

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**201152Orig1s000**

**RISK ASSESSMENT and RISK MITIGATION  
REVIEW(S)**

**Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology**

**Date:** February 15, 2011

**To:** Debra Birnkrant, MD, Director  
Division of Antiviral Products (DAVP)

**Through:** Claudia B. Karwoski, PharmD, Director  
Division of Risk Management (DRISK)

**From:** Mary Dempsey BS, Risk Management Programs Coordinator, DRISK  
Barbara Fuller, MSN, CWOCN, Acting TL, Patient Labeling  
Reviewer, DRISK  
Steve Morin, BSN, RN, Patient Labeling Reviewer, DRISK

**Subject:** Initial REMS review; Prior Approval Supplement; REMS  
Modification; REMS Assessment

**Drug Name:** Viramune (nevirapine)  
Tablets NDA 020636  
Oral Suspension NDA 020933  
Extended Release Tablets NDA 201152

**Applicant/Sponsor:** Boehringer-Ingelheim, Inc.

**OSE RCM #:** 2010-1415  
2010-1834

## **1 Background**

The Division of Division of Antiviral Products (DAVP) requested the Division of Risk Management (DRISK) review the Viramune (nevirapine) proposed Risk Evaluation Mitigation Strategy (REMS) Modification for the New Drug Applications (NDA) 020636, Viramune Tablets, and NDA 020933, Viramune Oral Suspension, and the proposed initial REMS for NDA 201152, Viramune (nevirapine) Extended Release Tablets, submitted by Boehringer Ingelheim, Inc on February 2, 2011. This submission proposes to combine the approved Viramune Tablets and Oral Suspension label and REMS to incorporate the currently under review Viramune Extended Release Tablets. Following approval of the Viramune Extended Release Tablets there will be one combined label and REMS for all Viramune (nevirapine) formulations.

The Viramune (nevirapine) REMS was initially approved June 24, 2008 with the following elements:

- Medication Guide
- Timetable for Submission of Assessments

## **2 Material Reviewed**

- June 24, 2008 initial REMS approval for NDAs 020636 and 020933
- June 3, 2011 REMS proposal for NDA 201152
- November 1, 2010 REMS Correspondence for NDA 201152
- January 7, 2011 approval of REMS Modification (NDAs 020636 and 020933) supplement that provided for revisions to the Medication Guide based on the first assessment of Viramune (nevirapine) REMS dated December 17, 2009 and modification to the approved REMS
- January 28, 2011 NDA 201152 REMS Amendment
- February 2, 2011 REMS Modification for NDAs 020636 and 020933

## **3 Proposed REMS Elements**

The February 2, 2011 cover letter states the following:

“Reference is made to your e-mail from 1/10/11 requesting submission of a PAS and NDA Amendment for a proposed REMS modification and updated combined IR/XR Medication Guide for nevirapine tablets/suspension (NDAs 020636 and

020933) and pending nevirapine extended-release tablets (NDA 201152), respectively.

Boehringer Ingelheim herein submits the following:

(1) Modified REMS (template A) which includes nevirapine IR tablet, oral suspension, and XR tablet. In line with our telcon discussion on 1/19/11., BI is proposing a modification to the REMS schedule of assessments. Please find below the rationale for this proposal.

(2) Updated Medication Guide (one proposed version of all nevirapine formulations) which is based on the recently approved (January 7, 2011) Medication Guide for Viramune Tablets and Oral Suspension with the following revisions: (b) (4) and the addition of nevirapine extended-release information from the original June 2010 NDA.”

“Proposed REMS Assessment Statement

It is Boehringer Ingelheim’s position that the proposed modification to the REMS should be adequate to achieve its purpose.”

“Proposal and Rationale for Modification to REMS Schedule of Assessments

The next scheduled REMS assessment within the currently approved REMS for Viramune tablets and suspension (version /2011) is a 3 year assessment (June 20, 2011). Based on communication with FDA which resulted in agreement for one REMS and Medication Guide for all nevirapine formulations, BI proposes postponement of the June 0, 2011 assessment by a period of 12 months to June 20, 2012. However, we wish to retain the currently approved timing of the 7-year assessment unaltered (June 20, 2015). The main rationale for this modification consists of the opportunity to gain experience with the proposed new combined Viramune IR/XR Medication Guide in order to support conducting the next survey. Additionally, this would allow for the potential to review with the Division the proposed methodology for this next survey, with lessons learned from the last survey conducted for the 18-month timeframe, and the availability of the new combined Viramune IR/XR Med Guide. Therefore, BI appreciates the Division’s consideration for this proposed revision to the 3 year REMS assessment timing.”

#### **4 Discussion and Conclusion**

The DAVP and DRISK consulted the Office of Compliance regarding Boehringer Ingelheim’s proposal to revise the REMS Timetable for Submission of Assessments and received the following response:

Boehringer Ingelheim shall amend the REMS timetable to include the 4 year date for submission of Assessment. But, the Office of Compliance requests that the sponsor, Boehringer Ingelheim Pharmaceuticals, Inc., submit a status update containing any data obtained for the 3year Assessment, due June 2011.

## 5. Recommendation

Send the following REMS Modification and Medication Guide comments to the sponsor and let DRISK know if you have any questions:

1. Regarding the February 2, 2011 proposed REMS Modification:

- a. See the appended Viramune (nevirapine) REMS proposal for tracked changes corresponding to comments in this review.
- b. The details of the distribution of the Medication Guide is more appropriate for the REMS Supporting Document
- c. We agree with your proposal to submit a 4 year assessment based upon the rationale you provided. However your 3 year assessment remains in effect and shall include the following:

Under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

d. REMS dates

It is now CDER policy to include dates on REMS in order to have the most recent version posted on the FDA web site. The standard format is as follows:

A header will appear on the top left-hand corner of the first page of the REMS document and will list the initial REMS approval date (mm/yyyy) on the first line, and the most recent REMS modification date (mm/yyyy) on the second line.

For example:

Initial REMS Approval: 06/2008

Most Recent Modification: XX/2011

2. DRISK reviewed and revised the Viramune (nevirapine) Medication Guide and it is appended to this review.

12 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MARY J DEMPSEY  
02/14/2011

CLAUDIA B KARWOSKI  
02/15/2011  
concur