DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-226/S-014
NDA 21-251/S-010

Mary Ellen Snyder
Global Pharmaceutical Regulatory Affairs
Dept RA76, AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms Snyder:

Please refer to your supplemental new drug applications dated December 19, 2003, received December 19, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for KALETRA (Lopinavir/Ritonavir) capsules and oral solution.

This supplemental new drug application provides for the use of KALETRA (Lopinavir/Ritonavir) capsules and oral solution for combination with other antiretroviral agents for the treatment of HIV-infection.

We completed our review of this application as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text. The approval was based on review of two phase II trials used to support long-term (Week 144-204) efficacy and safety data.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the package insert, and text for the patient package insert.

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-226/S-014." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages neonates to < 6months and adolescents from 12 years to 16 years until December 31, 2006.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

1. Multiple-dose pharmacokinetics, safety and activity study of ABT-378/ritonavir in combination with other antiretroviral agents in HIV-infected pediatric patients

   Submission date: December 31, 2006

2. Multiple-dose pharmacokinetic and safety study of ABT-378/ritonavir in HIV-exposed neonates (born to HIV-infected mothers).

   Submission date: December 31, 2006

We also remind you of an additional post-marketing commitment listed below:

3. Please submit resistance datasets according to DAVDP's HIV resistance template from the treatment-experienced studies (M97-765, M98-957, M98-888, and ANRS observation cohort) in order to further characterize the impact of baseline mutations and baseline susceptibility and virologic outcome. Please submit an integrated study report and an NDA labeling supplement to update the Microbiology: Cross Resistance section of the package insert based on results from baseline genotype and phenotype and virologic response analyses from the above referenced treatment-experienced studies.

   Protocol submission: Not applicable
   Study start: Not applicable
   Submission of resistance datasets, integrated study report and labeling supplement: within six months of the date of the letter.

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

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, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Vasavi Reddy, R.Ph., Regulatory Project Manager, at (301) 827-2413.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Division Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Food and Drug Administration

Attachment: Label

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

/s/

Jeffrey Murray

10/19/04 04:48:46 PM