CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215973Orig1s000
215974Orig1s000

OTHER REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	November 29, 2022
To:	Kevin Allen, MS Regulatory Project Manager **Division of Antivirals (DAV)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Jessica Chung, PharmD, MS Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Wendy Lubarsky, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name), Dosage Form and Route, Application Type/Number:	SUNLENCA (lenacapavir) injection, for subcutaneous use, NDA 215973 SUNLENCA (lenacapavir) tablets, for oral use, NDA 215974
Applicant:	Gilead Sciences, Inc.

1 INTRODUCTION

On June 27, 2022, Gilead Sciences, Inc. submitted for the Agency's review a Class 2 Resubmission of their original New Drug Application (NDA) 215973 for SUNLENCA (lenacapavir) injection and NDA 215974 for SUNLENCA (lenacapavir) tablets, in response to the Agency's Complete Response (CR) letters dated February 28, 2022. The proposed indication for SUNLENCA (lenacapavir) injection and SUNLENCA (lenacapavir) tablets, in combination with other antiretroviral(s), is for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Antivirals (DAV) on July 6, 2022, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for SUNLENCA (lenacapavir) injection and SUNLENCA (lenacapavir) tablets.

2 MATERIAL REVIEWED

- Draft SUNLENCA (lenacapavir) injection and SUNLENCA (lenacapavir) tablets PPI received on June 27, 2022 and November 9, 2022, and received by DMPP and OPDP on November 15, 2022.
- Draft SUNLENCA (lenacapavir) injection and SUNLENCA (lenacapavir) tablets Prescribing Information (PI) received on June 27, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on November 15, 2022.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss.

In our collaborative review of the PPI we:

- simplified wording and clarified concepts where possible
- ensured that the PPI is consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information

- ensured that the PPI is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

4 CONCLUSIONS

The PPI is acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPI.

Please let us know if you have any questions.

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11/29/2022 09:48:05 AM

BARBARA A FULLER
11/29/2022 09:55:05 AM

LASHAWN M GRIFFITHS
11/29/2022 09:55:57 AM

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: November 29, 2022

To: Kevin Allen, Regulatory Project Manager
Division of Antivirals (DAV)

From: Wendy Lubarsky, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Sam Skariah, Team Leader, OPDP

Subject: OPDP Labeling Comments for SUNLENCA (lenacapavir) injection, for subcutaneous use; SUNLENCA (lenacapavir) tablets, for oral use

NDA: 215973, 215974

Background:

In response to DAV's consult request dated July 5, 2022, OPDP has reviewed the proposed Prescribing Information (PI), Patient Package Insert (PPI), Instructions for Use (IFU), and carton and container labeling for the original NDA submission for SUNLENCA (lenacapavir) injection, for subcutaneous use, and SUNLENCA (lenacapavir) tablets, for oral use (Sunlenca).

PI/PPI/IFU:
OPDP's review of the proposed PI/IFU is based on the draft labeling emailed to OPDP on November 15, 2022 and accessed from SharePoint on November 28, 2022, and our comments are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed for the proposed PPI, and comments will be sent under separate cover.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling emailed to OPDP on November 28, 2022, and our comments are provided below.

Thank you for your consult. If you have any questions, please contact Wendy Lubarsky at (240) 402-7721 or wendy.lubarsky@fda.hhs.gov .

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WENDY R LUBARSKY
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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	October 12, 2022
Requesting Office or Division:	Division of Antivirals (DAV)
Application Type and Number:	NDA 215973 NDA 215974
Product Name and Strength:	Sunlenca (lenacapavir) Injection: 463.5 mg/1.5 mL (309 mg/mL) Tablet: 300 mg
Applicant/Sponsor Name:	Gilead Sciences, Inc. (Gilead)
TTT ID #:	2022-21-1
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph
DMEPA 1 Team Leader:	Madhuri Patel, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted a response, received on September 12, 2022 and September 28, 2022, to FDA's request to develop a 'Welcome Card' for the 4-count packaging configuration of Sunlenca Tablet. The Division of Antivirals (DAV) requested that we review the response to determine if it is acceptable from a medication error perspective. These submissions are in response to recommendations that we made during a previous label and labeling review.[a]

