

Kirk V. Shepard, MD  
Vice President  
Clinical & Scientific Affairs

## IMPORTANT NEW SAFETY INFORMATION

February 2004

### **Re: Clarification of risk factors for severe, life-threatening and fatal hepatotoxicity with VIRAMUNE® (nevirapine)**

Dear Health Care Professional:

Boehringer Ingelheim Pharmaceuticals Inc. (BIPI) is writing to inform you of important new labeling information being added to the Boxed Warning for VIRAMUNE, a non-nucleoside reverse transcriptase inhibitor indicated for the treatment of HIV-1 infection in combination with other antiretroviral agents. Specifically, we wish to draw your attention to the following:

Boehringer Ingelheim  
Pharmaceuticals, Inc.  
  
900 Ridgebury Rd./P.O. Box 368  
Ridgefield, CT 06877-0368  
Telephone (203) 798-9988  
Telefax (203) 791-6234

- Women with CD4+ counts  $>250$  cells/mm<sup>3</sup>, including pregnant women receiving chronic treatment for HIV infection, are at considerably higher risk (12 fold) of hepatotoxicity. Some of these events have been fatal. This subset of patients was identified by analyses of CD4 count at the time of initiation of VIRAMUNE therapy.
- The greatest risk of severe and potentially fatal hepatic events (often associated with rash) occurs in the first 6 weeks of VIRAMUNE treatment. However, the risk continues after this time and patients should be monitored closely for the first 18 weeks of treatment with VIRAMUNE.
- In some cases hepatic injury progresses despite discontinuation of treatment.

This new information is the result of recent post-marketing surveillance data and further analysis of the VIRAMUNE clinical trial database.

Although this new information describes patients at increased risk, it is important to note that any patient can experience hepatic events and should be monitored carefully. As is already described in the product labeling for VIRAMUNE, some experts recommend clinical and laboratory monitoring more often than once a month, and in particular would include monitoring of liver function tests at baseline, at the time of dose escalation, and two weeks after dose escalation. All patients developing a rash, at any time during VIRAMUNE treatment, but particularly during the first 18 weeks, should have liver function tests performed at that time. After the initial 18 week period, frequent clinical and laboratory monitoring should continue throughout VIRAMUNE treatment.

It is important to counsel all patients that if signs or symptoms of hepatitis, severe skin reactions or hypersensitivity reactions occur, they should discontinue VIRAMUNE treatment and seek medical evaluation immediately. VIRAMUNE should not be restarted in these patients.

You can assist us in monitoring the safety of VIRAMUNE by reporting adverse reactions to the Drug Information Unit at Boehringer Ingelheim Pharmaceuticals, Inc. at 1-800-542-6257, OPTION#4, by FAX at 1-800-821-7119 or via e-mail at [druginfo@rdg.boehringer-ingelheim.com](mailto:druginfo@rdg.boehringer-ingelheim.com). Alternatively, you can contact the FDA MedWatch program by telephone at 1-800-332-1088, by FAX at 1-800-332-0178, via [www.FDA.gov/medwatch](http://www.FDA.gov/medwatch), or by mail to MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 30857.

A copy of the newly revised package insert is enclosed with this letter for your review. Also included are Guidelines for the Management of Hepatic and Rash Events with VIRAMUNE, as an additional tool to assist you in managing these events.

Sincerely,

A handwritten signature in dark ink, appearing to read "Kirk V. Shepard".

Kirk V. Shepard, M.D.  
Vice President, Clinical & Scientific Affairs

Enclosures