DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21449/S-024

**SUPPLEMENT APPROVAL**

Gilead Sciences, Incorporated
Attention: Kat De Carlo
Senior Regulatory Affairs Associate
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. De Carlo:

Please refer to your Supplemental New Drug Application (sNDA) dated and received June 29, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for HEPSERA® (adefovir dipivoxil) 10 mg tablets.

We also refer to our approval letter dated December 28, 2018 which contained the following error in the approved labeling:

- Retention of Tradenames of tenofovir containing products
- Omission of drug interaction statement for products containing tenofovir disoproxil fumarate or tenofovir alafenamide instead of Tradenames of products from DRUG INTERATIONS and PATIENT COUNSELING INFORMATION
- Omission of the following statement from the Patient Package Insert "Especially tell your doctor if you take a medication that contains tenofovir disoproxil fumarate or tenofovir alafenamide."

This replacement approval letter incorporates the correction of the error. The effective approval date will remain December 28, 2018, the date of the original approval letter.

This Prior Approval supplemental new drug application provides for the following updates to the US Prescribing Information:

- **USE IN SPECIFIC POPULATIONS:** Updated to conform to the Pregnancy and Lactation Labeling Rule (PLLR)
- **CLINICAL PHARMACOLOGY, Microbiology**: Updated information regarding adefovir resistance-associated substitutions
- **PATIENT COUSELING INFORMATION**, and **PATIENT PACKAGE INSERT** were revised per current best labeling practices

## APPROVAL & LABELING

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

## 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 and Patient Package Insert), 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).

## 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 Linda C. Onaga, MPH, Senior Regulatory Project Manager, at (301) 796-0759 or the main line at (301) 796-1500.

Sincerely,

*{See appended electronic signature page}*

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
Prescribing Information
Patient Package Insert

---

**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/

---

POONAM MISHRA
12/28/2018 12:00:00 AM
on behalf of Debra Birnkrant