



ANDA 203053

Hetero USA, Inc.
U.S. Agent for: Hetero Labs Limited Unit V
Attention: Soma Raju
Director, Regulatory Affairs
1035 Centennial Avenue
Piscataway, NJ 08854

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated June 22, 2011, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Efavirenz, Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 600 mg/200 mg/300 mg.

This ANDA was reviewed under the expedited review provisions of the President's Emergency Plan for AIDS Relief (PEPFAR).

Reference is also made to our complete response letter dated June 14, 2013, and to your amendment dated June 24, 2013.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your ANDA at this time because of the patent issues noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the agency at this time, (i.e., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention.

The reference listed drug (RLD) upon which you have based your ANDA, Atripla Tablets, 600 mg/200 mg/300 mg of Gilead Sciences, LLC, is subject to periods of patent protection. The following patents and their expiration dates are currently listed in the agency's publication titled Approved Drug Products with

Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
5,519,021 (the '021 patent)	November 21, 2013*
5,663,169 (the '169 patent)	March 2, 2015*
5,814,639 (the '639 patent)	March 29, 2016*
5,914,331 (the '331 patent)	January 2, 2018*
5,922,695 (the '695 patent)	January 25, 2018*
5,935,946 (the '946 patent)	January 25, 2018*
5,977,089 (the '089 patent)	January 25, 2018*
6,043,230 (the '230 patent)	January 25, 2018*
6,939,964 (the '964 patent)	July 20, 2018*
6,639,071 (the '071 patent)	August 14, 2018
6,642,245 (the '245 patent)	May 4, 2021*
6,703,396 (the '964 patent)	September 9, 2021*

*with pediatric exclusivity

Your ANDA contains paragraph III certifications to each of these patents under section 505(j)(2)(A)(vii)(III) of the Act stating that Hetero Labs Limited Unit V will not market Efavirenz, Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 600 mg/200 mg/300 mg in the United States prior to the expiration of each of these patents. Therefore, final approval of your ANDA may not be made effective pursuant to section 505(j)(5)(B)(ii) of the Act until each of these patents has expired, currently, September 9, 2021.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

To reactivate your ANDA prior to final approval, please submit a "MINOR AMENDMENT - FINAL APPROVAL REQUESTED" 90 days prior to the date you believe that your ANDA will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in

your cover letter as a MINOR AMENDMENT - FINAL APPROVAL REQUESTED.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' compliance with cGMPs are subject to agency review before final approval of the ANDA will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

This drug product may not be marketed 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 301 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book." Should you believe that there are grounds for issuing the final approval letter prior to September 9, 2021, you should amend your ANDA accordingly.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in

prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self identification or fee payment.

Additionally, we note that the failure of any facility referenced in the application to self-identify and pay applicable fees means that FDA will not consider the GDUFA application review goal dates to apply to that application.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Sean Belouin, Project Manager, at (240) 276-8566.

Sincerely yours,

{See appended electronic signature page}

Kathleen Uhl, M.D.
Acting Director
Office of Generic Drugs
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/

ROBERT L WEST

10/31/2013

Deputy Director, Office of Generic Drugs, for
Kathleen Uhl, M.D.