



NDA 210251

**NDA APPROVAL**

Gilead Sciences, Inc.  
Attention: Kim Lindstrom, PhD.  
Senior Manager, Regulatory Affairs  
333 Lakeside Drive  
Foster City, CA 94404

Dear Dr. Lindstrom:

Please refer to your New Drug Application (NDA) dated June 10, 2017, and received on June 12, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for BIKTARVY (bictegravir, emtricitabine, and tenofovir alafenamide) tablets, 50 mg/200 mg/25mg.

We also acknowledge receipt of information related to BIKTARVY (bictegravir, emtricitabine, and tenofovir alafenamide), 50mg/200mg/25mg fixed-dose combination tablet for your Gilead Access Program that was reviewed as part of this application.

This new drug application provides for the use of BIKTARVY (bictegravir, emtricitabine, and tenofovir alafenamide), fixed-dose combination tablets, for the treatment of HIV-1 infection in adults who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of BIKTARVY.

We have completed our review of this 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, text for the patient package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible via publicly available labeling repositories.

### **CARTON AND IMMEDIATE CONTAINER LABELS**

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 210251.**” Approval of this submission by FDA is not required before the labeling is used.

### **MARKET PACKAGE**

Please submit one market package of the drug product when it is available to the following address:

Suzanne Strayhorn  
Food and Drug Administration  
Center for Drug Evaluation and Research  
White Oak Building 22, Room: 6317  
10903 New Hampshire Avenue  
Silver Spring, Maryland  
*Use zip code **20903** if shipping via United States Postal Service (USPS).*  
*Use zip code **20993** if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

### **ADVISORY COMMITTEE**

Your application for BIKTARVY was not referred to an FDA advisory committee meeting because there are previously approved drugs in this antiretroviral class available, safety data did not reveal issues that were unexpected for the class and efficacy results from the Phase 3 trials did not pose specific concerns.

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies from birth to <18 years, because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(C) of the FDCA. These required studies are listed below.

- 3322-1 Conduct a study in patients 2 years to <18 years old who are HIV-1 infected, virologically suppressed (HIV-1 RNA <50 copies/mL) and on a stable antiretroviral regimen at the time of enrollment, to assess the pharmacokinetics, safety and tolerability, and antiviral activity of bicitegravir/emtricitabine/tenofovir alafenamide as part of a fixed dose combination (FDC) product. Study participants must be monitored for a minimum of 24 weeks to assess safety and durability of antiviral response.

Final Protocol Submission: 08/2018  
Study Completion: 12/2020  
Final Report Submission: 05/2021

- 3322-2 Conduct a study in HIV-1 infected, treatment naïve patients at least 4 weeks and weighing 4 to 12 kg to assess the pharmacokinetics, safety and tolerability, and antiviral activity of bicitegravir/emtricitabine/tenofovir alafenamide. Study participants must be monitored for a minimum of 24 weeks to assess safety and durability of antiviral response.

Final Protocol Submission: 08/2019  
Study Completion: 02/2022  
Final Report Submission: 06/2022

- 3322-3 Conduct a study to evaluate the pharmacokinetics and safety of bicitegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in neonates (birth to less than 4 weeks of age) who are HIV-1 infected or exposed and at high risk of infection to identify the appropriate dose and establish the safety of B/F/TAF.

Final Protocol Submission: 01/2021  
Study Completion: 02/2022  
Final Report Submission: 06/2022

Submit the protocols to your IND 125589, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED**

**PEDIATRIC ASSESSMENTS"** in large font, bolded type at the beginning of the cover letter of the submission.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. 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 prescribing information, 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 20705-1266

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> ).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by Form FDA 2253. 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).

### **MEDWATCH-TO-MANUFACTURER PROGRAM**

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at

<http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

**POST APPROVAL FEEDBACK MEETING**

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Suzanne Strayhorn, Regulatory Project Manager, at (240) 402-4247.

Sincerely,

*{See appended electronic signature page}*

John Farley, M.D., MPH  
Deputy Director  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosure(s):

Content of Labeling  
Container Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JOHN J FARLEY  
02/07/2018