

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
201152Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 201-152

SUPPL # 000

HFD # 530

Trade Name Viramune XR extended release tablets

Generic Name nevirapine

Applicant Name Boehringer Ingelheim Pharmaceuticals Inc.

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

three years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

No

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 20636

Viramune (nevirapine) immediate release tablets

NDA# 20933

Viramune (nevirapine) suspension

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Trials 1100.1486 and 1100.1526.

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

- b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Trials 1100.1486 and 1100.1526 are the adult phase 3 trials that support labeling and were conducted to determine the safety and efficacy of the XR tablets. All trials were carried out under IND 74,744 with Boehringer Ingelheim as the sponsor.

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1
IND # 74744 YES ! NO
! Explain:

Investigation #2
IND # 74744 YES ! NO
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1
YES ! NO
Explain: ! Explain:

Investigation #2

!

YES

!

! NO

Explain:

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

Name of person completing form: Amalia Himaya

Title: Regulatory Project Manager

Date: March 7, 2011

Name of Office/Division Director signing form: Debra Birnkrant, M.D.

Title: Director, Division of Antiviral Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

AMALIA C HIMAYA
03/24/2011

JEFFREY S MURRAY
03/24/2011

DEBARMENT CERTIFICATION

Certification Requirement Section 306(k)(1) of the Act 21 U.S.C. 335a(k)

Boehringer Ingelheim Pharmaceuticals, Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.

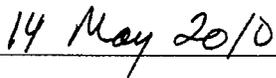
Signature:



Name of Applicant:

Christopher D. Corsico, M.D., MPH
U.S. Regional Medical Director
Boehringer Ingelheim Pharmaceuticals, Inc.

Date:



Mailing Address:

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P.O. Box 368
Ridgefield, CT 06877-0368

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 201-152 BLA #	NDA Supplement # Original BLA STN #	If NDA, Efficacy Supplement Type: n/a
Proprietary Name: Viramune XR Established/Proper Name: nevirapine Dosage Form: extended release tablets		Applicant: Boehringer Ingelheim Pharmaceuticals Inc Agent for Applicant (if applicable):
RPM: Amalia Himaya		Division: DAVP
<p>NDA: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action 3/25/11 • User Fee Goal Date is 4/2/11 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> None
<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>		<input type="checkbox"/> Received

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

❖ Application Characteristics ²	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): Type 3 (New Dosage Form)</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC </p> <p> NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies </p> <p> <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request </p> <p> BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies </p> <p> REMS: <input checked="" type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input type="checkbox"/> REMS not required </p> <p>Comments:</p>	
❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	<input type="checkbox"/> Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Press Office notified of action (by OEP)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information dissemination are anticipated	<input type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input checked="" type="checkbox"/> Other HIV-list serve

² Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	<input checked="" type="checkbox"/> Included
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) Approval- 3/25/11 Fileable/Standard Review- 7/30/10
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	3/24/11
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	6/3/10
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	

³ Fill in blanks with dates of reviews, letters, etc.
Version: 8/25/10

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>) 	<input checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	3/24/11
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	6/3/10
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent draft labeling 	2/17/11
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) 	Acceptability letter- 9/9/10 Reviews- 9/9/10 and 3/2/11
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 3/24/11 <input checked="" type="checkbox"/> DMEPA 2/3/11 and 3/2/11 <input checked="" type="checkbox"/> DRISK 2/15/11 <input checked="" type="checkbox"/> DDMAC 1/24/11 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	RPM Filing Review and Memo of Filing Meeting- 7/16/10 <input checked="" type="checkbox"/> Not a (b)(2) <input checked="" type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> 3/24/11
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm 	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>1/26/11</u> If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input checked="" type="checkbox"/> Verified, statement is acceptable
<ul style="list-style-type: none"> ❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>) 	Included

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 8/25/10

❖ Internal memoranda, telecons, etc.	n/a
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg 10/19/09
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 3/24/11
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 3/11/11
PMR/PMC Development Templates (<i>indicate total number</i>)	<input type="checkbox"/> None 1
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	
• Clinical review(s) (<i>indicate date for each review</i>)	7/23/10 (filing) and 2/27/11 (final)
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	Under Clinical review, page 15.
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	6/3/10 (REMS supporting document); 2/22/11 (REMS)
• REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)	
• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)	<input type="checkbox"/> None
• Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	Risk management review located under Labeling Review tab by DRISK on 2/15/11 pp. 2-5
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested 2/23/11 (review); 3/25/11 (letters to Drs. Santiago, Mallolas and

⁵ Filing reviews should be filed with the discipline reviews.
Version: 8/25/10

	Domingo); 2/22/11 (letter to Dr. Bogner); and 1/25/11 (letter to Dr. Ward).
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 7/27/10 (filing) and 2/24/11 (final)
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None 8/9/11 (filing) Trial 1100.1486-3/4/11 Trial 1100.1526-3/4/11
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 8/4/10 (filing) and 2/25/11 (final)
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None 9/1/10
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None requested

Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> None <u>Chemistry</u> - 7/20/10 (filing), 7/27/10 (initial quality assessment), and 2/24/11 (final) <u>Biopharmaceutics</u> - 7/15/10 (filing) and 2/25/11 (final)
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	Under Product Quality review, p. 47
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>	
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁶)</i>	Date completed: <input checked="" type="checkbox"/> Acceptable 7/13/10 (under Product Quality review, pp. 48-50) <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</i>	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁶ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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/s/

AMALIA C HIMAYA
03/28/2011

Himaya, Amalia

From: Himaya, Amalia
Sent: Wednesday, March 23, 2011 7:57 PM
To: 'maria.gigliotti@boehringer-ingelheim.com'
Subject: VXR BI Response to FDA 22MAR2011 (5).doc

Attachments: VXR BI Response to FDA 22MAR2011 (5) (2).doc

Minor edits similar to NVP IR/OS. If you agree, this will be the final label.

Please respond by 11AM tomorrow, Thursday.

Amalia



VXR BI
nse to FDA 22M.

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/s/

AMALIA C HIMAYA

03/24/2011

The email strings contain the agreed-upon final label. On 3/23/11, FDA sent the label which Boehringer Ingelheim accepted on 3/24/11.

Himaya, Amalia

From: Himaya, Amalia
Sent: Friday, March 18, 2011 12:28 PM
To: 'maria.gigliotti@boehringer-ingelheim.com'
Subject: NVP XR Label- Label#9

Attachments: Label#9_MG&PI_Mar_11.doc

Maria,

Reference is made to your submission dated 3/15/11. Attached is the label for NVP XR containing further edits.

1. The only substantive revision we propose is removal of Table 5 in subsection 14.1. In reviewing the label as a whole, we note that Table 5 "Demographic and Baseline Characteristics" is large in format for the information that it provides. We prefer including the key information in Table 5 in text format and have incorporated this information into the study description. In the interest of time, we are agreeable to negotiating this subsection via email before official submission.