2 DISCUSSION AND CONCLUSION

In the previous label and labeling review of Sunlenca, we noted that Gilead was proposing two packaging configurations of Sunlenca tablets (4-count and 5- count) to support the two oral dosing regimens proposed in the prescribing information. A 'Welcome Card' to provide patients with directions on their dosing regimen was also proposed but only for the 5-count packaging configuration, therefore, we requested submission of a proposed 'Welcome Card' for the 4-count packaging configuration. In their response to this request, Gilead stated a 'Welcome

[a] Fanari, M. Label and Labeling Review for Sunlenca (NDA 215973 & NDA 215974). Silver Spring (MD): FDA, CDER, OSE, DMEPA1 (US); 2022 SEPT 1. RCM No.: 2022-21.

Card' for the 4-count packaging configuration would not provide any additional benefit over the existing patient-directed labeling. In addition, Gilead noted that the 4-count packaging configuration of Sunlenca tablets would only be distributed to healthcare providers (HCP) from specialty pharmacies and not be available in retail or hospital pharmacies. Based on this information, we agree that a 'Welcome Card' is not required for the 4- count packaging configurations since HCP will be able to oversee its correct use and ensure patients have the correct count packaging for their prescribed dose regimen. However, for further clarity and to mitigate any potential for confusion between the two oral dosing regimens we have provided an additional recommendation in section 3 for Gilead.

3 RECOMMENDATIONS FOR GILEAD SCIENCES, INC. (GILEAD)

We agree with your proposal to not provide a 'Welcome Card' for the 4-count packaging configuration of Sunlenca tablets. However, we recommend that the carton labeling for this configuration be revised as follows to highlight that initiation of the Sunlenca tablets should occur on the same day as a Sunlenca injection:

A. Add the following statements to the principal display panel for the 4-count Sunlenca tablet carton labeling:

> Your healthcare provider will tell you when to take Sunlenca tablets.
> You will be given two injections of Sunlenca by your healthcare provider on the same day you take two Sunlenca tablets in this blister pack.

B. In addition, the two statements below should be deleted:

(b) (4)

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/s/

MELINA N FANARI
10/12/2022 09:43:40 AM

MADHURI R PATEL
10/12/2022 09:52:03 AM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	September 1, 2022
Requesting Office or Division:	Division of Antivirals (DAV)
Application Type and Number:	NDA 215973 NDA 215974
Product Name and Strength:	Sunlenca (lenacapavir) Injection: 463.5 mg/1.5 mL (309 mg/mL) Tablet: 300 mg
Product Type:	Combination Product and Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Gilead Sciences, Inc. (Gilead)
FDA Received Date:	June 27, 2022
TTT #:	2022-21
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph
Acting DMEPA 1 Team Leader:	Madhuri Patel, PharmD

1 REASON FOR REVIEW

As part of the approval process for Sunlenca (lenacapavir) injection and tablet, the Division of Antivirals (DAV) requested that we review the proposed Sunlenca prescribing information (PI), instruction for use (IFU), patient prescribing information (PPI), container labels and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

DMEPA previously reviewed the proposed prescribing information (PI), instruction for use (IFU), patient prescribing information (PPI), container labels and carton labeling for Sunlenca under the initial NDA submissions[a]. However, on February 28, 2021, a Complete Response action was issued for NDA 215974 and NDA 215974.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
ISMP Newsletters*	C-N/A
FDA Adverse Event Reporting System (FAERS)*	D-N/A
Other	E-N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 FINDINGS AND RECOMMENDATIONS

The proposed PI, PPI, IFU, container labels and carton labeling are reflective of the labels and labeling previously reviewed by DMEPA[b]. We note that there will be two proposed oral loading regimens for Sunlenca (consisting of 4-count or 5-count tablets) and Gilead has proposed the use of a 'Welcome card' (Appendix F.2) in the carton of the Sunlenca (5-count tablet) packaging

[a] Fanari, M., Label and Labeling Review for Sunlenca (NDA 215973 and NDA 215974). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Oct 21. Panorama No.: 2021-1278-1

[b] Fanari, M., Label and Labeling Review for Sunlenca (NDA 215973 and NDA 215974). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Oct 21. Panorama No.: 2021-1278-1

configuration to minimize the risk of dosing errors. In addition, the carton labeling for the two available tablet configurations (4-count or 5-count tablets) incorporate the use of color to provide visual differentiation. We consider this strategy appropriate, however, a 'Welcome Card' should also be developed and provided in the Sunlenca (4-count tablet) packaging configuration. We provide comments in Section 4 for Gilead Sciences, Inc.

