



NDA 20-972 SLR-033
NDA 21-360 SLR-021

SUPPLEMENT APPROVAL

Bristol-Myers Squibb Company
Attention: Katherine Takaki, Ph.D.
Director, Global Regulatory Strategy
5 Research Parkway
Signature 91 Building, 3 Sig-515
Wallingford, CT 06492

Dear Dr. Takaki:

Please refer to your supplemental new drug applications dated March 31, 2009, received April 1, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sustiva® (efavirenz) 50 mg and 200 mg capsules, and Sustiva® (efavirenz) 600 mg tablets.

We acknowledge receipt of your submission dated September 15, 2009.

These Prior Approval supplemental new drug applications provide for the following revisions to the package insert (PI):

- Additions to the Drug Interaction and Clinical Pharmacology sections based on the results of the two drug-drug interaction studies (efavirenz with atazanavir, a protease inhibitor of HIV-1, and efavirenz with an oral contraceptive)
- Addition of information from postmarketing reports of contraceptive failure in a few patients who were treated with efavirenz while on an implantable hormonal contraceptive
- Addition of information based on a literature review of the interaction of immunosuppressants metabolized by CYP3A4 (cyclosporine, sirolimus, tacrolimus) and inducers of the CYP3A4 isozyme

In addition, the following revisions were made to the patient package insert:

- Reyataz was added to “The following medicines may need to be replaced with another medicine when taken with Sustiva;” section.

- The immunosuppressant medicines cyclosporine (Gengraf, Neoral, Sandimmune and others) Prograf (tacrolimus) and Rapamune (sirolimus) were added to “The Following medicines may require a change in the dose of either SUSTIVA or other medicine,” section.

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

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)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. that is identical to the package insert and patient package insert enclosed. 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 NDA 20-972/S-033 and NDA 21-360/S-021.

LABELING

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the patient package insert).

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the following address or by facsimile at 301-847-8444:

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

In addition, as required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or

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publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

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

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 Sherly Abraham, R.Ph., Regulatory Project Manager, at (301)796-3198.

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

Enclosures:
Package Insert
Patient Package Insert

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20972	SUPPL-33	BRISTOL MYERS SQUIBB CO	SUSTIVA
NDA-21360	SUPPL-21	BRISTOL MYERS SQUIBB PHARMA CO	SUSTIVA (EFAVIRENZ) 300/600MG TABLETS

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
09/23/2009