2. In response to your 3/16/11 email, we agree with changing the symbol to "<" in Table 5 "Outcomes at Week 48 in Trial 1100.1486."

(b) (4)

Please respond by Monday 3/21/11.

Amalia



Label#9 MG&PI
Mar 11.doc (545)

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/s/

AMALIA C HIMAYA
03/18/2011

3. If the study/clinical trial is a **PMR**, check the applicable regulation.

If not a PMR, skip to 4.

- **Which regulation?**

- Accelerated Approval (subpart H/E)
 Animal Efficacy Rule
 Pediatric Research Equity Act
 FDAAA required safety study/clinical trial

- **If the PMR is a FDAAA safety study/clinical trial, does it: (check all that apply)**

- Assess a known serious risk related to the use of the drug?
 Assess signals of serious risk related to the use of the drug?
 Identify an unexpected serious risk when available data indicate the potential for a serious risk?

- **If the PMR is a FDAAA safety study/clinical trial, will it be conducted as:**

- Analysis of spontaneous postmarketing adverse events?
Do not select the above study/clinical trial type if: such an analysis will not be sufficient to assess or identify a serious risk
- Analysis using pharmacovigilance system?
Do not select the above study/clinical trial type if: the new pharmacovigilance system that the FDA is required to establish under section 505(k)(3) has not yet been established and is thus not sufficient to assess this known serious risk, or has been established but is nevertheless not sufficient to assess or identify a serious risk
- Study: all other investigations, such as investigations in humans that are not clinical trials as defined below (e.g., observational epidemiologic studies), animal studies, and laboratory experiments?
Do not select the above study type if: a study will not be sufficient to identify or assess a serious risk
- Clinical trial: any prospective investigation in which the sponsor or investigator determines the method of assigning investigational product or other interventions to one or more human subjects?

4. What type of study or clinical trial is required or agreed upon (describe and check type below)? If the study or trial will be performed in a subpopulation, list here.

Open-label, clinical trial to evaluate clinical pharmacology profile, safety and antiviral activity of Viramune XR (nevirapine) extended-release tablets in pediatric patients 3 to 18 years of age.
--

Required

- Observational pharmacoepidemiologic study
 Registry studies
 Primary safety study or clinical trial
 Pharmacogenetic or pharmacogenomic study or clinical trial if required to further assess safety
 Thorough Q-T clinical trial
 Nonclinical (animal) safety study (e.g., carcinogenicity, reproductive toxicology)

Continuation of Question 4

- Nonclinical study (laboratory resistance, receptor affinity, quality study related to safety)
 - Pharmacokinetic studies or clinical trials
 - Drug interaction or bioavailability studies or clinical trials
 - Dosing trials
 - Additional data or analysis required for a previously submitted or expected study/clinical trial (provide explanation)
-
- Meta-analysis or pooled analysis of previous studies/clinical trials
 - Immunogenicity as a marker of safety
 - Other (provide explanation)
-

Agreed upon:

- Quality study without a safety endpoint (e.g., manufacturing, stability)
 - Pharmacoepidemiologic study not related to safe drug use (e.g., natural history of disease, background rates of adverse events)
 - Clinical trials primarily designed to further define efficacy (e.g., in another condition, different disease severity, or subgroup) that are NOT required under Subpart H/E
 - Dose-response study or clinical trial performed for effectiveness
 - Nonclinical study, not safety-related (specify)
-
- Other
-

5. Is the PMR/PMC clear, feasible, and appropriate?

- Does the study/clinical trial meet criteria for PMRs or PMCs?
 - Are the objectives clear from the description of the PMR/PMC?
 - Has the applicant adequately justified the choice of schedule milestone dates?
 - Has the applicant had sufficient time to review the PMRs/PMCs, ask questions, determine feasibility, and contribute to the development process? n/a (PREA PMR is required and non-negotiable)
-

PMR/PMC Development Coordinator:

- This PMR has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.*

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/s/

AMALIA C HIMAYA
03/14/2011

KENDALL A MARCUS
03/14/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: March 11, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 IR Label

Reference is made to your submission dated March 8, 2011. We accepted your revisions and propose further recommendations as follows:

- minor editorial revisions
- consistency in the format of Tables 2 and 5
- In subsection 12.4, under Resistance, we corrected patients to subjects. However, please look over the entire label and make the necessary corrections between subjects and patients by using the following definition: *The use of "subjects" is preferred when referring to a participant in a clinical trial. The use of "patients" is preferred when referring to individuals being treated for their disease/condition.*

Please refer to the attached annotated label which will also be provided to you via email in word format.

If feasible, please provide your response by March 15, 2011. Please feel free to contact me at (301) 796-3391 or the Division's main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
03/11/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: March 4, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 IR Label #7 ; NDAs 20-636/S-37 and 20-933/S-2
Medication Guide and Package Inserts

Medication Guide

Reference is made to your proposed Medication Guide (MG) submitted on March 1, 2011 to the three nevirapine NDAs 201-152, 20-933/S-28, and 20636/S-37. We recommend further revisions to the MG, attached. This will also be provided to you in word format via electronic mail. Please review the entire MG and make note of all the content changes section by section.

Package Inserts

Reference is made to your electronic mail on February 25, 2011 containing your proposed labels for the extended release tablets, immediate release tablets, and oral suspension. We agree with all of your revisions *except* we propose the following wording in subsection 17.2 to reflect current thinking about effective ARV treatment and the risk of HIV transmission through sexual contact. This is consistent with language in the MG.

Inform patients that it is not known whether VIRAMUNE XR therapy reduces the risk of transmission of HIV-1 to others through sexual contact. Effective treatment combined with safer sex practices may reduce the chance of passing HIV to others through sexual contact. Patients should be advised to continue to practice safer sex and to use latex or polyurethane condoms to lower the chance of sexual contact with any body fluids such as semen, vaginal secretions or blood. Patients should be advised never to re-use or share needles.

(b) (4)



If feasible, please provide your response by March 8, 2011. Please feel free to contact me at (301) 796-3391 or the Division's main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

{see appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
03/04/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 23, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 IR Label #5

Reference is made to your February 18, 2011 submission. We accept your revisions and recommend further revisions to the package insert. Attached is FDA's revisions to the package insert which will also be provided to you in word format via electronic mail. Please review the entire package insert and make note of all the content changes section by section.

