

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

201152Orig1s000

Trade Name: Viramune XR Extended Release Tablets

Generic Name: Nevirapine

Sponsor: Boehringer Ingelheim Pharmaceuticals, Inc.

Approval Date: 03/25/11

Indications: Combination Antiretroviral Treatment of HIV-1 Infection in Adults.

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RESEARCH**

APPLICATION NUMBER:
201152Orig1s000

APPROVAL LETTER



NDA 201-152

NDA APPROVAL

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Maria Gigliotti, M.S.
Associate Director, Drug Regulatory Affairs
900 Ridgebury Rd
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Gigliotti:

Please refer to your New Drug Application (NDA) dated June 3, 2010, received June 3, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Viramune[®] XR[™] (nevirapine) extended-release tablets, 400 mg.

We acknowledge receipt of your amendments dated June 11, 2010, June 24, 2010, June 30, 2010, August 12, 2010, August 30, 2010, September 30, 2010, October 5, 2010, October 28, 2010, October 29, 2010, November 1, 2010, November 15, 2010, December 6, 2010, December 9, 2010, January 6, 2011, January 28, 2011, January 31, 2011, February 7, 2011, February 17, 2011, February 18, 2011, February 22, 2011, March 1, 2011, March 8, 2011, and March 15, 2011.

This new drug application provides for the use of Viramune[®] XR[™] (nevirapine) extended-release tablets once daily in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and proposes modifications to the approved Viramune[®] (nevirapine) Tablets¹ and Oral Suspension² REMS by including Viramune[®] XR[™] (nevirapine) extended-release tablets.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

¹ NDA 20-636

² NDA 20-933

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

IMMEDIATE CONTAINER LABELS

Submit final container labels that are identical to the enclosed immediate container labels submitted on February 17, 2011, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).” Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Container Labels for approved NDA 201-152.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

MARKET PACKAGE

Please submit one market package of the drug product when it is available.

If sending via USPS, please send to:

Amalia Himaya
Food and Drug Administration
Center for Drug Evaluation and
Research
White Oak Building 22, Room: 6317
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

If sending via any carrier other than USPS
(e.g., UPS, DHL), please send to:

Amalia Himaya
Food and Drug Administration
Center for Drug Evaluation and
Research
White Oak Building 22, Room: 6317
10903 New Hampshire Avenue
Silver Spring, Maryland 20903

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 indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for pediatric patients from birth to less than three years because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group. The extended release formulation is a solid dosage form that must not be chewed or crushed at the time of dosing. Therefore, this formulation is not appropriate for younger pediatric patients unable to swallow tablets. Viramune[®] (nevirapine) Oral Suspension is available and approved for use in children down to the age of 2 weeks and is an appropriate option in pediatric patients younger than 3 years.

We are deferring submission of your pediatric study for ages three to less than eighteen years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. This required study is listed below.

- 1741-1 Multiple-dose pharmacokinetic and safety study of nevirapine extended-release tablets, in combination with other antiretroviral agents, in HIV-infected pediatric patients from 3 to < 18 years old. Study report and datasets will include safety and antiviral activity data through 24 weeks of dosing with nevirapine extended-release tablets in a cohort of subjects.

Final Protocol Submission: December 2008
Final Report Submission: September 2011

Submit final reports to this NDA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated “**Required Pediatric Assessment(s)**”.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Viramune[®] (nevirapine) Oral Suspension and Tablets was originally approved on June 24, 2008 and a REMS modification was approved on January 7, 2011. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of inclusion of Viramune[®] XR[™] extended-release tablets in the REMS, related changes to the Medication Guide, and revision to the timetable for submission of assessments by including a 4-year assessment.

Your proposed modified REMS, submitted on February 22, 2011, and appended to this letter, is approved.

There are no changes to the REMS assessment plan described in our April 7, 2009 communication for Viramune® (nevirapine) Oral Suspension and Tablets.

We remind you that assessments of an approved REMS must include, 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.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you must submit a complete proposed REMS that relates only to the authorized generic product. Submit a proposed REMS, REMS supporting document, and any required appended documents as a prior approval supplement. Approval of the proposed REMS is required before you may market your authorized generic product.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 201-152 REMS ASSESSMENT

**NEW SUPPLEMENT FOR NDA 201-152
PROPOSED REMS MODIFICATION
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 201-152
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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 decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

REPORTING REQUIREMENTS

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 Amalia Himaya, Regulatory Project Manager, at (301) 796-3391 or the Division's main number at (301) 796-1500.

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:

REMS
Content of Labeling
Container 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 S MURRAY
03/25/2011