4 RECOMMENDATIONS FOR GILEAD SCIENCES, INC.

Identified Issues and Recommendations for Gilead Sciences, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Welcome Card			
	A welcome card was only proposed for the Sunlenca 5-count packaging configuration.	Minimize risk of dosing errors.	Please submit a proposed 'Welcome Card' for Agency review that is consistent with the Sunlenca 4-count packaging configuration.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Sunlenca injection and tablet that Gilead Sciences, Inc. submitted on June 27, 2022.

<table>
<tr><th colspan="2">Table 2. Relevant Product Information for Sunlenca</th></tr>
<tr><td>Initial Approval Date</td><td>N/A</td></tr>
<tr><td>Active Ingredient</td><td>lenacapavir</td></tr>
<tr><td>Indication</td><td>Treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults (b) (4) with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations</td></tr>
<tr><td>Route of Administration</td><td>Subcutaneous, Oral</td></tr>
<tr><td>Dosage Form</td><td>Injection, Tablet</td></tr>
<tr><td>Strength</td><td>Injection: 463.5 mg/1.5 mL (309 mg/mL); Tablet: 300 mg</td></tr>
<tr><td>Dose and Frequency</td><td>• Initiation with one of two options followed by once every 6-months maintenance dosing. Tablets may be taken without regard to food. (2.1)
<table>
<tr><td colspan="2">Initiation Option 1</td></tr>
<tr><td>Day 1</td><td>927 mg by subcutaneous injection (2 x 1.5 mL injections) and
600 mg orally (2 tablets)</td></tr>
<tr><td>Day 2</td><td>600 mg orally (2 tablets)</td></tr>
<tr><td colspan="2">Initiation Option 2</td></tr>
<tr><td>Day 1</td><td>600 mg orally (2 tablets)</td></tr>
<tr><td>Day 2</td><td>600 mg orally (2 tablets)</td></tr>
<tr><td>Day 8</td><td>300 mg orally (1 tablet)</td></tr>
<tr><td>Day 15</td><td>927 mg by subcutaneous injection (2 x 1.5 mL injections)</td></tr>
<tr><td colspan="2">Maintenance</td></tr>
<tr><td colspan="2">927 mg by subcutaneous injection (2 x 1.5 mL injections) every 6 months (26 weeks) from the date of the last injection +/-2 weeks.</td></tr>
</table></td></tr>
<tr><td>How Supplied</td><td>Injection: packaged in a dosing kit containing:
- 2 single-dose clear glass vials, each containing sufficient volume to allow withdrawal of 463.5 mg/1.5 mL (309 mg/mL) of lenacapavir. Vials are sealed with a stopper and aluminium overseal with flip-off cap.
- 2 vial access devices, 2 disposable syringes, and 2 injection safety needles for subcutaneous injection (22-gauge, ½ inch).
Tablets: packaged in a blister pack containing 4 tablets or 5 tablets. Each tablet contains 300 mg of lenacapavir.</td></tr>
</table>

Storage	Both formulations (oral loading dose and subcutaneous injection) of this product should be stored at 25 °C (77 °F), excursions permitted to 15–30 °C (59–86 °F)

APPENDIX B. PREVIOUS DMEPA REVIEWS

On August 19, 2022, we searched for previous DMEPA reviews relevant to this current review using the terms, Sunlenca. Our search did not identify any previous reviews with outstanding issues.

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error data, we reviewed the following Sunlenca injection and tablet labels and labeling submitted by Gilead Sciences, Inc.