Please provide your response by February 28, 2011 and feel free to contact me at (301) 796-3391 or the Division's main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
02/23/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 23, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
Narayan Rao, Senior Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 IR Label #6 ; NDAs 20-636/S-37 and 20-933/S-28

Reference is made to your proposed Medication Guide submitted on January 28, 2011 to NDA 201-152 and February 1, 2011 to NDAs 20933/S-28 and 20636/S-37. In consultation with FDA's Division of Risk Management (DRISK), attached is our revisions to the MG which will also be provided to you in word format via electronic mail. Please review the entire MG and make note of all the content changes section by section.

If feasible, please provide your response by February 28, 2011 via email followed by an official submission. Please feel free to contact me at (301) 796-3391 or the Division's main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

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Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
02/23/2011

Himaya, Amalia

From: maria.gigliotti@boehringer-ingelheim.com
Sent: Wednesday, February 16, 2011 11:26 AM
To: Himaya, Amalia
Subject: RE: NVP XR Peds submission

(b) (4)

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Reference ID: 2907838

2/18/2011

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/s/

AMALIA C HIMAYA
02/18/2011



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 16, 2011

TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
Narayan Rao, Senior Associate Director, Drug Regulatory Affairs

SPONSOR: Boehringer Ingelheim Pharmaceuticals, Inc.

SUBJECT: NDA 201-152 Request #R7, NDAs 20-636/S-37 and 20-933/S-28

Reference is made to your REMS amendment submitted on January 28, 2011 to NDA 201-152. Reference is also made to your REMS modification submitted on February 1, 2011 to NDAs 20933/S-28 and 20636/S-37. We have the following comments on your proposed REMS modification:

See the appended Viramune (nevirapine) REMS proposal for FDA's tracked changes.

REMS dates:

1. 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

REMS ELEMENTS:

2. In Medication Guide section, the details of the distribution of the Medication Guide is more appropriate for the REMS Supporting Document.
3. In Timetable for Submission of Assessments section, 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 should include a short status update of your assessment.

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.

Prominently identify the submission containing the REMS assessments with the following wording in bold capital letters at the top of the first page of the submission as appropriate: **NDA 20636 or NDA 20933 or NDA 201152 REMS ASSESSMENT.**

Please provide your response to above NDAs by February 22, 2011 and feel free to contact me at (301) 796-3391 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
02/16/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 10, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 IR Label #4 and Response to ex-US waiver request

I. Foreign Clinical Studies not conducted under an IND

Upon review of your October 5, 2010 and January 31, 2011 submissions, we are waiving the applicable requirements under 21 CFR 312.120 (b) that may not have been met. These apply to submitted data from foreign clinical studies not conducted under an IND as support for NVP XR.

II. Package Insert

Reference is made to your January 28, 2011 and February 7, 2011 submissions. We recommend further revisions to the package insert. The package insert will also be provided to you in word format via electronic mail. Please review the entire package insert and make note of all the content changes section by section. A few notables:

A. In Section 12.4, Microbiology, we consider patient # 10238 as a virologic failure based on the genotypic resistance and viral load data. Therefore, we are retaining “23” as the total value of virological failures. Also, we further revised *Resistance* subsection to include all virological failure subjects who developed NVP resistance during therapy.

B. We further revised Table 6, Outcomes at Week 48 in Study 1100.1486, based on the snapshot algorithm and the DAVP’s updated format for the study outcome table. In addition, we revised the change from baseline in CD4+ cell count using the same time window for the snapshot at Week 48 (Week 44 to Week 52) and recalculated the corresponding values using SAS Proc Mixed. The results with the LOCF for missing CD4+ after Day 29 (Week 4) will be reported. Hence, the sentence below Table 6 was revised accordingly.

C. As agreed during our February 8, 2011 teleconference, [REDACTED] (b) (4)

Please provide your response by February 18, 2011. Please feel free to contact me at (301) 796-3391 or the Division’s main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
02/10/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 4, 2011

TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs

SPONSOR: Boehringer Ingelheim Pharmaceuticals, Inc.

SUBJECT: NDA 201-152 Request #R6, container label

In consultation with FDA's Division of Medication Error Prevention and Analysis (DMEPA), we have the following comments on your container label:

Container Labels (30 count) Trade/Sample

1. The entire established name is '(Nevirapine) Extended-release Tablets'. As currently presented 'Extended-release Tablets' has a greater prominence due to the font size. Modify the presentation of the established name so that '(nevirapine)' and 'Extended-release Tablets' have equal prominence. Additionally, ensure that the established name is at least 1/2 the size of the proprietary name and the established name shall have a prominence commensurate with the prominence with which such proprietary name appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features per 21 CFR 201.10(g)(2).
2. Delete the (b) (4) located on the principal display panel. (b) (4)
3. Per 21 CFR 208.24, modify the medication guide statement, (b) (4) to include how the medication guide is provided. For example, the statement could read "Pharmacist: Dispense with attached Medication Guide to each patient" (b) (4). Change the font to a color that increases the contrast with the white background.
4. Minimize the prominence of the company name 'Boehringer Ingelheim' and accompanying graphic. As currently presented it distracts from more important information on the principal display panel.
5. Increase the prominence of the product code segment (0597-0123-30) of the NDC number located at the top of the principal display panel. Additionally, decrease the prominence of the net quantity statement.

6. De-bold and minimize the “Rx Only” statement on the principal display panel.

Please provide your response by **February 17, 2011**. Please feel free to contact me at (301) 796-3391 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
02/04/2011



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 3, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim Pharmaceuticals, Inc.
SUBJECT: NDA 201-152 Request #R5

Reference is made to your submission dated January 28, 2011. We have the following comment on your request for clarification in Section 12 of the package insert:

BIPI: Based on the definition of virologic failure provided in the resistance report, the number of virologic failures that BI was able to include from Trial 1100.1486 is (b) (4) in the XR group and (b) (4) in the IR group. As the numbers mentioned in the proposed label do not match (57 vs (b) (4)), could the FDA provide the algorithm used to define virologic failure and the list of patients which are considered as VF? We would like to confirm the results cited in the newly proposed wording.

FDA response: (b) (4)

(b) (4)

If feasible, please provide your response with the information request we sent you yesterday, February 2, 2011. Please feel free to contact me at (301) 796-3391 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products

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/s/

AMALIA C HIMAYA
02/03/2011



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: February 2, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim Pharmaceuticals, Inc.
SUBJECT: NDA 201-152 Request #R4

Reference is made to your submission dated January 28, 2011. We have the following comment:

[Redacted content] (b) (4)

If feasible, please provide your response via email by this Friday, February 4, 2011 but no later than February 8, 2011. Official submission to the application can follow. Please feel free to contact me at (301) 796-3391 if you have any questions regarding the contents of this transmission.

{see appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

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/s/

AMALIA C HIMAYA
02/02/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: January 21, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 IR Label #3

Reference is made to your January 6, 2011 submission containing your proposed labeling for NVP XR. Reference is also made to the FDA information request sent to you on January 12, 2011. Attached is FDA's further revisions to the package insert also incorporating FDA's proposed revision dated January 12, 2011. The package insert will also be provided to you in word format via electronic mail. Please review the entire package insert and make note of all the content changes section by section.

