



NDA 204119

**TENTATIVE APPROVAL**

Hetero USA, Inc.  
Attention: Dr. Soma Raju  
U.S. Agent for Hetero Labs Limited Unit III  
1035 Centennial Ave.  
Piscataway, NJ 08854

Dear Dr. Raju:

Please refer to your New Drug Application (NDA) 204119 dated May 9, 2012, received May 11, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Efavirenz, Lamivudine, and Tenofovir disoproxil fumarate Tablets, 600 mg/300 mg/300 mg.

We acknowledge receipt of your submissions dated:

June 7, 2012  
August 1, 2012

August 20, 2012  
September 24, 2012

October 18, 2012  
November 6, 2012

This NDA provides for the use of Efavirenz, Lamivudine, and Tenofovir disoproxil fumarate Tablets, 600 mg/300 mg/300 mg alone or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 40 kg.

This NDA was reviewed under the President's Emergency Plan for AIDS Relief (PEPFAR).

We completed our review of this application. It is **tentatively approved** under 21 CFR 314.105 for use as recommended in the agreed-upon labeling (refer to the enclosed text for the package insert, patient package insert, immediate container and carton labels). Also refer to your November 6, 2012, submission for the agreed-upon labeling. Based on the data provided, the expiration dating period for Efavirenz, Lamivudine, and Tenofovir disoproxil fumarate Tablets, 600 mg/300 mg/300 mg is 24 months when packaged in HDPE bottles of 30 tablets with desiccant and child resistant closure, and stored below 30°C.

This determination is based upon information available to the Agency at this time [i.e., information in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in manufacturing and testing of the drug product]. This determination is subject to change on the basis of any new information that may come to our attention.

The listed reference drug products [Sustiva<sup>®</sup> (efavirenz), Epivir<sup>®</sup> (lamivudine) and Viread<sup>®</sup> (tenofovir disoproxil fumarate)] upon which you base your application are subject to a period of

patents' protection and therefore, final approval of your application under section 505(c)(3) of the Act [21 U.S.C. 355(c)(3)] may not be made effective until the period has expired. If you have questions as to when this date will be, please contact the Agency at the information provided below.

Two or six months prior to the expiration of the patents' protection, as appropriate, submit an amendment to this application identifying changes, if any, in the conditions under which your product was tentatively approved. Any changes to the conditions outlined in this NDA require our review before final approval and the goal date for our review will be set accordingly. Your amendment should include updated labeling, chemistry, manufacturing and controls data, and a safety update. This amendment should include draft final printed labels and labeling which comply with all United States regulations (uniqueness of drug product appearance per 21 CFR 206; child-resistant packaging per 16 CFR 1700, etc.). This amendment should be designated clearly in your cover letter as a "**FINAL APPROVAL REQUESTED.**"

We remind you that you are expected to comply with the reporting requirements provided in 21 CFR 314.80 and 314.81. If the product is to be mass distributed in developing countries, a system of collecting and reporting adverse drug reactions by the distributor would be desirable (e.g., through governmental or nongovernmental agencies distributing the products).

We remind you that, should you intend to market this product in the United States after the period of patents' protection, you are required to join the antiretroviral pregnancy registry at that time and make the appropriate labeling change that references the existence of the pregnancy registry. In addition, an updated package insert (PI) must be submitted under the Structured Product Labeling requirements (<http://www.fda.gov/oc/datacouncil/spl.html>) as defined by the Physician's Labeling Rule [21 CFR 201.56, 201.57].

Before we issue a final approval letter, this NDA is not deemed approved. If you believe that there are grounds for issuing the final approval letter before the period of patents' protection has expired, you should amend your application accordingly.

Please note that this drug product may not be marketed in the United States without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d).

If you have any questions, please contact David Araojo, Pharm.D., Senior Program Consultant, at (301) 796-0669 or email at [david.araojo@fda.hhs.gov](mailto:david.araojo@fda.hhs.gov).

Sincerely yours,

*{See appended electronic signature page}*

Jeffrey Murray, M.D., M.P.H.  
Deputy Director  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosures: PI, PPI, immediate container and carton labels

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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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JEFFREY S MURRAY  
11/08/2012