAUTIONS section
- Revision of the DRUG INTERACTIONS Table 5 and/or CLINICAL PHARMACOLOGY Table 7 and/or Table 8 with
    - revised lopinavir/ritonavir information
    - revised saquinavir information
    - new antimalarial (artemether/lumefantrine) information
- Revision of DRUG INTERACTIONS, Cannabinoid Test Interaction subsection; and
- Revision of the USE IN SPECIFIC POPULATIONS, Nursing Mothers subsection to include information regarding the presence of Sustiva (efavirenz) in human breast milk.

In addition, major revisions requested by the Office of Surveillance and Epidemiology were incorporated in the Patient Information document, patient package insert.

APPROVAL & LABELING

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.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

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, text for the patient package insert, 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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

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 Karen Winestock, Chief, Project Management Staff, at (301) 796-0834 or 301-796-1500.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD
Director
Division of Antiviral Products
Office of Antimicrobial Products
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/

DEBRA B BIRNKRANT
05/23/2014