Please provide your response by January 28, 2010. Please feel free to contact me at (301) 796-3391 or the Division's main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

enclosure:
FDA's revision to the package insert

17 Pages of Draft Labeling have been Withheld in Full as
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/s/

AMALIA C HIMAYA
01/21/2011



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: January 18, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim Pharmaceuticals, Inc.
SUBJECT: NDA 201-152 Request #R3

Reference is made to your submissions dated June 3, 2010 and October 5, 2010 containing your request for a waiver for foreign clinical studies and your rationale for including the non-US data in the evaluation of NVP XR, respectively. We have an additional comment:

[Redacted content] (b) (4)

Please provide your response by **January 31, 2011** and feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

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/s/

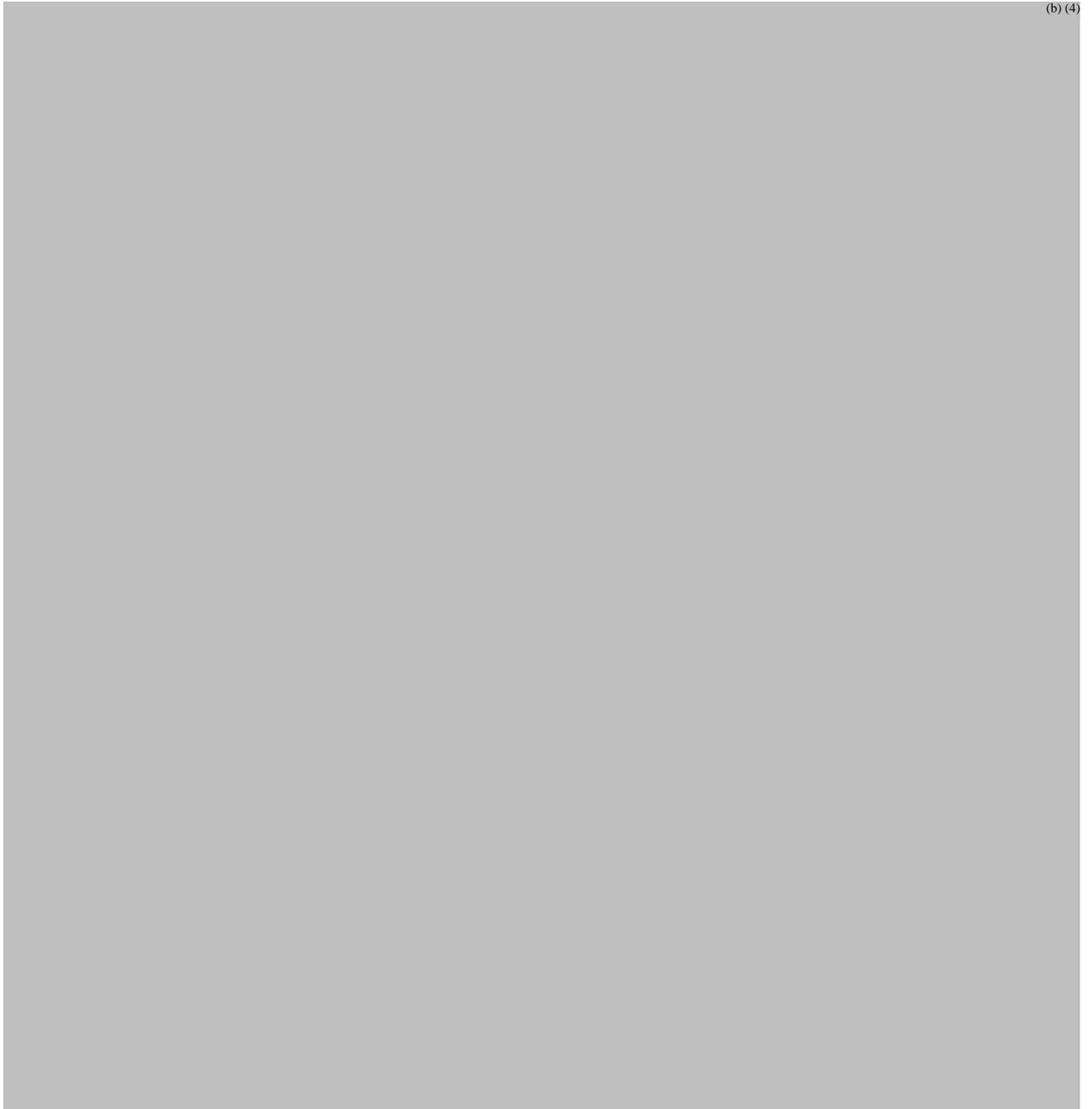
AMALIA C HIMAYA
01/18/2011

Himaya, Amalia

From: Himaya, Amalia
Sent: Wednesday, January 12, 2011 3:05 PM
To: 'maria.gigliotti@boehringer-ingelheim.com'
Subject: RE: NVP XR Peds submission

Thank you for the response.

Amalia



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/s/

AMALIA C HIMAYA
01/12/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: January 12, 2011
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 (NVP XR) IR Label #2

Reference is made to your January 6, 2011 submission containing your proposed labeling in response to our December 22, 2010 proposed revisions to the package insert. We have the following comments:

1. We agree with all of your proposed revisions except we do not agree with your proposal to (b) (4)

[Redacted content]

2. We propose revisions to subsection 12.3, Pharmacokinetics, under Absorption and Bioavailability. (b) (4)

[Redacted content]

[Redacted content]

[The single-dose pharmacokinetics of VIRAMUNE XR was studied in 17 healthy volunteers. Nevirapine was absorbed with a median \$t_{max}\$ of approximately 24 hrs. The mean \$C_{max}\$ and \$AUC_{0-\infty}\$ of nevirapine were 2060 ng/mL and 161000 ng*hr/mL, respectively. The](#)

bioavailability of 400 mg NVP XR, relative to 400 mg VIRAMUNE IR, was approximately 75%.

The multiple-dose pharmacokinetics of VIRAMUNE XR was studied in 24 HIV-1 infected patients who switched from chronic VIRAMUNE IR to VIRAMUNE XR. The mean nevirapine $AUC_{0-24,ss}$ and $C_{min,ss}$ after 19 days of VIRAMUNE XR dosing under fasted conditions were 82000 ng*hr/mL and 2920 ng/mL, respectively. When VIRAMUNE XR was administered under fed conditions, the mean nevirapine $AUC_{0-24,ss}$ and $C_{min,ss}$ were 96700 ng*hr/mL and 3150 ng/mL, respectively. The bioavailability of 400 mg NVP XR, relative to 400 mg VIRAMUNE IR, under fasted and fed conditions, was 80 % and 94 %, respectively. The difference in the bioavailability of nevirapine, when VIRAMUNE XR is dosed under fasted or fed conditions, is not considered clinically relevant. VIRAMUNE XR can be taken with or without food.