- Container label(s) received on June 27, 2022
- Carton labeling received on June 27, 2022
- Instructions for Use, Prescribing Information and Patient Prescribing Information (Images not shown) received on June 27, 2022, available from \\CDSESUB1\evsprod\NDA215973\0036\m1\us\114-labeling\draft and \\CDSESUB1\evsprod\NDA215974\0027\m1\us\114-labeling\draft

F.2 Label and Labeling Images

Container label(s)

Injection

[c] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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MADHURI R PATEL
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FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: March 14, 2022

To: Kevin Allen, Regulatory Project Manager
Division of Antivirals (DAV)

From: Wendy Lubarsky, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Sam Skariah, Team Leader, OPDP

Subject: OPDP Labeling Comments for SUNLENCA (lenacapavir) injection, for subcutaneous use and SUNLENCA (lenacapavir) tablets, for oral use

NDA: 215973 and 215974

This memo is in response to Division of Antivirals (DAV) labeling consult request dated July 14, 2021. Reference is made to a Complete Response letter that was issued on February 28, 2021. Therefore, OPDP defers comment on the proposed labeling at this time, and request that DAV submit a new consult request during the subsequent review cycle. If you have any questions, please contact Wendy Lubarsky at (240) 402-7721 or wendy.lubarsky@fda.hhs.gov.

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Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy Initiatives
Division of Medical Policy Programs

REVIEW DEFERRAL MEMORANDUM

Date:	January 13, 2022
To:	Kevin Allen, MS Regulatory Project Manager **Division of Antivirals (DAV)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Jessica Chung, PharmD, MS Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
Subject:	Review Deferred: Patient Package Insert (PPI)
Drug Name (established name:	SUNLENCA (lenacapavir)
Dosage Form and Route, Application Type/Number:	injection, for subcutaneous use, NDA 215973 tablets, for oral use, NDA 215974
Applicant:	Gilead Sciences, Inc.

1 INTRODUCTION

On June 28, 2021, Gilead Sciences, Inc. submitted for the Agency's review an original New Drug Application (NDA) 215973 and NDA 215974 for SUNLENCA (lenacapavir) injection and tablets, respectively. The proposed indication for SUNLENCA (lenacapavir) injection and tablets, in combination with other antiretroviral(s), is for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults (b) (4) with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations. On July 14, 2021, the Division of Antivirals (DAV) requested that the Division of Medical Policy Programs (DMPP) review the Applicant's proposed Patient Package Insert (PPI) for SUNLENCA (lenacapavir) injection and tablets.

This memorandum documents the DMPP review deferral of the Applicant's proposed PPI for SUNLENCA (lenacapavir) injection and tablets.

2 CONCLUSIONS

Due to outstanding deficiencies, DAV plans to issue a Complete Response (CR) letter. Therefore, DMPP defers comment on the Applicant's patient labeling at this time. A final review will be performed after the Applicant submits a complete response to the Complete Response (CR) letter. Please send us a new consult request at such time.

Please notify us if you have any questions.

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LASHAWN M GRIFFITHS
01/13/2022 11:52:18 AM

Clinical Inspection Summary

Date	16 December 2021
From	Cheryl Grandinetti, PharmD Clinical Pharmacologist Good Clinical Practice Assessment Branch Division of Clinical Compliance Evaluation Office of Scientific Investigations
To	Kevin Allen, RPM Benjamin Lorenz, MD, Medical Reviewer Sarah Connelly, MD, Medical Team Leader Division of Antivirals (DAV)
NDAs #	215973 and 215974
Applicant	Gilead Sciences, Inc.
Drug	Lenacapavir subcutaneous injection (NDA 213973) and lenacapavir tablets (NDA 215974)
NME	Yes
Proposed Indication	For the treatment HIV-1 Infection in adults (b) (4) who have multidrug resistance HIV-1 infection and are failing their current regimen
Consultation Request Date	4 August 2021
Summary Goal Date	17 December 2021
Action Goal Date	25 February 2022
PDUFA Date	28 February 2022

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Routine PDUFA inspections were conducted for 2 clinical investigators, Drs. DeJesus and Ruane, in support of this application (NDA 215973 and 215974). The inspections covered one clinical trial, Protocol GS-US-200-4625. Overall, the study appears to have been conducted adequately, and the data generated by these two sites appear acceptable in support of the respective indication.

