DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020628 / S-046
NDA 021785 / S-022

SUPPLEMENT APPROVAL

Hoffmann-La Roche, Inc.
Patricia Smith, PhD.
Regulatory Agent on behalf of Roche
c/o Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080

Dear Dr. Smith:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received on September 15, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for INVIRASE® (saquinavir mesylate) capsules, 200 mg (NDA 020628) and tablets, 500 mg (NDA 021785).

These Prior Approval supplemental new drug applications provide for updates to the US Prescribing Information (USPI) as follows:

SECTION 2 DOSAGE AND ADMINISTRATION: Rilpivirine information was removed from this section and added to Section 4, "Contraindications" section of the USPI.

SECTION 4 CONTRAINDICATIONS & SECTION 7 DRUG INTERACTIONS: These sections were updated per current regulatory requirements [21 CFR 201.57 (c)(8)]. The names of the drugs contraindicated with INVIRASE/ritonavir are listed in Section 4 and the corresponding pharmacokinetic effects and clinical comments are detailed in Section 7. Information related to concomitant use and/or switch to rilpivirine has been updated. Information regarding the concomitant use of tyrosine inhibitors, dasatinib and sunitinib, has been added. Section 7 was updated to revise language regarding concomitant use of alfuzosin. Dapsone was removed from Section 4 and added to Section 7. Cautionary statements regarding coadministration with nefazodone, itraconazole and omeprazole have been added to Section 7 due to the potential risk of cardiac arrhythmias.

SECTION 5 WARNINGS AND PRECAUTIONS: A new subsection header 5.1 "Importance of Co-administration with Ritonavir" was added to emphasize that INVIRASE must be combined with ritonavir. The language in subsection 5.5 "Hepatotoxicity", was revised per current best practices and guidance.

SECTION 17 PATIENT COUNSELING INFORMATION: This section was reorganized and reordered per current best labeling practices and guidance.

The Medication Guide has also been updated to reflect changes made to the USPI and current best practices.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are 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 and 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 include 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).

REPORTING REQUIREMENTS

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

If you have any questions, call Suzanne Strayhorn, Regulatory Project Manager, at (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
03/15/2018
on behalf of Debra Birnkrant, MD