



ANDA 090894

ANDA APPROVAL

Teva Pharmaceuticals USA, Inc.
425 Privet Road
Horsham, PA 19044
Attention: Rich Leone
Senior Director, Regulatory Affairs

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on September 26, 2008, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 200 mg/300 mg.

Reference is also made to the tentative approval letter issued by this office on August 16, 2011, the complete response letter issued by this office on March 3, 2016, and to your amendments received on April 8, May 5, July 29, August 5, August 30 and September 13, 2016; and March 2, May 1, May 12, May 18, May 22, May 31 and June 2, 2017.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 200 mg/300 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Truvada Tablets, 200 mg/300 mg, of Gilead Sciences, Inc. (Gilead). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

The RLD upon which you have based your ANDA, Gilead's Truvada Tablets, 200 mg/300 mg, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
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*
6,642,245 (the '245 patent)	May 4, 2021*
6,703,396 (the '396 patent)	September 9, 2021*

8,592,397 (the '397 patent)	January 13, 2024
8,716,264 (the '264 patent)	January 13, 2024
9,457,036 (the '036 patent)	January 13, 2024

* with pediatric exclusivity added

Your ANDA contains paragraph IV certifications to each of the patents¹ under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 200 mg/300 mg, under this ANDA. You have notified the Agency that TEVA Pharmaceuticals USA, Inc. (TEVA) complied with the requirements of section 505(j)(2)(B) of the FD&C Act and that litigation was initiated within the statutory 45-day period against TEVA for infringement of the '245, '396, '695, '946, '089, '230, and '331 patents in the United States District Court for the Southern District of New York [Gilead Sciences, Inc. and Emory University, v. TEVA Pharmaceuticals USA, Inc. and TEVA Pharmaceutical Industries, Ltd., Civil Action Nos. 08-cv-10838 ('245 and '396 patents), 10-cv-1796 ('695, '946, '089, and '230 patents), and 10-cv-1798 ('331 patent)]. You have also notified the Agency that the cases have been dismissed.

With respect to 180-day generic drug exclusivity, we note that TEVA was the first ANDA applicant for Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 200 mg/300 mg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, TEVA may be eligible for 180 days of generic drug exclusivity for Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 200 mg/300 mg. This exclusivity, which is provided for under 505(j)(5)(B)(iv) of the FD&C Act, would begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The Agency notes that TEVA failed to obtain tentative approval of this ANDA within 30 months after the date of which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The Agency is not, however, making a formal determination at this time of TEVA's eligibility for 180-day generic drug exclusivity. It will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after TEVA begins commercial marketing of Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 200 mg/300 mg, or (b) at any time prior to the expiration of the '245 and '396 patents if TEVA has not begun commercial marketing. Please submit correspondence to this ANDA informing the Agency of the date commercial marketing begins.

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

¹ The Agency notes that the '397, '264, and '036 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

Section 505-1 of the FD&C Act authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. In accordance with section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA under section 505(j) is subject to certain elements of the REMS required for the applicable listed drug.

The details of the REMS requirements were outlined in our REMS notification letter dated August 31, 2012. In that letter, you were also notified that pursuant to section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA and the listed drug it references must use a single, shared system for elements to assure safe use (ETASU), unless FDA waives that requirement.

Your REMS, known as the Emtricitabine/Tenofovir Disoproxil Fumarate REMS Program, submitted on May 22, 2017, and appended to this letter, is approved. The Emtricitabine/Tenofovir Disoproxil Fumarate REMS is a single, shared system that consists of ETASU.

Your REMS must be fully operational before you introduce Emtricitabine and Tenofovir Disoproxil Fumarate into interstate commerce.

The Emtricitabine/Tenofovir Disoproxil Fumarate REMS uses a single, shared system for the ETASU and the REMS assessments. This single shared system REMS Program currently includes the products listed on the FDA REMS website, available at <http://www.fda.gov/remis>. Other products may be added in the future if additional NDAs or ANDAs are approved.

Under section 505-1(g)(2)(C) of the FD&C Act, FDA can require the submission of a REMS assessment if FDA determines an assessment is needed to evaluate whether the REMS should be modified to ensure the benefits of the drug outweigh the risks or to minimize the burden on the healthcare delivery system of complying with the REMS.

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

We also remind you that section 505-1(f)(8) of the FD&C Act prohibits holders of an approved covered application from using any element to assure safe use to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

ANDA 090894 REMS ASSESSMENT

**NEW SUPPLEMENT FOR ANDA 090894/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR ANDA 090894/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR ANDA 090894/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING
CHANGES SUBMITTED IN SUPPLEMENT XXX**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISION FOR ANDA 090894

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

ANNUAL FACILITY FEES

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 1st 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.

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 in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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 via publicly available labeling repositories.

The Electronic Common Technical Document (eCTD) is CDER’s standard format for electronic regulatory submissions. Beginning May 5, 2017, ANDAs must be submitted in eCTD format and beginning May 5, 2018, drug master files must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: www.fda.gov/ectd.

Sincerely yours,

{See appended electronic signature page}

Heidi Lee, PharmD
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

ENCLOSURE:
REMS



Heidi
Lee

Digitally signed by Heidi Lee
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