ANDA 209721

ANDA APPROVAL

Amneal Pharmaceuticals of New York, LLC
U.S. Agent for Amneal Pharmaceuticals Co. GmbH
50 Horseblock Road
Brookhaven, NY 11719
Attention: Candis Edwards
Senior Vice President, Regulatory Affairs

Dear Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on December 9, 2016, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 100 mg/150 mg, 133 mg/200 mg, 167 mg/250 mg, and 200 mg/300 mg.

Reference is also made to the complete response letter issued by this office on May 17, 2018, and to any amendments thereafter.

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, 100 mg/150 mg, 133 mg/200 mg, 167 mg/250 mg, and 200 mg/300 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Truvada Tablets, 100 mg/150 mg, 133 mg/200 mg, 167 mg/250 mg, and 200 mg/300 mg, of Gilead Sciences, Inc. (Gilead).

The RLD upon which you have based your ANDA, Gilead's Truvada Tablets, 100 mg/150 mg, 133 mg/200 mg, 167 mg/250 mg, and 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.S. Patent Number	Expiration Date
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 (200 mg/300 mg strength only)
8,716,264 (the '264 patent)	January 13, 2024 (200 mg/300 mg strength only)
9,457,036 (the '036 patent)	January 13, 2024 (200 mg/300 mg strength only)
9,744,181 (the '181 patent)	January 13, 2024 (200 mg/300 mg strength only)

* with pediatric exclusivity added

Your ANDA contains paragraph IV certifications to each of the patents[1] 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, 100 mg/150 mg, 133 mg/200 mg, 167 mg/250 mg, and 200 mg/300 mg, under this ANDA. With respect to the 200 mg/300 mg strength, you have notified the Agency that Amneal Pharmaceuticals Co. GmbH (Amneal) 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 Amneal for infringement of the '245, '396, and '264 patents in the United States District Court for the District of New Jersey [Gilead Sciences, Inc. and Emory University v. Amneal Pharmaceuticals, LLC, Civil Action No. 17-02335]. With respect to the 100 mg/150 mg, 133 mg/200 mg, and 167 mg/250 mg strengths, you have notified the Agency that Amneal 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 for infringement of the '245 and '396 patents in the United States District Court for the District of Delaware [Gilead Sciences, Inc. and Emory University v. Amneal Pharmaceuticals LLC, Civil Action No. 17-00943]. You have also notified the Agency that these cases were dismissed.

With respect to 180-day generic drug exclusivity, we note that Amneal was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 100 mg/150 mg, 133 mg/200 mg, and 167 mg/250 mg. Therefore, with this approval, Amneal is eligible for 180 days of generic drug exclusivity for Emtricitabine and Tenofovir Disoproxil Fumarate Tablets, 100 mg/150 mg, 133 mg/200 mg, and 167 mg/250 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit a correspondence to this ANDA informing the Agency of the date you begin commercial marketing. Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

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.

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 February 2, 2017. 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 final proposed REMS, submitted on June 21, 2018; is approved, and will be posted on the FDA REMS website: http://www.fda.gov/rems

The REMS consists of elements to assure safe use (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/rems. 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 a REMS assessment 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 209721 REMS ASSESSMENT

NEW SUPPLEMENT FOR ANDA 209721/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 209721/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 209721/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 209721

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.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

In addition to submitting the proposed REMS as described above, you can also submit the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, include the SPL file with your proposed REMS submission.

For more information on submitting REMS in SPL format, please email REMS_Website@fda.hhs.gov

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

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[2] 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.

Sincerely yours,

{See appended electronic signature page}

For Vincent Sansone, PharmD
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

[1] The Agency notes that the '181 patent was submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to this patent would not create a statutory stay of approval.

[2] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Heidi Lee

Digitally signed by Heidi Lee
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