DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021-906/S-024
NDA 021-251/S-031

SUPPLEMENT APPROVAL

Abbott Laboratories
Attention: Mary Konkowski
Manager, Global Pharmaceutical Regulatory Affairs
Dept. PA76/ Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your supplemental new drug applications dated and received June 29, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for:

Kaletra® (lopinavir/ritonavir) Tablets, 200mg/50mg and 100mg/25mg
Kaletra® (lopinavir/ritonavir) Oral Solution, 80mg/ml; 20mg/ml

We acknowledge receipt of your submissions to these supplements dated July 31, 2009, August 6, 2009, August 26, 2009, September 3, 2009, October 30, 2009, November 3, 2009, November 10, 2009, December 23, 2009, January 8, 2010, January 25, 2010, February 4, 2010, February 10, 2010, March 4, 2010, March 9, 2010, and March 24, 2010, and your risk evaluation and mitigation strategy (REMS) assessment dated April 12, 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 Kaletra® (lopinavir/ritonavir) Tablets and Oral Solution. This information pertains to the risk of drug interactions with the use of the class of protease inhibitors.

These Prior Approval supplemental new drug applications provide for:

- A new once daily dosing regimen in adult patients with less than three lopinavir resistance-associated substitutions.
- Proposed modifications to the approved REMS.
- Revisions to the labeling consistent with our January 13, 2010 letter as follows regarding coadministration with Kaletra®:
  i) The addition of alfuzosin as a contraindicated medication.
  ii) The addition of new dosing recommendations for bosentan and tadalafil when prescribed for the treatment of pulmonary arterial hypertension.
  iii) The addition of new dosing recommendations for colchicine when prescribed for the treatment of familial Mediterranean fever or gout.

In addition, the following labeling revisions were also made regarding coadministration with Kaletra®:

- The addition of new dosing recommendations for colchicine for the prophylaxis of gout.
- The addition of the recommendation that colchicine should not be co-administered 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 enclosed, agreed-upon labeling text.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for the evaluation of once daily dosing tablets in pediatric patients weighing less than 15kg because necessary studies are impossible or highly impractical.

We are deferring submission of your pediatric studies for the evaluation of once daily dosing tablets in pediatric patients weighing 15 kg through 18 years of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

We are deferring submission of your pediatric studies for the evaluation of the once daily dosing oral solution because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1632 - 1. Please submit the 24 week results of PENTA 18 evaluating the pharmacokinetic, safety and activity of twice daily and once daily dosing of Kaletra tablets in a reviewable format. Submit a final report that includes detailed summaries of pharmacokinetic, safety and activity data as well as electronic datasets.

Protocol Submission Date: April 30, 2010
Study Completion Date: November 30, 2012
Final Report Submission: December 31, 2013

Submit all final study reports to your NDA. Use the following designator to prominently label all submissions: "**Required Pediatric Assessment(s)**".

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Kaletra (lopinavir/ritonavir) Tablets and Oral Solution was originally approved on April 6, 2009 and a REMS modification was approved on January 29, 2010. The REMS consisted of a Medication Guide and a timetable for submission of assessments of the REMS. The proposed modified REMS contains a revised Medication Guide to add the drug-drug interaction information described above.

Your proposed modified REMS, submitted on March 24, 2010, and appended to this letter, is approved. The REMS consists of the Medication Guide and a timetable for submission of assessments.
The timetable for submission of assessments of the REMS will remain the same as that approved on April 6, 2009.

There are no changes to the REMS assessment plan described in our April 6, 2009 letter.

Assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. 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 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.

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

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

NDA 021-906 and/or 021-251 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 021-906 and/or 021-251
PROPOSED REMS MODIFICATION
REMS ASSESSMENT
NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021-906 and/or 021-251
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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

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 (text for the package insert and Medication Guide) 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 these NDAs, 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 product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, 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 this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA 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).

If you have any questions, call Robert G. Kosko, Jr., Pharm.D., M.P.H., Regulatory Project Manager, at (301) 796-3979 or the Division's main number (301) 796-1500.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21906	SUPPL-24	ABBOTT LABORATORIES	KALETRA TABLETS
NDA-21251	SUPPL-31	ABBOTT LABORATORIES	KALETRA

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/s/

JEFFREY S MURRAY
04/27/2010