



NDA 21-906/S-022  
NDA 21-251/S-029

**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 April 28, 2009, received April 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 both supplements dated July 31, 2009, October 19, 2009, October 22, 2009, and December 15, 2009.

These Prior Approval supplemental new drug applications provide for:

- Updates to the U.S package insert to include drug-drug interaction information for concurrent lopinavir/ritonavir administration with inhaled medicines such as salmeterol or salmeterol in combination with fluticasone propionate (Serevent®, Advair®) and the related changes to the Medication Guide.
- Updates to the U.S package insert to include drug-drug interaction information for concurrent lopinavir/ritonavir administration with sildenafil (Revatio®) and the related changes to the Medication Guide.
- Proposed modifications to your approved risk evaluation and mitigation strategy (REMS), as described below.

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.

## **CONTENT OF LABELING**

Within 14 days from the date of this letter, please amend any pending supplemental application(s), including “Changed Being Effected” supplements for which the labeling is in effect, but for which FDA has not yet issued an action letter, for this NDA with 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/ucm155657.htm> that includes the changes approved in this application.

As soon as possible, but no later than 14 days from the date of this letter, please 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/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide). For administrative purposes, please designate this submission, “**SPL for approved NDA 21-906/S-022 and NDA 21-251/S-029**”.

## **RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for Kaletra® (lopinavir/ritonavir) Tablets and Oral Solution was originally approved on April 6, 2009, and consists of a single Medication Guide for both products and a timetable for submission of assessments of the REMS. A modification to the approved REMS was required because of the revisions to the Medication Guide to add the drug-drug interaction information described above and the modification to the timetable for submission of assessments of the REMS included in your July 31, 2009 and December 15, 2009 submissions. Your December 31, 2009 submission included a statement that the revised Medication Guide would be adequate with the proposed modifications to achieve its purpose.

Your proposed modified REMS, submitted on December 31, 2009, and appended to this letter, is approved. The REMS consists of the Medication Guide and a timetable for submission of assessments.

There are no changes to the REMS assessment plan included 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 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 21-906 and 21-251 REMS ASSESSMENT**

**NEW SUPPLEMENT for NDA 21-906 and 21-251  
PROPOSED REMS MODIFICATION  
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR<<insert application #>>  
REMS ASSESSMENT  
PROPOSED REMS MODIFICATION (if included)**

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

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

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

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 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

Carton and Container Labeling

REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21906	SUPPL-22	ABBOTT LABORATORIES	KALETRA TABLETS
NDA-21251	SUPPL-29	ABBOTT LABORATORIES	KALETRA

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

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/s/

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KENDALL A MARCUS  
01/29/2010