CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

220018Orig1s000
220020Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number	220018
Applicant Name	Gilead Sciences, Inc.
Drug Product Name	YEZTUGO (lenacapavir) injection
Dosage Form	Injection
Proposed Strength(s)	463.5 mg/1.5 mL (309 mg/mL)
NDA Classification	Type 10 – New Indication Submitted as Distinct NDA – Not Consolidated
Route of Administration	Subcutaneous
Maximum Daily Dose	927 mg
Rx/OTC Dispensed	Rx
Proposed Indication	Pre-exposure prophylaxis (PrEP) to prevent sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg.
Drug Product Description	Lenacapavir Injection is a sterile, preservative-free solution for subcutaneous administration, packaged in a glass vial with (b) (4) (overfill of (b) (4) to allow for withdrawal of 1.5 mL.
Co-packaged product information	Vial kit includes two vials of lenacapavir injection, two (b) (4) disposable syringes, two withdrawal needles, and two injection safety needles.
Device information	Withdrawal needle: 18G 1.5-inch withdrawal needle with Luer lock fitting; (b) (4) Disposable syringe: 3 mL (b) (4) disposable syringe with Luer lock fitting; (b) (4) Injection safety needle: 22G 0.5-inch injection safety needle with Luer lock fitting; (b) (4)

Storage Temperature/ Conditions	Store at 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) (see USP Controlled Room Temperature). Keep vials in the original carton until ready for use to protect from light.		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Not assigned this review cycle	
	Drug Product/ Labeling	Akshata Nevrekar	Hudson Roth
	Manufacturing	Ruth Moore	Kshitij Patkar
	Biopharmaceutics	Not assigned this review cycle	
	Microbiology	Shannon Heine	Neal Sweeney
	Other (specify)	Not assigned this review cycle	
	RBPM	Omolara Oyinlola-Adeyemi	
	ATL	Hudson Roth	
Consults	N/A		

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating:

36 months when stored at 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F), protect from light.

b. Additional Comments for Action: N/A

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

Lenacapavir injection was originally approved under NDA 215973 for the treatment of HIV-1 infection in adults (b) (4) Gilead submitted NDA 220018 to seek approval for lenacapavir injection for the new indication of pre-exposure prophylaxis (PrEP) of HIV-1. The Applicant cross-references the entirety of Module 3 in NDA 215973 for the CMC information to support approval of NDA 220018; no new CMC information has been submitted under NDA 220018.

Lenacapavir injection will be supplied as a sterile, preservative-free, yellow solution with a strength of 309 mg/mL for subcutaneous injection. The drug

product will be packaged in a vial kit, containing two vials of the drug product, two withdrawal needles, two syringes, and two safety injection needles. Lenacapavir injection proposed for PrEP for HIV-1 under NDA 220018 has the same active ingredient and formulation as lenacapavir injection for HIV-1 treatment approved under NDA 215973. The drug product quality information has already been assessed and found adequate under NDA 215973, and there are no changes proposed for NDA 220018. Therefore, the application is acceptable from a drug product quality perspective.

The proposed labeling for NDA 220018 has been reviewed from the product quality perspective and found adequate.

The manufacturing process for lenacapavir injection (b) (4) . The manufacturing design and control strategy for the finished product have already been assessed and approved in NDA 215973 and there are no changes proposed for NDA 220018. The manufacturing facilities listed for NDA 220018 have been approved for NDA 215973 and are currently in satisfactory CGMP compliance status. Therefore, the application is acceptable from a manufacturing and facilities perspective.

The information related to sterility assurance referenced to NDA 215973 was reviewed and considered adequate. (b) (4)

As all review disciplines found NDA 220018 adequate from the CMC perspective, OPQ recommends approval for NDA 220018 for lenacapavir injection.

