

NDA 221104

NDA APPROVAL

Gilead Sciences, Inc.
Attention: April Raj, MS
Associate Director, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear April Raj:

Please refer to your new drug application (NDA) received February 27, 2026, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Bixlenvo (bictegravir and lenacapavir), tablets.

This NDA provides for the use of Bixlenvo (bictegravir and lenacapavir) fixed-dose combination tablets as a complete regimen for the treatment of HIV-1 in adults 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 with no known or suspected resistance to the individual components of Bixlenvo.

APPROVAL & LABELING

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.

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 [FDA.gov](http://www.fda.gov).¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible via publicly available labeling repositories.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on August 11, 2026, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to guidance for industry *SPL Standard for Content of Labeling Technical Qs & As*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 221104.**” Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Bixlenvo (bictegravir and lenacapavir), tablets shall be 24 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F).

MARKET PACKAGE

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

Yolande Togbe
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 6493
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 Bixlenvo was not referred to an FDA advisory committee because:

- (1) this drug is not the first in its class
- (2) the application did not raise significant safety or efficacy issues that were unexpected for a drug of this class

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

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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.

We are waiving the pediatric study requirement for ages birth to less than 2 years of age because the drug does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group and it is not likely to be used by a substantial number of pediatric patients in that age group. This is due to the small number of virologically suppressed patients with HIV-1 under 2 years of age who would be eligible to switch to a bictegravir and lenacapavir fixed-dose combination product.

We are deferring submission of your pediatric studies for ages greater than 2 to less than 18 years of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of FD&C Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FD&C Act. These required studies are listed below.

- 5039-1 Conduct a study to evaluate the pharmacokinetics, safety, and tolerability of bictegravir/lenacapavir in pediatric participants with HIV-1 infection who are less than 18 years of age and weigh at least 35 kg. Study participants must be evaluated for a minimum of 24 weeks to assess safety and durability of antiviral response.

Study Completion: 11/2026
Final Report Submission: 07/2027

- 5039-2 Conduct a study to evaluate the pharmacokinetics, safety, and tolerability of bictegravir/lenacapavir in pediatric participants with HIV-1 infection who are at least 2 years old and weigh at least 10 kg and less than 35 kg. Study participants must be evaluated for a minimum of 24 weeks to assess safety and durability of antiviral response.

Study/Trial Completion: 06/2030
Final Report Submission: 12/2030

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial. See guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act*.

Submit the protocol(s) to your IND 158963, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as an 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.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FD&C Act authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FD&C Act will not be sufficient to assess a signal of a serious risk of virologic failure due to the emergence of potential novel treatment resistance substitutions from the use of bictegravir and lenacapavir.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FD&C Act will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

- 5039-3 Conduct a phenotypic study to determine the impact of the integrase amino acid substitution R263G on bictegravir susceptibility and the capsid substitution K70E on lenacapavir susceptibility against HIV-1 in cell culture. Include as references integrase strand transfer inhibitor (INSTI) resistance-associated substitution (RAS) and capsid inhibitor RAS conferring low to high reductions in susceptibility to bictegravir and lenacapavir, respectively

The timetable you submitted on August 5, 2026, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 11/2026
Study Completion: 04/2027
Final Report Submission: 06/2027

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.³

³ See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act* (October 2019).
<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

Submit clinical protocol(s) to your IND 158963 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

REQUIRED POSTMARKETING PROTOCOL UNDER 505(o) , REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o), REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o).

Section 505(o)(3)(E)(ii) of the FD&C Act requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FD&C Act, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FD&C Act section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.

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 a Form FDA 2253. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website⁶.

If you have any questions, contact Yolande Togbe, Regulatory Project Manager, at (301) 796-7647 or yolande.togbe@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Prabha Viswanathan, MD
Director (Acting)
Division of Antivirals
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert
- Carton and Container Labeling

⁶ <https://www.uspnf.com/>

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/

PRABHA VISWANATHAN
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