(b) (4)



We anticipate additional labeling comments will be provided to you next week. Please feel free to contact me at (301) 796-3391 or the Division's main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

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/s/

AMALIA C HIMAYA
01/12/2011

Himaya, Amalia

From: Himaya, Amalia
Sent: Monday, January 10, 2011 9:43 AM
To: 'maria.gigliotti@boehringer-ingelheim.com'; 'narayan.rao@boehringer-ingelheim.com'
Cc: 'pam.strode@boehringer-ingelheim.com'
Subject: NVP formulations (NDAs 20933, 20636, & 201152): combined MG and REMS

Maria and Narayan, please find below the information that should be submitted to the IR/suspension and XR formulations.

Maria, for NVP XR (NDA 201152) I anticipate sending you additional labeling comments for the package insert no later than middle of next week with a requested response from you by January 28. Please submit the modified REMS and updated MG sooner than this date, if feasible, to give DRISK a headstart on review.

Please note the REMS supporting document is not required to be submitted until 90 days before the next assessment is due. A reminder to submit this by 3/24/11 for the 3-year assessment.

	NVP IR Tablet and Suspension	NVP XR
Submission Type	Submit as new PAS supplements with REMS modification (NDA 20636 and NDA 20933)	Submit as REMS Modification and Labeling Amendment to NDA 201152
REMS	Include the following in your submission: 1. Modified REMS to include NVP XR 2. <u>REMS Assessment Statement</u> There should only be one version of REMS for all 3 formulations.	Include the following in your submission: 1. Modified REMS to include IR tablet and suspension There should only be one version of REMS for all 3 formulations.
MG	1. As per your 12/19/10 email, (b) (4) to be consistent with proposed language in USPI. 2. Update MG to include NVP XR information. There should only be one version of MG for all 3 formulations.	1. As per your 12/19/10 email, (b) (4) to be consistent with proposed language in USPI. 2. Update MG to incorporate the most recent January 2011 MG approval of NVP IR tablet and suspension. There should only be one version of MG for all 3 formulations.
Word Document (REMS and MG)	1. Each time you submit a modified REMS document, include a word file in the submission in addition to the pdf file. 2. MG and any revisions thereafter should be provided in PDF and word file.	1. Each time you submit a modified REMS document, include a word file in the submission in addition to the pdf file. 2. MG and any revisions thereafter should be provided in PDF and word file.

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/s/

AMALIA C HIMAYA
01/10/2011



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: December 22, 2010
TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs
SPONSOR: Boehringer Ingelheim
SUBJECT: NDA 201-152 IR Label #1

Reference is made to your June 3, 2010 submission to NDA 201-152 containing your proposed labeling for NVP XR. Attached is FDA's revisions to the package insert which will also be provided to you in word format via electronic mail. Please review the entire package insert and make note of all the content changes section by section. Medication Guide comments and revisions will be provided at a later time.

Please provide your response by January 6, 2010. Please feel free to contact me at (301) 796-3391 or the Division's main number at (301) 796-1500 if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

enclosure:
FDA's revision to the package insert

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/s/

AMALIA C HIMAYA
12/22/2010



NDA 201,152

INFORMATION REQUEST

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

Dear Ms. Gigliotti:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nevirapine Extended Release Tablet, 400 mg.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. No information was provided for developing the prototype Formulation as reported in Table 5, page 21, Document No. U10-3066-01. Please provide information on the development of the prototype formulation, i.e. rationale for selection of the excipients and the % concentration.
2. [REDACTED] (b) (4)
3. Data was provided [REDACTED] (b) (4)
4. The manufacturing flow diagram [REDACTED] (b) (4)
5. The optimum process parameters reported in the submission were [REDACTED] (b) (4)
6. Provide updated stability data as per agreement reached at the Pre-NDA telecon.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Khushboo Sharma, Regulatory Project Manager in the Office of New Drug Quality Assessment (Khushboo.Sharma@fda.hhs.gov), and Amalia Himaya, Regulatory Project Manager the Office of New Drugs (Amalia.Himaya@fda.hhs.gov).

If you have any questions please call Khushboo Sharma, Regulatory Project Manager, at (301) 796-1270.

Sincerely,

{See appended electronic signature page}

Stephen P. Miller, Ph.D.
Acting Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

RAPTI D MADURAWA
11/10/2010
(for Stepehn Miller, secondary reviewer)

Himaya, Amalia

From: Himaya, Amalia
Sent: Monday, October 25, 2010 12:29 PM
To: 'maria.gigliotti@boehringer-ingelheim.com'
Subject: FW: NDA 201-152 NVP XR R2_JMP_clinical.pdf - Adobe Acrobat Professional

Maria, our response is in red font below.

Thanks,
Amalia

From: maria.gigliotti@boehringer-ingelheim.com [mailto:maria.gigliotti@boehringer-ingelheim.com]
Sent: Thursday, October 21, 2010 11:52 AM
To: Himaya, Amalia
Subject: RE: NDA 201-152 NVP XR R2 JMP clinical.pdf - Adobe Acrobat Professional

Dear Amalia,

Reference is made to your e-mail request dated 10/20/10 for NDA 201-152 (attached). I have met with the team and we would like clarification of a few points to ensure that we adequately address the request and meet the reviewer's needs.

Question 1: Please clarify whether the requested CDISC datasets (ADSL, AE, CM, DM, DS, LB, MH, and VS) should be filed as a sequence to the eCTD NDA (or whether these datasets should be provided on a CD separate from the eCTD).

It would be fine to submit these as a sequence to the eCTD NDA

Question 2: If we are filing the requested datasets to the eCTD NDA, we would like clarification about the folders in which these datasets should reside. Per the CDISC Minimal Data Requirements for JMP Clinical, it is noted that the ADSL dataset should reside in the "ADaM" folder and the datasets AE, CM, DM, DS, LB, MH, and VS should reside in the "SDTM" folder. We note that in our eCTD NDA structure, we currently have an "analysis" and a "tabulations" folder within each study. Within our eCTD tool, it is not possible to create additional folders such as the folders mentioned above "ADaM" and "SDTM". Therefore, we would propose to include the requested ADSL dataset in the "analysis" folder within the respective trial and the AE, CM, DM, DS, LB, MH, and VS datasets in the "tabulations" folder within the respective trial. These datasets would be submitted as a sequence which would append these datasets to the eCTD NDA. Please advise on whether this is acceptable.