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:

Drug Substance	**-**	**N/A**
Drug Product	**-**	**Adequate**
Quality Labeling	**-**	**Adequate**
Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**N/A**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): No

5. Life-Cycle Considerations
Established Conditions per ICH Q12: No

Comparability Protocols (PACMP): No

Additional Lifecycle Comments:
N/A

Application Technical Lead Name and Date:
Hudson Roth, Ph.D., 5/7/2025

Hudson Roth

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CHAPTER IV: LABELING

NDA Number	220018
Assessment Cycle Number	01
Drug Product Name	220018: (lenacapavir) injection, for subcutaneous use

Assessment Recommendation: Adequate

Item	Assessment Conclusion	SDN # where labeling is adequate ("N/A" otherwise)
Prescribing Information Labeling	Adequate	**3**
Patient Information	Adequate	**3**
Instruction for Use (IFU)	Adequate	**3**
Container Labels	Adequate	**3**
Carton Labeling	Adequate	**3**

Brief Description of Outstanding Issues: No outstanding issues. Revisions/edits have been made to the PI as a part of labelling negotiations.

The Applicant is asked (comment to the Applicant in the PI) to include temperature excursion statement on the carton/container label for the drug product.

Submissions being reviewed:

Document Reviewed (eCTD #, SDN #)	Date Received	Information Provided
Prescribing information	12/19/2024	yes
Container and carton label	12/19/2024	yes
Instructions for use	12/19/2024	yes

1.0 PRESCRIBING INFORMATION[1]

Assessment of Product Quality Related Aspects of the Prescribing Information:

[1] Labeling Review Tool (LRT) (March 2022), including use of consistent terminology for dosage form and unit of measure for strength in the product title and DOSAGE FORMS AND STRENGTHS heading in Highlights, in the DOSAGE AND ADMINISTRATION, DOSAGE FORMS AND STRENGTHS, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING sections (see page 2 of LRT)

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

(b) (4)

[redacted]

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights[2] [21 CFR 201.57(a)(2)]		
Established name(s)[3]	Adequate	
Route(s) of administration	Adequate	
Controlled drug substance symbol (if applicable)	N/A	

[2] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018)

[3] Established name = [Drug] [Route of Administration] [Dosage Form]. Do use not "USP" descriptor in the product title or within the Highlights (see page 3 of LRT).

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Initial U.S. Approval [§201.57(a)(3)]	Adequate	
Dosage Forms and Strengths Heading in Highlights [§ 201.57(a)(8)]		
Dosage form(s)[4] and strength(s) in metric system[5]	Adequate	
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).[6]	Adequate	Included drug name 'lenacapavir' during labelling negotiations.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."[7]	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.[8]	Adequate	

Assessment: *Adequate*

[4] Draft guidance: *Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format* (January 2018); USP <1151>; USP Nomenclature Guideline
[5] Labeling Review Tool (March 2022, page 13), include limited packaging information; USP <7>
[6] Guidance: *Naming of Drug Products Containing Salt Drug Substances* (June 2015); MAPP 5021.1
[7] Guidance: *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation* (March 2013)
[8] Guidance: *Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use* (October 2018); USP <659>

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)[9]

(b) (4)

[redacted]

[9] See § 201.57(c)(3); draft guidance: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023); Labeling Review Tool (March 2022, page 25)

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents and/or soft food[10], storage conditions needed to maintain the stability of the reconstituted or diluted product).	N/A	
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food).	Adequate	

[10] Draft Guidance: Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
For parenteral products: include statement: *"Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*[11]	Adequate	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.[12] Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.*[x]*"* with x numerical citation to "OSHA Hazardous Drugs."	N/A	

Assessment: *Adequate*

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)[13]

[11] §201.57(c)(3)(iv)
[12] USP General Notices 2.30 Legal Recognition
[13] See § 201.57(c)(4); Labeling Review Tool (March 2022, page 29)

3 DOSAGE FORMS AND STRENGTHS

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	
Strength(s) in metric system	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride). No equivalency statement.	Adequate	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable.	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package (see USP <659>).	Adequate	

Assessment: *Adequate*

1.2.3 Section 11 (DESCRIPTION)[14]

11 DESCRIPTION

(b) (4)

[redacted]

