



NDA 020628/S-032
NDA 021785/S-009

SUPPLEMENT APPROVAL

Hoffmann-La Roche Inc.
Attention: Barbara Taylor, Ph.D.
Director, Regulatory Affairs
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Dr. Taylor:

Please refer to your supplemental new drug applications dated February 12, 2010 and received February 16, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: INVIRASE[®] (saquinavir mesylate) CAPSULES
NDA Number: 020628
Supplement Number: 032

Name of Drug Product: INVIRASE[®] (saquinavir mesylate) TABLETS
NDA Number: 021785
Supplement Number: 009

We also acknowledge receipt of your submissions dated March 5, 2010 and March 15, 2010.

Reference is also made to our letter dated January 13, 2010, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for INVIRASE (saquinavir mesylate) CAPSULES and INVIRASE (saquinavir mesylate) TABLETS. This information pertains to the risk of drug-drug interactions with the use of protease inhibitors, including INVIRASE (saquinavir mesylate).

These supplemental new drug applications provide for revisions to the labeling regarding coadministration of certain drugs with INVIRASE (saquinavir mesylate) CAPSULES and INVIRASE (saquinavir mesylate) TABLETS.

The following changes are consistent with our January 13, 2010 Safety Labeling Change Notification letter: the CONTRAINDICATIONS and PRECAUTIONS: Drug Interactions sections of the labeling have been updated with the following information:

- The addition of sildenafil as a contraindicated medication when prescribed for the treatment of pulmonary arterial hypertension.
- The addition of alfuzosin as a contraindicated medication.
- The addition of the recommendation that salmeterol should not be coadministered.
- The addition of new dosing recommendations for bosentan and tadalafil when prescribed for the treatment of pulmonary arterial hypertension.
- The addition of new dosing recommendations for colchicine when prescribed for the treatment of familial Mediterranean fever or gout.

Agreed-upon changes are as follow:

- The addition of new dosing recommendations for colchicine when prescribed for the prophylaxis of gout.
- The addition of the recommendation that colchicine should not be coadministered with INVIRASE (saquinavir mesylate) in patients with hepatic or renal impairment.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling and include the labeling changes proposed in any pending “Changes Being Effected” (CBE) supplements. 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 for this NDA, including pending “Changes Being Effected” (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.

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

PROMOTIONAL MATERIALS

All promotional materials for your drug products that include representations about your drug products must be promptly revised to make it consistent with the labeling changes approved in these supplements, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to

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 following address or by facsimile at 301-847-8444:

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

In addition, as required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about these drug products (i.e., a “Dear Health Care Professional” letter), we request that you submit an electronic copy of the letter to both these NDAs and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

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, please contact 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

Enclosure
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21785	SUPPL-9	HOFFMANN LA ROCHE INC	INVIRASE (SAQUINAVIR MESYLATE) 500 MG
NDA-20628	SUPPL-32	HOFFMANN LA ROCHE INC	INVIRASE(SAQUINAVIR MESYLATE) 200MG CAPS

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/s/

KENDALL A MARCUS
04/27/2010