It will be fine to submit them using the prior structure and to submit ADSL in the "analysis folder" and the SDTM files in the "tabulation" folder.

Question 3: BI proposes to create the requested datasets for studies 1100-1486 and 1100-1526. Please advise if this is acceptable.

Yes, this is fine, since these are the pivotal trials.

ADDITIONAL ISSUE:

There is an outstanding data problem that has been noted for the original data submission. For the original Study 1486 submission, analysis files ADAMEFF and SNAPSHOT use a different USUBJID than

the other datasets. This prevents the data from being machine readable for the purposes of analysis across the datasets. In the ADAMEFF and SNAPSHOT datasets, the USUBJID has removed the "0" that exists in the other datasets prior to the patient id portion of the USUBJID. Please re-submit these datasets with a corrected USUBJID variable. This same problem exists for the ADAMEFF file for study 1526 as well and should be corrected.

Thank you in advance.

Maria

Maria Gigliotti, MS

Associate Director, Drug Regulatory Affairs

Boehringer Ingelheim Pharmaceuticals, Inc.

Phone: 203 798 5609

Mobile: (b) (6)

Fax: 203 778 7880

maria.gigliotti@boehringer-ingelheim.com

From: Himaya, Amalia [mailto:Amalia.Himaya@fda.hhs.gov]

Sent: Wednesday, October 20, 2010 4:22 PM

To: Gigliotti, Maria DRA BIP-US-R

Subject: NDA 201-152 NVP XR R2 JMP clinical.pdf - Adobe Acrobat Professional

Maria, please confirm receipt. I also just received your email re: IND 74744.

Amalia

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/s/

AMALIA C HIMAYA
10/26/2010



NDA 201,152

INFORMATION REQUEST

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

Dear Ms. Gigliotti:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nevirapine Extended Release Tablet, 400 mg.

We are reviewing the Biopharmaceutics section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Submit all the input and output files generated during the application of your proposed IVIVC model in setting the proposed dissolution specifications.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Khushboo Sharma, Regulatory Project Manager in the Office of New Drug Quality Assessment (Khushboo.Sharma@fda.hhs.gov), and Amalia Himaya, Regulatory Project Manager the Office of New Drugs (Amalia.Himaya@fda.hhs.gov).

If you have any questions please call Khushboo Sharma, Regulatory Project Manager, at (301) 796-1270.

Sincerely,

{See appended electronic signature page}

Stephen P. Miller, Ph.D.
Acting Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

STEPHEN P MILLER
10/25/2010



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: October 20, 2010

TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs

SPONSOR: Boehringer Ingelheim Pharmaceuticals, Inc.

SUBJECT: NDA 201-152 Request #R2

The review team is interested in evaluating a new review tool, JMP Clinical, for this application. In order to do so, we are requesting the CDISC minimal data requirements in the attachment.

Please provide your response by **October 29, 2010** and feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Attachment (CDISC Minimal Data Requirements JMP Clinical)

CDISC Minimal Data Requirements for JMP Clinical

Rules and conventions of CDISC apply (such as ISO 8601 date format).

Folder	Data Set	Variable	Type	Label	Notes
ADaM	ADSL	AGE	N	Age	
ADaM	ADSL	AGEGR1	C	Age Group 1	
ADaM	ADSL	ARM	C	Description of Planned Arm	On y one of ARM, TRT01A, or TRT01P s requ red
ADaM	ADSL	DEATHDSC	C	Death Descrip on	Nonstandard, used on y n Morta ty Cause Comparison
ADaM	ADSL	RACE	C	Race	
ADaM	ADSL	SEX	C	Sex	
ADaM	ADSL	STUDYID	C	Study Ident fier	Must be coded cons stent y across data sets
ADaM	ADSL	TRTEDT	N	Date of Last Exposure to Treatment	E ther TRTEDT or TRTEDTM s requ red
ADaM	ADSL	TRTEDTM	N	Date of Last Exposure to Treatment	E ther TRTEDT or TRTEDTM s requ red
ADaM	ADSL	TRTSDT	N	Date of First Exposure to Treatment	E ther TRTSDT or TRTSDTM s requ red
ADaM	ADSL	TRTSDTM	N	Date of First Exposure to Treatment	E ther TRTSDT or TRTSDTM s requ red
ADaM	ADSL	TRT01A	C	Actual Treatment for Period 01	On y one of ARM, TRT01A, or TRT01P s requ red
ADaM	ADSL	TRT01P	C	Planned Treatment for Period 01	On y one of ARM, TRT01A, or TRT01P s requ red
ADaM	ADSL	USUBJID	C	Unique Subject Identifier Body System or Organ Class	Must be coded cons stent y across data sets
SDTM	AE	AEBODSYS	C	Body System or Organ Class	
SDTM	AE	AEDECOD	C	Dictionary-Derived Term	
SDTM	AE	AEENDY	N	Study Day of End of Adverse Event	
SDTM	AE	AEREL	C	Causa ty	
SDTM	AE	AESEV	C	Severity/Intensity	E ther AESEV or AETOXGR s requ red; va ues must be M d, Moderate, Severe, L fe Threatening, or Death
SDTM	AE	AESTDY	N	Study Day of Start of Adverse Event	
SDTM	AE	AETOXGR	C	Toxicology Grade	E ther AESEV or AETOXGR s requ red; va ues must be M d, Moderate, Severe, L fe Threatening, or Death
SDTM	AE	STUDYID	C	Study Identifier	Must be coded cons stent y across data sets
SDTM	AE	USUBJID	C	Unique Subject Identifier Standardized Medication Name	Must be coded cons stent y across data sets
SDTM	CM	CMDECOD	C	Standardized Medication Name	
SDTM	CM	CMENDY	C	Study Day of End of Medication	
SDTM	CM	CMSTDY	C	Study Day of Start of Medication	
SDTM	CM	STUDYID	C	Study Identifier	Must be coded cons stent y across data sets
SDTM	CM	USUBJID	C	Unique Subject Identifier	Must be coded cons stent y across data sets

