DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 021976/S-016 **SUPPLEMENT APPROVAL**

Tibotec, Incorporated
Attention: Susan Fiordeliso
Sr. Manager, Global Regulatory Affairs
1125 Trenton-Harbourton Rd.
Titusville, NJ 08540

Dear Ms. Fiordeliso:

Please refer to your supplemental new drug application dated and received February 12, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for PREZISTA® (darunavir) Tablet.

We also acknowledge receipt of your submissions dated March 12, 2010 and March 24, 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 PREZISTA (darunavir) Tablet. This information pertains to the risk of drug-drug interactions with the use of protease inhibitors, including PREZISTA (darunavir).

This supplemental application provides for revisions to the labeling regarding coadministration of certain drugs with PREZISTA (darunavir) Tablet.

The following changes are consistent with our January 13, 2010 Safety Labeling Change Notification letter: section 4 (CONTRAINDICATIONS) and section 7 (DRUG INTERACTIONS) of the labeling have been updated with the following information:

- The addition of sildenafil as a contraindicated medication when prescribed for the treatment of pulmonary arterial hypertension.
- The addition of the recommendation that salmeterol should not be coadministered.
- The addition of new dosing recommendations for bosentan and tadalafil when prescribed for the treatment of pulmonary arterial hypertension.
- The addition of new dosing recommendations for colchicine when prescribed for the treatment of familial Mediterranean fever or gout.

Agreed-upon changes are as follow:

- The addition of new dosing recommendations for colchicine when prescribed for the prophylaxis of gout.
- The addition of the recommendation that colchicine should not be coadministered with PREZISTA (darunavir) in patients with hepatic or renal impairment.

We have 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.

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 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 this NDA, 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, please contact Amalia Himaya, Regulatory Project Manager, at (301) 796-3391 or the Division's main number at (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

Enclosure
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21976	SUPPL-16	CENTOCOR ORTHO BIOTECH INC	PREZISTA

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

/s/

KENDALL A MARCUS
04/26/2010