DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-906/S-014
NDA 21-251/S-023

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

Dear Ms. Konkowski:

Please refer to your supplemental new drug applications dated December 28, 2007, received December 28, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for KALETRA® (lopinavir/ritonavir) Tablets and KALETRA® (lopinavir/ritonavir) Oral Solution.

We acknowledge receipt of your submissions dated January 17, 2008, February 15, 2008, May 14, 2008, June 05, 2008, June 26, 2008, October 6, 2008, October 23, 2008, and January 02, 2009, March 25, 2009, April 1, 2009, and April 2, 2009.

These supplemental applications proposed the following changes:

- To update the WARNINGS and PRECAUTIONS, ADVERSE REACTIONS, Post-marketing, CLINICAL PHARMACOLOGY, and PATIENT COUNSELING INFORMATION sections of the package insert with QT/QTc interval and PR interval information from Study M06-809, and to convert the patient package insert to a Medication Guide that includes information related to cardiac abnormalities.

We 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, please submit the content of labeling [21 CFR 314.50(l)] 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 Medication Guide). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 21-906/SLR-014 and NDA 21-251/SLR-023.**"

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 21-906/S-014 AND 21-251/S-023**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) for an approved drug if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

Since KALETRA® (lopinavir/ritonavir) was approved in 2000 for use in combination with other antiretroviral agents for the treatment of HIV-infection, we have become aware of increases in the QTcF and PR intervals of the electrocardiogram associated with the use of KALETRA® (lopinavir/ritonavir), thus putting certain patients at increased risk for cardiac arrhythmias. This information was not available when KALETRA®(lopinavir/ritonavir) was granted marketing authorization. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that KALETRA® (lopinavir/ritonavir) poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of KALETRA® (lopinavir/ritonavir). FDA has determined that KALETRA® (lopinavir/ritonavir) is a product that has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decision to use, or to continue to use KALETRA® (lopinavir/ritonavir). This includes the new safety information regarding increased risk for cardiac abnormalities identified above. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed KALETRA® (lopinavir/ritonavir).

Your proposed REMS, submitted on April 1, 2009 and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS that was included in your April 1, 2009 submission.

Information needed for assessment of the REMS will include but may not be limited to a survey of patients' understanding of the serious risks associated with the use of KALETRA® (lopinavir/ritonavir), including the risk of potential cardiac arrhythmias.

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, 21-251 REMS ASSESSMENT

NEW SUPPLEMENT for NDA 21-906, 21-251
PROPOSED REMS MODIFICATION
REMS ASSESSMENT (if included)

If you do not submit electronically, please send 5 copies of submissions containing REMS assessments or proposed modifications of the REMS.

Please note that:

- This Medication Guide must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(f)(2)];

- You are responsible for ensuring that this Medication Guide is available for distribution to every patient who is dispensed a prescription for this product [21 CFR 208.24];

- The final printed Medication Guide distributed to patients must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text; and

- You are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided [21 CFR 208.24(d)].

In addition, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the revised product labeling and has determined that it contains significant new risk information relating to your drug product. We are hereby requesting that all promotional materials for your drug product that include representations about your drug product be revised to include the new risk information immediately. These revisions should include prominent disclosure of the important new information described in the WARNINGS AND PRECAUTIONS sections that appear in the revised package labeling. Please submit a written response to this request within one week of receipt of this letter, stating whether you intend to comply with this request, to the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications by facsimile at (301) 847-8444 or at 5901-B Ammendale Road, Beltsville, MD 20705.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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 Rashmi Kalla, Regulatory Project Manager, at (301) 796-3931.

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: Package Insert
Medication Guide
Approved REMS
Carton and Container Labels

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

/s/

Kendall Marcus
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