SDTM	DM	AGE	N	Age	
SDTM	DM	ARM	C	Description of Planned Arm	
SDTM	DM	RACE	C	Race	
SDTM	DM	RFENDTC	C	Subject Reference End Date/Time	
SDTM	DM	RFSTDTTC	C	Subject Reference Start Date/Time	
SDTM	DM	SEX	C	Sex	
SDTM	DM	STUDYID	C	Study Identifier	Must be coded consistently across data sets
SDTM	DM	USUBJID	C	Unique Subject Identifier Category for Disposition Event	Must be coded consistently across data sets
SDTM	DS	DSCAT	C	Standardized Disposition Term	
SDTM	DS	DSDECOD	C		
SDTM	DS	STUDYID	C	Study Identifier	Must be coded consistently across data sets
SDTM	DS	USUBJID	C	Unique Subject Identifier Study Day of Specimen Collection	Must be coded consistently across data sets
SDTM	LB	LBDY	N		
SDTM	LB	LBSTNRHI	N	Reference Range Upper Limit-Std Units	
SDTM	LB	LBSTNRLO	N	Reference Range Lower Limit-Std Units	
SDTM	LB	LBSTRESN	N	Numeric Result/Finding Standard Units Lab Test or Examination Name	
SDTM	LB	LBTEST	C	Study Identifier	Must be coded consistently across data sets
SDTM	LB	USUBJID	C	Unique Subject Identifier Body System or Organ Class	Must be coded consistently across data sets
SDTM	MH	MHBODSYS	C		
SDTM	MH	MHDECOD	C	Dictionary-Derived Term	
SDTM	MH	STUDYID	C	Study Identifier	Must be coded consistently across data sets
SDTM	MH	USUBJID	C	Unique Subject Identifier	Must be coded consistently across data sets
SDTM	VS	STUDYID	C	Study Identifier	Must be coded consistently across data sets
SDTM	VS	USUBJID	C	Unique Subject Identifier Study Day of Visit Signs	Must be coded consistently across data sets
SDTM	VS	VSDY	N		
SDTM	VS	VSSTRESN	N	Numeric Result/Finding Standard Units	
SDTM	VS	VSTEST	C	Visit Signs Test Name	

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/s/

AMALIA C HIMAYA
10/20/2010



NDA 201,152

INFORMATION REQUEST

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

Dear Ms. Gigliotti:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nevirapine Extended Release Tablet, 400 mg.

We are reviewing the Biopharmaceutics sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Please provide your response by October 6, 2010.

1. You have provided information on the in vitro alcohol interaction study for Nevirapine extended release (ER) tablets using the proposed QC method. However, in order to rule out a possible dose-dumping (DD) effect in the presence of alcohol in the acidic environment of the stomach, we recommend that you conduct an additional drug-alcohol interaction study in 0.1 N HCl with the following alcohol concentrations; 0 %, 5 %, 10 %, 20 %, and 40 % as the dissolution media. Dissolution testing should be conducted using the same apparatus and paddle speed as the QC method. Dissolution data should be generated from 12 dosage units (n 12) at multiple time points to obtain a complete dissolution profile.

Please include the following information as part of your study report:

- The comparison dissolution profile data to determine if the modified release characteristics are maintained, especially in the first 2 hours.
 - The similarity f2 values to assess the similarity (or lack thereof) in the dissolution profiles.
2. For your proposed QC method, submit the dissolution method report including the complete dissolution profile data (individual, mean, SD, profiles) collected during the development and validation of the proposed dissolution method.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug

Quality Assessment (Jeannie.David@fda.hhs.gov), and Amalia Himaya, Regulatory Project Manager the Office of New Drugs (Amalia.Himaya@fda.hhs.gov).

If you have any questions regarding this letter, call Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Stephen P. Miller, Ph.D.
Acting Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

STEPHEN P MILLER
09/24/2010



NDA 201152

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Boehringer Ingelheim Pharmaceuticals, Inc
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877

ATTENTION: Maria Gigliotti, MS
Associate Director, Drug Regulatory Affairs

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 for Nevirapine Extended-release Tablets, 400 mg.

We also refer to your June 11, 2010, correspondence, received June 11, 2010, requesting review of your proposed proprietary name, Viramune XR. We have completed our review of the proposed proprietary name, Viramune XR and have concluded that it is acceptable.

The proposed proprietary name, Viramune XR, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your June 11, 2010, submission is altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Twanda Scales, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5056. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Amalia Himaya, at (301) 796-3391.

Sincerely,

{See appended electronic signature page}

Denise P. Toyer, PharmD
Deputy Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-201152

ORIG-1

BOEHRINGER
INGELHEIM
PHARMACEUTICA
LS INC

Nevirapine Extended Release
Tablets

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/s/

DENISE P TOYER
09/09/2010



NDA 201-152

FILING COMMUNICATION

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, for Viramune® XR™ (nevirapine) extended-release tablets, 400 mg.

We also refer to your submissions dated June 24, 2010 and June 30, 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is April 3, 2011.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by March 6, 2011.

During our filing review of your application, we identified the following potential review issue:

Chemistry- Biopharmaceutics

It is noted that only two formulations used in the construction of the proposed *In Vitro/In Vivo* Correlation (IVIVC) meet the requirements of showing at least a (b)(4) difference in both, the *in vitro* and *in vivo* performance. Specifically, we find that the dissolution

profiles for K25 vs. K30 and for K30 vs. K40 were similar (f_2 values were 53 and 59, respectively). Therefore, you will need to conduct an external predictability analysis of the model in order for you to implement your proposed IVIVC. Otherwise, your proposed IVIVC will only be limited to Category 2a applications (refer to Guidance for Industry - Extended Release Oral Dosage Forms: Development, Evaluation and Application of *In Vitro/In Vivo* Correlation). **Please note this comment supercedes the earlier version sent to you on July 22, 2010. Please provide your response by August 11, 2010.**

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

We also request that you submit the following information:

Clinical

1. For your pediatric plan, please provide a timeline for the submission of the protocol, study completion date, and final study report submission date.
2. Please submit a rationale for assuming the applicability of foreign data in the submission to the U.S. population.

Statistics

3. Please submit the SAS programs used to generate tables and figures in your clinical study report for Studies 1100-1486 and 1100-1526 to facilitate the regulatory review process. Please also submit a 'define.pdf' to describe the SAS programs in the submission.

Virology

4. Please provide the resistance data for Study U10-3152-01 in accordance to the "Guidance for Submitting HIV Resistance Data" available on the following link: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070955.pdf>.

Chemistry- Biopharmaceutics

5. Please submit the complete dissolution profile data (raw data and mean values) from the clinical and primary stability batches supporting the selection of the dissolution acceptance criteria (i.e., specification-sampling time points and specification values) for Nevirapine Extended Release (ER) Tablets, 400 mg. **Please provide your response by August 11, 2010.**

6. Please submit complete dissolution profile data (raw data and mean values) for the *in vitro* effect of alcohol on the dissolution profile of Nevirapine ER Tablets or indicate where this information is located in the submission received on June 3, 2010. **Please provide your response by August 11, 2010.**

If you have not already done so, you must submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

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 acknowledge receipt of your request for a partial waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial waiver request is denied.

We acknowledge receipt of your request for a partial deferral of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial deferral request is denied.

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

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-201152

ORIG-1

BOEHRINGER
INGELHEIM
PHARMACEUTICA
LS INC

Nevirapine Extended Release
Tablets

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/s/

JEFFREY S MURRAY
07/30/2010



NDA 201,152

INFORMATION REQUEST

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

Dear Ms. Gigliotti:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nevirapine Extended Release Tablet, 400 mg.

