

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

220018Orig1s000

Trade Name: YEZTUGO injection, for subcutaneous use

Generic or Proper Name: lenacapavir

Sponsor: Gilead Sciences, Inc.

Approval Date: June 18, 2025

Indication: For pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating YEZTUGO.

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APPROVAL LETTER



NDA 220018

NDA APPROVAL

Gilead Sciences, Inc.
Attention: Jamie Lam, MBS
Senior Manager, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Jamie Lam:

Please refer to your new drug application (NDA) received December 19, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Yeztugo (lenacapavir) injection, for subcutaneous use.

We also acknowledge receipt of information related to lenacapavir injection for your Gilead Access Program that was reviewed as part of this application.

This NDA provides for the use of Yeztugo (lenacapavir) injection for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition.

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.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use) 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 *SPL Standard for Content of Labeling Technical Qs and As*.²

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>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the 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 220018.**" 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 Yeztugo (lenacapavir) injection shall be 36 months from the date of manufacture when stored at 20°C to 25°C (68°F to 77°F) and protected from light.

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.

We are waiving the pediatric study requirement for ages birth to less than 16 years because necessary studies are impossible or highly impracticable. This is because PrEP is intended to reduce the risk of sexually acquired HIV-1 infections. Clinical trials of PrEP would be highly impracticable in a pediatric population who are not sexually mature and active or in whom the likelihood of sexual behavior is very low.

We note that you have fulfilled the pediatric study requirement for ages 16 to less than 18 years for this application.

POSTMARKETING COMMITMENT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 4836-1 Conduct a study to determine the phenotype of lenacapavir against the following HIV-1 capsids: 1) subtype A1 containing the P111T substitution; 2) subtype C containing the T54A, Q67R, I73V, and A105V substitutions, 3) subtype C containing the T54S and T107A substitutions, and 4)

subtype D containing the L56M and L69V substitutions, assessed individually and in the context in which these were identified. In your study, use a wildtype control and known resistance-associated substitutions, such as a subtype B capsid with the K70N substitution (24-fold change in EC₅₀ value) representing the range of reductions in susceptibility for comparison.

The timetable you submitted on May 13, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2026

Submit clinical protocols to your IND 153858 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

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

REPORTING REQUIREMENTS

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

³ For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/media/128163/download>.

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

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

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.⁶

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 website⁷.

If you have any questions, contact Kevin Allen, Regulatory Project Manager, at 301-837-7467 or Kevin.Allen@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Wendy Carter, DO
Director
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
 - Instructions for Use
- Carton and Container Labels

⁶ <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

⁷ <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/

WENDY W CARTER
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