DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-976/S-009

Tibotec, Incorporated
Attention: Susan Fiordeliso
Manager, Global Regulatory Affairs
1020 Stony Hill Road, Suite 300
Yardley, PA 19067

Dear Ms Fiordeliso:

Please refer to your supplemental new drug application dated and received June 20, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PREZISTA (darunavir) 75 mg and 150 mg tablets.

We acknowledge receipt of your submissions dated July 18, 2008, August 8, 2008, August 11, 2008, September 12, 2008, September 18, 2008, October 8, 2008, October 15, 2008, November 6, 2008, November 10, 2008, November 21, 2008, and December 17, 2008.

This supplemental new drug application was submitted to provide dosing recommendations for human immunodeficiency virus (HIV-1) infected pediatric patients 6 to less than 18 years of age and to include two new dosage strengths, 75 mg and 150 mg tablets.

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. (b) (4) [redacted]

Approval of this supplement fulfills the following postmarketing commitment as numbered in the June 23, 2006, approval letter. This commitment is listed below:

3. Please assess the pharmacokinetics, safety, tolerability and antiviral activity of two alternative doses of a suitable pediatric formulation in combination with ritonavir, in treatment-experienced pediatric children and adolescents between 6 and 17 years of age.

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

We are waiving the pediatric study requirement for ages 0 to below 3 years of age because of evidence strongly suggesting the drug would be unsafe in this pediatric age group. This decision is based on the

results of juvenile rat toxicology studies that provide evidence of a potential safety risk as a result of overt toxicity in this age group and evidence of potential drug accumulation in brain tissue.

Your deferred pediatric studies required by section 505B(a) of the Federal Food and Drug and Cosmetic Act (FDCA) 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 FDCA. We remind you of the deferred pediatric studies as listed in the October 21, 2008, approval letters for NDA 21-976/006 and NDA 21-976/007, respectively.

1. Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric subjects 3 to 6 years of age. Please evaluate dose requirements and safety in treatment-experienced pediatric patients 3 to 6 years of age with HIV-1 infection after preliminary review of data from the 6 to 17 year olds in trial TMC114-C212 with the Division of Antiviral Products (DAVP).

Protocol Submission:	December 31, 2008
Final Report Submission:	June 30, 2011

1. Deferred pediatric study under PREA for the treatment of HIV-1 infection in treatment-naïve pediatric subjects from 12 to <18 years of age. Conduct a pediatric safety and activity study of darunavir, in combination with ritonavir, in the treatment-naïve population with activity based on the results of virologic response over at least 24 weeks of dosing and safety monitored over 48 weeks.

Submission of final protocol:	June, 2009
Submission of final study report:	July, 2012

2. Deferred pediatric study under PREA for the treatment of HIV-1 infection in treatment-naïve pediatric subjects from 3 to <12 years of age. Conduct a pediatric safety and activity study of darunavir, in combination with ritonavir, in the treatment-naïve population with activity based on the results of virologic response over at least 24 weeks of dosing and safety over 48 weeks.

Submission of final protocol:	March, 2011
Submission of final study report:	March, 2015

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

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(1)] 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 and text for the patient package insert). 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 21-976/S-009."**

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

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.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Antiviral Products and two copies of both the promotional materials and the package insert directly to:

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

LETTERS TO HEALTH CARE PROFESSIONALS

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
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

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 Stacy Powers Newalu M.P.H., Regulatory Project Manager, at (301) 796-3978.

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

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
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