

NDA 215973/S-06
NDA 215974/S-08

SUPPLEMENT APPROVAL

Gilead Sciences, Inc.
Attention: Ketki Malgaonkar
Senior Manager Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ketki Malgaonkar:

Please refer to your supplemental new drug applications (sNDAs) dated and received January 31, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sunlenca (lenacapavir) injection and Sunlenca (lenacapavir) tablet.

These Prior Approval supplemental new drug applications provide for:

- An alternative 300 mg once weekly, oral bridging dosing regimen for Sunlenca (lenacapavir) tablet for the treatment of HIV-1 infection in heavily treatment experienced adults with multidrug resistant HIV-1 infection, when a patient plans to miss a scheduled subcutaneous injection
- Labeling changes to WARNINGS AND PRECAUTIONS, 5.3 Injection Site Reactions and ADVERSE REACTIONS, 6.1 Clinical Trials Experience, regarding improper administration (intradermal injection) and associated serious injection site reactions, including necrosis and ulcer
- Labeling changes to DRUG INTERACTIONS, 7.3 Established and Other Potentially Significant Drug Interactions, regarding interactions with systemically-administered dexamethasone
- Labeling changes to CLINICAL PHARMACOLOGY, 12.4 Microbiology, regarding lenacapavir resistance with suboptimal adherence to other antiretroviral drugs in the regimen
- Updates to Patient Information, “How should I receive and take Sunlenca?” section with instructions on how to proceed if a patient plans to miss an injection

APPROVAL & LABELING

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

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 FDA.gov.¹ 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 *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, 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 these supplemental applications, 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.

We are waiving the pediatric study requirement from birth to less than 12 years of age because the necessary studies are impossible or highly impracticable. This is because

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>.

most children living with HIV-1 will not experience multiple courses of antiretroviral regimens and will therefore not be considered highly treatment experienced until adolescence.

We are deferring submission of your pediatric study for ages 12 to less than 18 years of age and weighing at least 35 kg for this application because this product is ready for approval for use in adults and pediatric studies have not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of FDCA. This required study is listed below.

- 4728-1 Conduct a study to evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of lenacapavir, including oral bridging, in treatment-experienced children living with HIV-1 infection who are less than 18 years of age and weighing at least 35 kg. The safety and antiretroviral activity of lenacapavir in pediatric subjects must be evaluated for a minimum of 24 weeks. Pharmacokinetic and safety data for oral bridging may be obtained from other ongoing studies, (b) (4)

Study Completion: 03/2027

Final Report Submission: 09/2027

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

Reports of this required pediatric postmarketing study 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 this study. 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. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-*

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>.

*Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*⁴

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 FDA.gov.⁵ Information and Instructions for completing the form can be found at FDA.gov.⁶

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplements for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDAs that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplements pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

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

Your product, approved under NDA 215973, 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.⁷

⁴ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁶ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁷ <https://www.fda.gov/comboination-products/guidance-regulatory-information/postmarketing-safety-reporting-comboination-products>

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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 (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
 - Instructions for Use (Healthcare Provider)

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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