During the inspections, the primary efficacy endpoint source data [i.e., the HIV-1 RNA test results at baseline (Day 1) and at the end of the Functional Monotherapy Period (Day 15)] were verified against the sponsor's data line listings for all subjects randomized at the 2 sites selected for inspection. No discrepancies were noted.

Important enrollment and other protocol deviations were noted for 3 out of the 5 subjects enrolled at Dr. DeJesus' site (Site 00698). These protocol deviations are not likely to have an impact on the overall study results and are discussed in more detail in Section III of the Clinical Inspection Summary (CIS).

II. BACKGROUND

NDAs 215973 and 215974 were submitted in support of the use of lenacapavir subcutaneous injection and oral tablets in adults (b) (4) who have multidrug resistance HIV-1 infection and are failing on their current regimen. The pivotal study supporting the application was the following:

- Protocol GS-US-200-4625, "A Phase 2/3 Study to Evaluate the Safety and Efficacy of Long-Acting Capsid Inhibitor GS-6207 in Combination with an Optimized Background Regimen in Heavily Treatment Experienced People Living With HIV-1 Infection With Multidrug Resistance."

This was a Phase 2/3, randomized, placebo-controlled, multicenter study of lenacapavir administered together with an optimized background regimen in patients with HIV with multi-drug resistance (to ≥ 2 antiretroviral medications from each of ≥ 3 of the 4 main classes) who are failing their current regimen (defined as plasma HIV-1 RNA ≥ 400 copies/mL). The primary objective was to evaluate the antiviral activity of lenacapavir administered as an add-on to a failing regimen (functional monotherapy) for patients with HIV with multi-drug resistance. Participants who completed a screening visit returned to the clinic between 14 and 30 days later for a cohort-selection visit. HIV-1 RNA results from this cohort-selection visit were used to determine whether eligible participants participated in Cohort 1 or Cohort 2.

Once eligibility and availability of the optimized background regimen was confirmed, participants were assigned to one of two cohorts (i.e., Cohort 1 and 2). Eligible participants were enrolled in Cohort 1 if they had a < 0.5 $\log_{10}$ HIV-1 RNA decline compared to the Screening visit and HIV-1 RNA ≥ 400 copies/mL at the Cohort Selection visit (occurred between 14 and 30 days after the screening visit)

Participants were enrolled into Cohort 2 if Cohort 1 was fully enrolled or if they did not meet the criteria for randomization in Cohort 1 (i.e., they had ≥ 0.5 $\log_{10}$ copies/mL HIV-1 RNA decline compared with the screening visit or HIV-1 RNA < 400 copies/mL at the cohort-selection visit). Cohort 2 subjects received open-label lenacapavir.

<u>Cohort 1:</u>

Participants enrolled in Cohort 1 were randomized using an IWRS to receive (in a 2:1 ratio) oral lenacapavir or placebo for 14 days, starting on Day, 1 while they continued their existing failing regimen as follows:

- Cohort 1A: Oral lenacapavir 600 mg (2 x 300 mg) on Days 1 and 2 and then oral lenacapavir 300 mg (1 x 300 mg) on Day 8 plus their failing regimen

- Cohort 1B: Matching placebo on Days 1, 2 and 8 plus their failing regimen.

14-Day Functional Monotherapy Period:

In Cohort 1, the sponsor, participants, investigators, and study staff at the sites were blinded to the treatment assignment during the 14-day Functional Monotherapy Period. Functional monotherapy of lenacapavir was assessed while participants continued their failing regimen. After each participant completed the 14-day Functional Monotherapy Period, the participant's treatment assignment was

unblinded by the investigator site using the IWRS to determine the treatment regimen in the Maintenance Period. The sponsor staff did not receive the treatment codes from IWRS until all participants in Cohort 1 had completed the Functional Monotherapy Period.

Maintenance Period: After unblinding, Cohort 1 study participants received the following:

- Participants in Cohort 1A (who received oral lenacapavir) received open label lenacapavir subcutaneous (SC) injection (927 mg; 309 mg/mL; 2 X 1.5 mL) on Day 1 of the Maintenance Period and initiated their optimized background regimen (i.e., 14 days after the first dose of oral lenacapavir).

