



NDA 020628/S-041
NDA 021785/S-017

SUPPLEMENT APPROVAL

Hoffmann-La Roche, Inc.
c/o Genentech, Inc.
Attention: Elizabeth Wishart
Regulatory Agent on behalf of Roche
1 DNA Way
South San Francisco, CA 94080

Dear Ms. Wishart,

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received on August 12, 2014, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for INVIRASE® (saquinavir mesylate), 200 mg capsules and 500 mg tablets.

We acknowledge receipt of your amendments dated August 26, 2015, which constituted a complete response to our June 16, 2015, action letter.

These “Prior Approval” labeling supplements proposed the following changes to the Package Insert (PI) for INVIRASE® capsules (NDA 20628) and INVIRASE® tablets (NDA 21785):

- **DOSAGE AND ADMINISTRATION:** Addition of a lower starting dose specific to treatment-naïve patients initiating treatment with INVIRASE® in combination with ritonavir. Updated recommendations for patients switching immediately (no washout period) from treatment with another ritonavir containing regimen, NNRTI or delavirdine or rilpivirine containing regimens
- **WARNINGS AND PRECAUTIONS:** Language added related to ECG monitoring and management of QT interval increases
- **DRUG INTERACTIONS:** Language revised as related to drug interaction potential between INVIRASE®/ritonavir and intravenously administered midazolam (Table 3, benzodiazepine)
- **CLINICAL PHARMACOLOGY:** Addition of information related to the pharmacodynamic and pharmacokinetic parameters in HIV-1 treatment naïve patients who initiated treatment with a modified INVIRASE®/ritonavir regimen

APPROVAL & LABELING

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.”

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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If you have any questions, call Suzanne Strayhorn, Regulatory Project Manager, at (301) 796-1500 or (240) 402-4247.

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

ENCLOSURE(S):

Content of Labeling

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

/s/

POONAM MISHRA
02/26/2016