DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-636 (S-027)
NDA 20-933 (S-017)

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: John Barry, Ph.D.
Associate Director, Drug Regulatory Affairs
900 Ridgebury Rd
P.O. Box 368
Ridgefield, CT 06877-0368

Dear Dr. Barry:

Please refer to your February 15, 2007 supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Viramune® (nevirapine) Tablets (200 mg) and Viramune® (nevirapine) Oral Suspension (10 mg/ml).

Reference is made to your submissions dated December 27, 2007 and February 12, 2008, February 21, 2008, two dated February 25, 2008, March 14, 2008, April 18, 2008, May 30, 2008, June 2, 2008, June 12, 2008, June 16, 2008, June 17, 2008, June 18, 2008, June 19, 2008, June 23, 2008 and June 24, 2008.

These supplemental new drug applications provide for changes to the package insert that include dosing recommendations for the treatment of HIV-1 infection in pediatric patients 15 days and older and for patients with hepatic impairment. In addition, the Indications and Usage section was updated to limit the lead-in period to 28 days for patients who experience skin rash. The Medication Guide section titled "Who should not take Viramune® (nevirapine)" was updated to state "Do not take VIRAMUNE if you have severe liver problems." and the section titled "How should I take VIRAMUNE" was updated to limit the lead-in period to 28 days for patients who experience skin rash.

We 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 enclosed below.

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 indications 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.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENT

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a REMS for an approved drug if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(2)). This provision took effect on March 25, 2008.

Since Viramune® (nevirapine) was approved in 1996, for use in combination with other antiretroviral agents for the treatment of HIV-1-infection, we have become aware that patients with moderate (Child Pugh Class B) or severe hepatic impairment (Child Pugh Class C) should not take Viramune® (nevirapine) due to the risk of increased nevirapine levels and because a safe dose has not been identified for these patients. In addition, there are concerns for decreased Viramune® (nevirapine) efficacy with prolonged once-daily dosing in the lead-in period. The above information was not available when Viramune® (nevirapine) was granted marketing authorization for use in combination with other antiretroviral agents for the treatment of HIV-1-infection. Therefore, we consider this information to be “new safety information” as defined in FDAAA.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. FDA previously approved a Medication Guide required for distribution with Viramune® (nevirapine) in accordance with 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Viramune® (nevirapine) poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Viramune® (nevirapine). FDA has determined that Viramune® (nevirapine) is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use, Viramune® (nevirapine). This includes the new safety information identified above regarding the use of nevirapine by patients with moderate or severe hepatic impairment and regarding the duration of once-daily dosing. The Medication Guide now clarifies that the total duration of the once-daily lead-in dosing period should not exceed 28 days, at which point an alternative regimen may need to be started.

Your proposed REMS, submitted on June 17, 2008 is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS that was included in your June 17, 2008 submission. The timetable you submitted is as follows:

1st FDAAA assessment:	December 20, 2009 (18 months from approval)
2nd FDAAA assessment:	June 20, 2011 (3 years from approval)
3rd FDAAA assessment:	June 20, 2015 (7 years from approval)

Information needed for assessment of the REMS should include but may not be limited to:

a. A survey of patients' understanding of the serious risks of Viramune® (nevirapine)
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

Use the following designator(s) to prominently label all submissions, including supplements, relating to this REMS:

NDA 20-636/20-933 REMS Assessment
NDA 20-636/20-933 Proposed REMS Modification

Please note that:

- This Medication Guide must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(f)(2)];

- You are responsible for ensuring that this Medication Guide is available for distribution to every patient who is dispensed a prescription for this product [21 CFR 208.24];

- The final printed Medication Guide distributed to patients must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text; and

- You are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided [21 CFR 208.24(d)].

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)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert, text for the patient package insert). 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 NDA20-636/S-027 and 20-933/S-017."

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

PROMOTIONAL MATERIALS

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Antiviral Products and two copies of both the promotional materials and the package insert(s) directly to:

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

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, please contact Tanima Sinha, M.S., Regulatory Project Manager, at (301) 796-0812.

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: Final agreed upon labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jeffrey Murray

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