DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20972/S-43
NDA 21360/S-31

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Bristol-Myers Squibb Company
Attention: Hwei-Gene (Heidi) Wang, Ph.D.
Associate Director, Global Regulatory and Safety Sciences, US
5 Research Parkway, Room 285B,
Mailstop 2DW-206,
Wallingford, CT 06492

Dear Dr. Wang:

Please refer to your Supplemental New Drug Applications (sNDAs) dated October 31, 2012, received November 2, 2012 (NDA 21360) and November 5, 2012 (NDA 20972), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sustiva (efavirenz) 600 mg tablets and Sustiva (efavirenz) 200 mg and 50 mg capsules.

We acknowledge receipt of your amendments dated:

December 7, 2012	January 31, 2013	March 15, 2013	May 1, 2013
December 11, 2012	February 1, 2013	March 20, 2013	May 2, 2013
December 12, 2012	February 11, 2013	March 26, 2013	
January 4, 2013	March 1, 2013	April 9, 2013	
January 29, 2013	March 8, 2013	April 29, 2013	

These "Prior Approval" supplemental new drug applications propose:

- To update the labeling with dosing recommendations for pediatric patients 3 months to 3 years of age and weighing at least 3.5 kg. using a "capsule sprinkle" method of administration (contents of the open capsule sprinkled into a small amount of food or formula).

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

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), 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 these NDAs, 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.

We note that you have fulfilled the pediatric study requirement for all relevant pediatric age groups for this application.

We are waiving the pediatric study requirement for ages 0 months to less than 3 months because the product would be ineffective and/or unsafe in one or more of the pediatric group(s) for which a waiver is being requested. This is because the difficulty of administering an adequate dosage in this group and the high risk of developing HIV resistance to Sustiva (efavirenz) in patients who are underdosed.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated October 31, 2012 containing the final report for the following postmarketing requirement listed in the September 17, 1998 approval letter.

752-3 Continue with the development of a pediatric program, with emphasis on developing a liquid formulation along with obtaining safety, tolerability, pharmacokinetic and antiviral activity data.

We have reviewed your submission and conclude that the above requirement was fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our September 17, 1998, letter.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

2042-1 Perform a label comprehension study to determine whether patients and/or caregivers can understand and follow the instructions for use of Sustiva (efavirenz) capsule sprinkles. The protocol for this study should be provided to the Division of Antiviral Products for review and comment prior to study initiation.

The timetable you submitted on May 1, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	08/2013
Study Completion:	05/2014
Final Report Submission:	05/2014

Submit clinical protocols to your IND 49465 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. 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 Abiola Olagundoye-Alawode, Pharm.D., Regulatory Project Manager, at (301) 796-3982.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
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/

KENDALL A MARCUS
05/02/2013