[14] See § 201.57(c)(12); Labeling Review Tool (March 2022, page 56)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)[15] [§ 201.57(c)(12)(i)(A)].	Adequate	
Dosage form(s) and route(s) of administration [§ 201.57(c)(12)(i)(B)].	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)" [§ 201.57(c)(12)(i)(C)].	Adequate	
List inactive ingredients (not required for oral use, except for colorant) by the USP/NF names in alphabetical order.[16] Avoid brand names. [§ 201.57(c)(12)(i)(C)].	Adequate	
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	Adequate	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of	N/A	

[15] Use of "USP" descriptor is not required to be included next to the established name throughout Prescribing Information (PI) labeling. If an applicant wants to use the "USP" descriptor next to the established name in the PI, recommend limiting its use to the product quality sections of the Full Prescribing Information (FPI) (i.e., DOSAGE FORMS AND STRENGTHS, DESCRIPTION, HOW SUPPLIED/STORAGE AND HANDLING) (see page 3 of LRT).

[16] Per § 201.100(b)(5)(i) and (ii), flavoring and colorants may be designated as such without naming their components except for FD&C Yellow No 5 and FD&C Yellow No 6, which must be listed per § 201.20. Per § 201.100(b)(5)(iii), trace amounts of harmless substances added solely for individual product identification need not be named. If an applicant wants to use the National Formulary (NF) descriptor next to excipients, recommend limiting its use to the product quality sections of the FPI (see page 3 of LRT). Do not list brand names, e.g., Opadry, Eudragit, Polistirex, etc.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].		
Sterility statement (if applicable) [§ 201.57(c)(12)(i)(D)].	Adequate	
Pharmacological/Therapeutic class[17] [§ 201.57(c)(12)(i)(E)].	Adequate	
Chemical name[18], structural formula, molecular weight [§ 201.57(c)(12)(i)(F)].	Adequate	
If radioactive, statement of important nuclear characteristics [§ 201.57(c)(12)(i)(G)].	N/A	
Other important chemical or physical properties (such as pKa or pH) [201.57(c)(12)(ii)].	Adequate	
For oral prescription drug products, include gluten statement[19] (if applicable).	N/A	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity").	Adequate	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

Assessment: *Adequate*

[17] Listed before "indicated for" in INDICATIONS AND USAGE of Highlights section [§ 201.57(a)(6)]; can also search the term "FDA EPC Text Phrases" in FDA's Labeling Resources for Human Prescription Drugs for the most recent EPC list.

[18] Chemical names do not need to be capitalized unless it appears at the beginning of a sentence (see *Preferred IUPAC Names Provisional Recommendation*, September 2004; Chapter 1, par. 16 Name writing, p.80-90).

[19] Draft guidance: *Gluten in Drug Products and Associated Labeling Recommendations* (December 2017)

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)[20]

(b) (4)

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s) [§ 201.57(c)(17)].	Adequate	
Strength(s) in metric system. [§ 201.57(c)(17)(i)] If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety. No equivalency statement.	Adequate	
Available units (e.g., bottles of 100 tablets) [§ 201.57(c)(17)(ii)].	Adequate	

[20] See § 201.57(c)(17); Labeling Review Tool (March 2022, page 70). Consider including proprietary name and established name.

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s) [§ 201.57(c)(17)(iii)].	Adequate	
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored."	N/A	
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package (see USP <659>).	Adequate	
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs." [§ 201.57(c)(17)(iv)]	Adequate	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature. (see USP <659>).	Adequate	
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of	Adequate	

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*[21]		
Include information about child-resistant packaging[22] (if chosen by manufacturer).	N/A	

Assessment: *Adequate*

1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug review division if the product contains any of these inactive ingredients.

Please include your comments about other sections of labeling if they contain product quality information.