We are reviewing the Biopharmaceutics and Chemistry, Manufacturing and Controls sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA. Please provide your response by August 11, 2010.

1. Submit the complete dissolution profile data (raw data and mean values) from the clinical and primary stability batches supporting the selection of the dissolution acceptance criteria (i.e., specification-sampling time points and specification values) for Nevirapine Extended Release (ER) Tablets, 400 mg.
2. Submit complete dissolution profile data (raw data and mean values) for the *in vitro* effect of alcohol on the dissolution profile of Nevirapine ER Tablets or indicate where this information is located in the submission received on June 3, 2010.
3. It is noted that only two formulations used in the construction of the proposed IVIVC meet the requirements of showing at least a ^{(b) (4)} difference between the *in vitro* and *in vivo* performance. We find that comparison of the dissolution profiles for K25 vs. K30 and for K30 vs. K40 generated f2 values higher than 50 (53 and 59, respectively). Therefore, you will need to conduct an external predictability study of the model in order for you to implement your proposed IVIVC. Otherwise, your proposed IVIVC will only be limited to Category 2a applications (refer to Guidance for Industry - Extended Release Oral Dosage Forms: Development, Evaluation and Application of *In Vitro/In Vivo* Correlation).

These comments will be re-iterated in the filing communication letter.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Amalia Himaya, Regulatory Project Manager the Office of New Drugs (Amalia.Himaya@fda.hhs.gov).

If you have any questions regarding this letter, call Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Stephen P. Miller, Ph.D.
Acting Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-201152

ORIG-1

BOEHRINGER
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Nevirapine Extended Release
Tablets

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/s/

STEPHEN P MILLER
07/22/2010



MEMORANDUM OF ELECTRONIC MAIL CORRESPONDENCE

DATE: June 17, 2010

TO: Maria Gigliotti, M.S., Associate Director, Drug Regulatory Affairs

SPONSOR: Boehringer Ingelheim Pharmaceuticals, Inc.

SUBJECT: NDA 201-152 Request #R1

Reference is made to your June 3, 2010 submission. We have reviewed the Study 1486 protocol, BYSITE define file, and BYSITE dataset.

Based on our review, it appears that the primary endpoint data included in the dataset may be incorrect as ENDPOINT is defined as "Sustained virologic response at Week 24 using the LLOQ 50 copies/mL and TLOVR algorithm" rather than at Week 48 (as would be expected based on our review of the protocol and the BYSITE define file) in the dataset itself. In addition, data is missing for a significant percentage of sites for the TRTEFFR, TRTEFFV, SITEEFFE, and SETEEFFV variables. Please provide a revised BYSITE dataset, which addresses these issues, to facilitate DSI's review.

Please provide your response by **June 24, 2010** and feel free to contact me at (301) 796-3391, if you have any questions regarding the contents of this transmission.

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-201152

ORIG-1

BOEHRINGER
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PHARMACEUTICA
LS INC

Nevirapine Extended Release
Tablets

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/s/

AMALIA C HIMAYA
06/17/2010

David, Jeannie C

From: David, Jeannie C
Sent: Tuesday, June 15, 2010 5:10 PM
To: 'mark.debellis@boehringer-ingelheim.com'
Cc: maria.gigliotti@boehringer-ingelheim.com; Himaya, Amalia
Subject: RE: FDA Request for Clarification - NDA 201-152

Hi Mark,

Thank you for providing the additional clarification by phone just now. We will look forward to your amendment by the end of this month to specify what "testing" functions occur at the drug substance manufacturing, drug product manufacturing, and drug product contract testing sites. Also, per your earlier communication below, please clearly state that BIPI is withdrawing the (b) (4) site, in addition to adding the (b) (4) site.

As mentioned, I am the Project Manager in support of the CMC review. Please continue to cc: Amalia Himaya, Division of Anti-Viral Products, in your communications with me.

Best regards,

Jeannie

Jeannie David, M.S.
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drug Quality Assessment
10903 New Hampshire Avenue
Building 22, Mail Room 1491
Silver Spring, MD 20993
Phone: (301) 796-4247
Fax: (301) 796-9877

jeannie.david@fda.hhs.gov

From: mark.debellis@boehringer-ingelheim.com [mailto:mark.debellis@boehringer-ingelheim.com]
Sent: Tuesday, June 15, 2010 4:30 PM
To: David, Jeannie C
Cc: maria.gigliotti@boehringer-ingelheim.com; Himaya, Amalia; mark.debellis@boehringer-ingelheim.com
Subject: FDA Request for Clarification - NDA 201-152
Importance: High

Dear Jeannie,

My name is Mark DeBellis and I am handling the CMC aspects of the Nevirapine extended-release tablet NDA 201-152. Reference is made to a phone call held with yourself and Maria Gigliotti on June 14, 2010 regarding your request for clarification concerning the two Roxane sites listed in the Establishment Information of NDA 201-152.

With regard to the two Roxane sites listed in both 3.2.P.3.1 and Establishment Information, both sites are proposed to perform routine drug product testing, including stability testing.

6/15/2010

In addition, subsequent to the NDA submission BIPI was informed that the proposed excipients testing site cited in both 3.2.P.3.1 and Establishment Information, (b) (4), is no longer in business.

The following contract laboratory has been identified as the site which will perform testing of excipients:

(b) (4)

The (b) (4) site was last inspected by FDA from 8/12/2009 to 8/14/2009. No Form 483 was issued.

BIPI intends to amend the NDA with updated Establishment Information and a revised Drug Product Manufacturer document (3.2.P.3.1) by June 30, 2010. Please let me know if you concur with the approach/timeline to amend the NDA as described. My contact information is described below.

Thanks in advance.

Best regards,
Mark

Mark J. DeBellis
Manager, CMC Regulatory Affairs
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
Ridgefield, CT 06877 0368
203 791 6056 (Office)
203 791 6262 (Fax)
mark.debellis@boehringer ingelheim.com

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-201152

ORIG-1

BOEHRINGER
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LS INC

Nevirapine Extended Release
Tablets

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/s/

JEANNIE C DAVID
06/15/2010



NDA 201-152

NDA ACKNOWLEDGMENT

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:

We have received your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Viramune[®] XR[™] (nevirapine) extended-release tablets, 400 mg

Date of Application: June 3, 2010

Date of Receipt: June 3, 2010

Our Reference Number: NDA 201-152

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on August 2, 2010 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>

If you have any questions, call me at (301) 796-3391 or the Division's main number at (301) 796-1500.

Sincerely,

{See appended electronic signature page}

Amalia Himaya
Regulatory Project Manager
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application
Type/Number

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AMALIA C HIMAYA
06/09/2010