



NDA 021356/S-57
NDA 022577/S-13

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
REQUIREMENT(S)**

Gilead Sciences, Inc.
Attention: Kat DeCarlo
Sr. Associate, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. DeCarlo:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received on June 14, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for VIREAD[®] (tenofovir disoproxil fumarate) tablets, for oral use 150mg, 200mg, 250mg, 300mg and for VIREAD[®] (tenofovir disoproxil fumarate) powder, for oral use 40mg/1g.

These Prior Approval supplemental new drug applications provide for the following changes to the VIREAD[®] USPI:

- Revisions to INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS, USE IN SPECIFIC POPULATIONS, CLINICAL PHARMACOLOGY, CINICAL STUDIES, and PATIENT COUNSELING INFORMATION to include the expansion of the chronic hepatitis B (CHB) indication to include pediatric patients 2 years and older weighing at least 10 kg supported by Week 48 data from trial GS-US-174-0144
- Revisions to USE IN SPECIFIC POPULATIONS to conform to Pregnancy and Lactation Labeling Rule (PLLR)
- Revisions to the Patient Package Insert (PPI) and Instructions for Use (IFU) for consistency with changes made to the Full Prescribing Information (FPI)

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, Instructions for Use) with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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 from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)

These supplemental New Drug Applications (sNDAs) provided the final reports for the following postmarketing requirements listed in both the August 11, 2008 (NDA 021356/S-25) and March 24, 2010 (NDA 021356/S-33) approval letters.

- 283-2 Deferred pediatric studies under PREA for the treatment of chronic hepatitis B virus infection in pediatric patients ages 2 to <12 years of age
- 1618-1 Conduct a controlled trial (trial of pediatric HBV-infected subjects required under PREA) that elucidates the mechanism of tenofovir's effects on bone. Evaluations of adequate numbers of pediatric subjects must include the following:
- a. Measurement of renal excretion of calcium, phosphorous, and magnesium through calculation of the renal phosphate threshold (TmP/GFR).
 - b. Measurement of urine bicarbonate, urine n-telopeptide, serum bone-specific alkaline phosphatase, parathyroid hormone, osteocalcin, c-telopeptide, 25 hydroxyvitamin D, 1,25 (dihydroxyvitamin) D levels, albumin, calcium, phosphate, magnesium, and bicarbonate.
 - c. Correlation of renal parameters with measurements of bone mineral density (DEXA)

We have reviewed your submissions and conclude that the above requirements are fulfilled.

We remind you that there is a postmarketing requirement listed in the March 8, 2006, approval letter that is still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the Prescribing Information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

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 submit final promotional materials and Prescribing Information, 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>.

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 Alicia Moruf, PharmD, MPH, Regulatory Project Manager, at 301-796-3953.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD

Director

Division of Antiviral Products

Office of Antimicrobial Products

Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling

Prescribing Information

Patient Package Insert

Instructions for Use

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JEFFREY S MURRAY
12/11/2018