1.2.6 Manufacturing Information After Section 17 (for drug products)[23]

Item	Item in Proposed Labeling (choose "Adequate" or "Inadequate")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer.	Adequate	

Assessment: *Adequate*

[21] Guidance: *Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex* (December 2014)
[22] Guidance: *Child-Resistant Packaging Statements in Drug Product Labeling* (August 2019)
[23] § 201.1(h)(5) and 201.1(i); Labeling Review Tool (March 2022, page 74)

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information):

Item	Item in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[24]	Adequate	
Special preparation instructions (if applicable).	N/A	
Storage and handling information (if applicable).	Adequate	
If the product contains a desiccant, ensure the desiccant has a warning (e.g., "Do not eat.") and the size and shape of the desiccant differ from the dosage form.	N/A	
Active ingredient(s) (if applicable).	Adequate	
Alphabetical listing of inactive ingredients (if applicable).	Adequate	
Name and location of business (street address, city, state, and zip code) of manufacturer, distributor, and/or packer.	Adequate	

Assessment: *Adequate*

3.0 CONTAINER AND CARTON LABELING[25]

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[24] Established name = [Drug] [Route of Administration] [Dosage Form]
[25] Carton and Container Labeling Resources

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Proprietary name and established name[27], (font size and prominence) [§ 201.10(g)(2)].	Adequate	Yes	
Strength(s) in metric system [§ 201.100(b)(4) & 201.100(d)].[28]	Adequate	Yes	
Route(s) of administration, not required for oral use [§ 201.100(b)(3)].	Adequate	Yes	
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP [§ 201.10(d)(1) & 201.100(b)(4), USP <1121>].	Adequate	No	
Net contents (e.g., tablet count, volume of liquid) [§ 201.51(a)].[29]	Adequate	Yes	
"Rx only" displayed on the principal display [§ 201.100(b)(1)].	Adequate	Yes	
NDC (requested, but not required for all labels or labeling) [§ 201.2 & 207.35].	Adequate	Yes	
Lot number and expiration date [§ 201.18 & 201.17].	Adequate	Yes	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the beyond-use-date (BUD).	Adequate	Yes	Temperature excursions included on carton label. Excursions not included on container (vial) label due to space limitation.

[27] Established name = [Drug] [Route of Administration] [Dosage Form]

[28] Express as " XX mg per tablet" or "XX mg per capsule" for strength of professional samples of solid oral dosage form with small net quantities per container (e.g., 5 or less) or blister pack/carton. See Guidance: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)

[29] § 201.51(h): A drug shall be exempt from compliance with the net quantity declaration required by this section if it is an ointment labeled "sample", "physician's sample", or a substantially similar statement and the contents of the package do not exceed 8 grams.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
For injectable drug products for parenteral administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement. (See USP <659>).	Adequate	Yes	
Name of all inactive ingredients, in alphabetical order [§ 201.10(a)] [except for oral drug per § 201.100(b)(5) or limited space per § 201.10(i)(2)].	Adequate	No	
For parenteral injectable dosage forms, include quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. [§ 201.100(b)(5)(iii)].	N/A	No	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol at 60 °F. (15.56 °C) [§ 201.10(d)(2)].	N/A	Yes	
Linear Bar code [§ 201.25(c)(2)].[30]	Adequate	Yes	
Adequate directions for use: "Recommended Dosage: See Prescribing Information" [§ 201.5 & 201.55].	Adequate	Yes	

[30] See § 201.25(b)(1)(i) for a list where bar code is not required, e.g., prescription drug samples, medical gases, radiopharmaceuticals, etc.

Item	Item in Proposed Carton Labeling (choose "Adequate", "Inadequate", or "N/A")	Is item in Container Labels same as that of Carton Labeling?	Assessor's Comments about Container Labels and Carton Labeling (If an item is Inadequate or different, provide more details, as appropriate)
Name of manufacturer/distributor /packer [§ 201.1(a), 201.1(h)(5)].	Adequate	Yes	
"Keep out of reach of children" statement, optional for Rx, required for OTC [§ 201.66(c)(5)(x)].	Adequate	No	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	Yes	
No text on Ferrule and Cap overseal of a vial of injectable products unless a cautionary statement is required. (USP <7>).	Adequate	Yes	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	Yes	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.[31]	N/A	Yes	
And others if space is available.	N/A	Yes	

Assessment of Carton Labels and Container Labeling: *Adequate*

[31] USP General Notices 3.20 Indicating Conformance

4. OUTSTANDING ISSUES AND RECOMMENDATIONS

No Outstanding issues. Comments have been issued to the Applicant in the PI and revisions/edits have been made to the PI during labelling negotiations.

