



NDA 20-636/S-021

NDA 20-933/S-011

Boehringer Ingelheim Pharmaceuticals, Inc.  
Attention: Mr. Kevin Dransfield  
Associate Director, Regulatory Affairs  
900 Ridgebury Rd./P.O. Box 368  
Ridgefield, CT 06877-0368

Dear Mr. Dransfield:

Please refer to your supplemental new drug applications dated October 22, 2003, received October 23, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for VIRAMUNE<sup>®</sup> (nevirapine) Tablets and VIRAMUNE<sup>®</sup> (nevirapine) Suspension.

These "Changes Being Effected" supplemental new drug applications provide for the inclusion of changes in the VIRAMUNE<sup>®</sup> (nevirapine) labels regarding risk factors for hepatic toxicity associated with VIRAMUNE<sup>®</sup>, as follows.

The inclusion of an additional sentence in the last paragraph of the **BOXED WARNING** section, to read:

**Women and patients with higher CD4 counts are at increased risk of these hepatic events.**

A revision of the third paragraph of the **WARNINGS: Hepatic Events** section, to read:

Increased AST or ALT levels and/or co-infection with hepatitis B or C at the start of antiretroviral therapy are associated with a greater risk of hepatic adverse events. Women appear to have a three fold higher risk than men for rash-associated hepatic events (4.6% versus 1.5%). Patients with higher CD4 counts may also be at higher risk for rash-associated hepatic events with VIRAMUNE. In a retrospective review, women with CD4 counts >250 cells/mm<sup>3</sup> had a 9 fold higher risk of rash-associated hepatic adverse events compared to women with CD4 counts <250 cells/mm<sup>3</sup> (8.4% versus 0.9%). An increased risk was observed in men with CD4 counts >400 cells/mm<sup>3</sup> (4.5% versus 0.7% for men with CD4 counts <400 cells/mm<sup>3</sup>).

We completed our review of these supplemental new drug applications. They are approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on October 22, 2003 (Package insert, Patient Package insert.)

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, HFD-410  
FDA  
5600 Fishers Lane

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Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Destry Sullivan, Regulatory Project Manager, at (301) 827-2335.

Sincerely,

*{See appended electronic signature page}*

Debra Birnkrant, M.D.

Director

Division of Antiviral Drug Products

Office of Drug Evaluation IV

Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Debra Birnkrant  
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NDA 20-933, 20-636