DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21752/S-044

SUPPLEMENT APPROVAL

Gilead Sciences, Inc.
Attention: Janette Meyer, RAC
Associate Director, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Meyer:

Please refer to your Supplemental New Drug Application (sNDA) dated December 20, 2013, received December 20, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TRUVADA (emtricitabine/tenofovir disoproxil fumarate) tablets, 200 mg and 300 mg.

We acknowledge receipt of your amendments dated January 31, 2014, February 14, 2014, March 29, 2014, April 22, 2014, May 19, 2014, June 3, 2014, June 11, 2014 and June 16, 2014 and your risk evaluation and mitigation strategy (REMS) assessment dated July 9, 2013. We also refer to our REMS Modification Notification letter dated November 1, 2013.

This "Prior Approval" supplemental new drug application proposes modifications to the approved REMS for TRUVADA (emtricitabine/tenofovir disoproxil fumarate) for a Pre-Exposure Prophylaxis (PrEP) indication.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for TRUVADA (emtricitabine/tenofovir disoproxil fumarate) tablets was originally approved on July 16, 2012, and last modified on June 17, 2013. The REMS consists of a Medication Guide, elements to assure safe use (ETASU) and a timetable for submission of assessments of the REMS.

In accordance with our REMS modification letter of November 1, 2013, your proposed modifications to the REMS consist of the following:

- Revision to the goal of the REMS to remove "other healthcare professionals" because the REMS training program only target prescribers and to add "uninfected" to be consistent with the REMS document and labeling.
- Revision of the ETASU to provide a mechanism for prescribers to report completion of the prescriber training program (whether the training is completed online or via hard copy), which will improve data collection of the number and specialty of prescribers who report completion of the prescriber training materials.
- A revised Medication Guide (dated December 16, 2013) that includes changes based on patient comprehension testing.
- Revision of the ETASU to require the maintenance of a secure database to capture the number and specialty of prescribers who report completion of the prescriber training.
- Revision of the timetable for submission of assessments from annually to every 18 months to allow adequate time to capture increased provider and patient participation in surveys.
- Revision of the appended REMS materials to be consistent with current labeling.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element 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.

Your proposed modified REMS, submitted on June 16, 2014 and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on June 18, 2014.

In accordance with our REMS Assessment Revision letter dated November 1, 2013, you have also revised the TRUVADA REMS assessment plan to enhance the methodology to more clearly reflect the REMS goals and elements. The revised REMS assessment plan should include, but is not limited to, the following:

1. Evaluation of an uninfected individual's knowledge of the following:
    a. Importance of strict adherence to the recommended dosing regimen
    b. Importance of regular monitoring of HIV-1 serostatus
    c. Understanding that TRUVADA for a PrEP Indication must be part of a comprehensive prevention strategy that includes safer sex practices
2. Evaluation of prescriber knowledge of the following information:
    a. Importance of strict adherence to the recommended dosing regimen

b. Importance of regular monitoring of HIV-1 serostatus to avoid continuing to take TRUVADA for a PrEP Indication, if seroconversion has occurred, to reduce the risk of development of resistant HIV-1 variants

c. Understanding that TRUVADA for a PrEP Indication must be considered as only a part of a comprehensive preventive strategy in order to reduce the risk of HIV-1 infection and that other preventive measures should also be used

3. Number and specialty of prescribers who report completion of the prescriber training materials
4. Evaluation of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
5. With respect to the REMS goals, an assessment of the extent to which the elements are meeting the goal or whether the goal or such elements should be modified.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 21752 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the 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:

NDA 21752 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 21752

PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 21752
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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, call Kyong Hyon, Safety Regulatory Project Manager, at (301) 796-0734.

Sincerely,

{See appended electronic signature page}

William Tauber, M.D.
Acting Deputy Director for Safety
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

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

/s/

WILLIAM B TAUBER
06/18/2014