Primary Labeling Assessor Name and Date: Akshata Nevrekar; 5/6/2025

Secondary Assessor Name and Date (and Secondary Summary, as needed): David Claffey; 5/6/2025

Akshata Nevrekar

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David Claffey

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U.S. FOOD & DRUG ADMINISTRATION

CHAPTER VII: MICROBIOLOGY

IQA ANDA Assessment Guide Reference

Product Information	
NDA Number	220018
Assessment Cycle Number	1
Drug Product Name / Strength	Lenacapavir (GS-6207) / 309 mg/mL
Route of Administration	Subcutaneous
Applicant Name	Gilead Sciences, Inc.
Therapeutic Classification/ OND Division	Type 10-New Indication Submitted as Distinct NDA – Not Consolidated / CDER/OND/OID/DAV
Manufacturing Site	(b) (4)
Method of Sterilization	

Assessment Recommendation: **Adequate**

Assessment Summary:

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
Seq 0002 (3)	19 December 2024
Seq 0014 (15)	18 March 2025

Highlight Key Issues from Last Cycle and Their Resolution: N/A

Remarks: The subject drug is proposed for subcutaneous injection as indicated for pre-exposure prophylaxis (PrEP) of human immunodeficiency virus type 1 (HIV-1) infection. The applicant cross-references relevant quality documents and data of lenacapavir LEN previously submitted under the approved NDA for Sunlenca injection, NDA 215973. The applicant provided an LoA from Gilead Sciences, Inc., dated 17 December 2024, for NDA 215973.

The submission is recommended for approval from the standpoint of product quality microbiology.

Concise Description of Outstanding Issues: N/A

Supporting Documents:

- (b) (4) .
- Microbiology Reviews of NDA 215973 (N215973MR01.docx, overall inadequate), dated 23 January 2022 (*N215973MR02.docx*, adequate), dated 1 July 2022 regarding the manufacture of the subject drug product at the (b) (4) manufacturing facility.

(b) (4)

Select Number of Approved Comparability Protocols: 0

The subject submission is in support of a new indication for the subcutaneous (SC) injection of lenacapavir (LEN; GS-6207). LEN (Sunlenca®) was approved in combination with other antiretrovirals for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection on 22 December 2022. The subject application is regarding the use of LEN for HIV-1 pre-exposure prophylaxis (PrEP) in adults and adolescents for the previously approved 309 mg/mL injection dosage forms.

The SC LEN injection has the same active ingredient, formulation, and dose as the FDA approved SC LEN injection for Sunlenca®, the relevant quality documents and data of LEN are incorporated via cross-reference to the previously submitted and reviewed NDA for Sunlenca® injection, NDA 215973. The applicant states that the CMC information for LEN for PrEP injection, 309 mg/mL in its entirety is submitted via the cross-reference letter to Sunlenca injection NDA 215973.

(See Section 1.4.1, pg. 2-3 of *Letter of Authorization – Gilead, NDA 215973, NDA 220020)*

Letter of Authorization (LoA) for NDA # 215973

The applicant provided an LoA from Gilead Sciences, Inc., dated 17 December 2024, for NDA 215973 for Sunlenca® (Lenacapavir) Injection.

(See Section 1.4, pg. 4-6 of *Cross-reference to Other Applications – NDA 215973 SN 001, 0036, 0047, 0088, 0094, 0095, 0096, 0099, 0117, 0124, 0131, 0141)*

A detailed table indicating the sequence number where specific information is contained in referenced NDA 215973 was provided. The cross-referenced information regarding the subject drug product manufacturing and sterility assurance validation studies for both manufacturing facilities was listed. This information has been previously assessed.

(See Section 1.14.1.3, *Draft Labeling Text – Clean – PDF*)

NOTE: According to the previous reviews and the referenced sequence for NDA 215973, the bacterial endotoxins specification is NMT (b) (4)

Maximum dose according to the package insert:
927 mg by subcutaneous injection in adults and adolescents weighing at least 35 kg.

(b) (4)

(b) (4)

The endotoxins dose at the specification and the maximum dose when administered to adolescents weighing 35 kg exceeds the USP <85> recommendation of 5 EU/kg/hr.

The draft labeling for the subject drug product states that the product is “indicated for pre-exposure prophylaxis (PrEP) to prevent sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg.” While the proposed maximum dose and route of administration remain the same as approved, the target patient population has expanded to include adolescents. The potential endotoxins dose at the specification and the maximum dose when administered to adolescents weighing 35 kg exceeds the USP <85> recommendation of 5 EU/kg/hr. Therefore, the following therefore the following Product Quality Microbiology Information Request was sent to the applicant on 5 March 2025.

We acknowledge the referenced sequence for NDA 215973 regarding the drug product specification. We also acknowledge that the current submission proposes to expand the target patient population for the subject drug product to include adolescents weighing at least 35 kg. Although the proposed maximum dose and route of administration remain the same as the approved drug product, based on the a maximum dose of 927 mg for subcutaneous administration to adolescents weighing at least 35 kg and the proposed endotoxins specification of NMT (b) (4) *the maximum potential bacterial endotoxins dose administered to an adolescent patient weighing 35 kg would exceed the USP <85> recommended maximum level of NMT 5 EU/kg/hr for routes of administration other than intrathecal. Therefore, revise the proposed bacterial endotoxins specification for the subject drug product to be within the USP recommended limit when administered to adolescent patients based on the maximum dose in the labeling. Additionally, provide the appropriate documentation to reflect the change, e.g. finished product specification, stability protocol, justification of specification, and revised maximum valid dilution calculation for bacterial endotoxins testing.*

Summary of the applicant’s response received 18 March 2025
(See Seq 0014, Section 1.11.1, pg. 2-3 of *Response to FDA Information Request (Microbiology) Regarding Endotoxin Limit in DP dated 2025-03-05*)
The applicant agreed to revise the bacterial endotoxins acceptance limit from not more than (b) (4) to not more than (b) (4) in the drug product specification to ensure that patients weighing 35 kg will not exceed the USP <85> recommended maximum level of NMT 5 EU/kg/hr for routes of administration other than intrathecal.

The applicant provided the following calculation:

(b) (4)

[redacted]

The applicant also states that revised Sections 3.2.P.5.1 and 3.2.P.5.6 reflecting the revised acceptance limit for bacterial endotoxins, a revised finished product specification, and an updated Method Verification document were provided. This information was assessed in the cross-referenced NDA 215973.

Assessment: *Adequate*

The information regarding the description of the drug product and composition as well as the description of the container closure system referenced in the subject submission was previously assessed and found adequate in Microbiology Reviews of NDA 215973 (b) (4) [redacted]. The information regarding the manufacture of the subject drug product at the (b) (4) [redacted]. manufacturing facility referenced in the subject submission, including the validation of the (b) (4) [redacted] sterilization process, was assessed for sterility assurance in Microbiology Reviews of NDA 215973 (*N215973MR01.docx*, overall inadequate), dated 23 January 2022 and (*N215973MR02.docx*, adequate), dated 1 July 2022. (b) (4) [redacted] The applicant has provided an adequate description of the drug product composition and the container closure system. Therefore, the applicant has cross-referenced an approved application for which multiple product quality microbiology reviews have been performed and cover the sequences referred to in the subject application. The information related to sterility assurance that was referenced was considered adequate. Since the draft labeling for the subject drug product states that the product is "indicated for pre-exposure prophylaxis (PrEP) to prevent sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg." (b) (4) [redacted]

(b) (4)

MICROBIOLOGY LIST OF DEFICIENCIES

None.

Primary Microbiology Assessor Name and Date: Shannon Heine, PhD, 01 April 2025
Secondary Assessor Name and Date: Neal Sweeney, PhD, 01 April 2025
"I concur."

Shannon Heine

Digitally signed by Shannon Heine
Date: 4/02/2025 09:20:52AM
GUID: 5d3b22d0000f55e971f4d77300610879

Neal Sweeney

Digitally signed by Neal Sweeney
Date: 4/02/2025 08:19:10PM
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/s/

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