- Participants in Cohort 1B (who were randomized to receive placebo on Days 1,2 and 8) received a 14-day oral dosing with open label oral lenacapavir on Days 15, 16, and 22, and initiated their optimized background regimen on Day 15. Cohort 1B received lenacapavir SC injection (927 mg; 309 mg/mL) at Day 1 (i.e., 14 days after the first dose of oral lenacapavir) while continuing their optimized background regimen.

Lenacapavir SC injection 900 mg (300 mg/mL Sodium Injection) was administered on Day 1, Weeks 26, 52, and every 6 months (26 weeks) thereafter. After the Day 1 SC visit, all Cohort 1 participants continued with study visits at Weeks 4, 10, 16, 22, 26, 36, and 52. Participants received their subsequent SC lenacapavir injection at the Week 26 visit.

The *primary efficacy endpoint* was the proportion of participants in Cohort 1 achieving a reduction in HIV-1 RNA of ≥ 0.5 $\log_{10}$ copies/mL from baseline at the end of the Functional Monotherapy Period.

Rationale for Site Selection

The clinical sites were chosen primarily based on numbers of enrolled subjects, site efficacy, and prior inspectional history.

III. RESULTS (by site):

1. Edwin DeJesus, MD
   Site # 00698
   Orlando Immunology Center
   1707 North Mills Ave
   Orlando, FL, 32803
   PDUFA Inspection Dates: 20 to 28 Sep 2021

At this site, 5 subjects were screened and enrolled. Per the sponsor's BIMO data line listings, 3 subjects were enrolled and randomized into Cohort 1 and 2 subjects were enrolled in Cohort 2. The study is ongoing but closed to enrollment. There was one subject who was enrolled in Cohort 2 (Subject (b) (6)) who died during the trial secondary to a cancer. The death was deemed not related to the study drug.

A full audit of the study records for the 5 enrolled subjects in Cohort 1 and 2 was conducted. Records

reviewed during the inspection included, but were not limited to, the study protocol and amendments; IRB submissions, approvals, and correspondence; subject eligibility criteria; informed consent process and forms; source records, including medical records and other regulatory documentation (e.g., Form FDA 1572s); primary efficacy endpoint data related to the HIV-1 RNA test results at baseline (Day 1) and at the end of the Functional Monotherapy Period (Day 15); adverse event reporting; protocol deviations; drug accountability logs; and monitor logs and follow-up letters.

There was no evidence of under-reporting of adverse events. The source records documenting the HIV-1 RNA test results at baseline (Day 1) and at the end of the Functional Monotherapy Period (Day 15) were reviewed and verified against the sponsor's data line listings for the 3 subjects enrolled in Cohort 1. No discrepancies were noted.

During the inspection, the following important protocol enrollment deviations were noted:

- Subject (b) (6), randomized to lenacapavir: Subject (b) (6) was enrolled despite meeting exclusion criteria #13, which excludes subjects who are participating or planning to participate in any other clinical trial (including observational trials) without prior approval from the sponsor throughout the study. This protocol deviation for Subject (b) (6) was not reported to FDA in the listings of protocol deviations (i.e., Appendix 16.2.2.2 and BIMO data line listing 7).

  Specifically, it was noted that this subject was also enrolled in another clinical trial of investigational fostemsavir (BMS-663068) and taking the fostemsavir as part of his failing regimen. In addition to fostemsavir, this subject's failing regimen included Trogarzo IV, T-20, abacavir and Biktarvy. Dr. DeJesus did not obtain prior approval from the sponsor, Gilead, to enroll this subject who was also in another clinical trial as required in exclusion criteria #13. Moreover, after the subject was randomized into Cohort 1A, the fostemsavir trial sponsor did not approve the co-enrollment, and the subject was subsequently withdrawn from the fostemsavir trial and fostemsavir treatment. Dr. DeJesus later obtained sponsor approval to continue this subject in the lenacapavir trial even though the subject would no longer be taking the fostemsavir as part of his failing regimen due to the other trial prohibiting co-enrollment. The subject was noted to have continued his failing regimen minus the fostemsavir throughout the Functional Monotherapy Period.

- Subject (b) (6), randomized to lenacapavir: This subject did not meet inclusion criteria #3, which states that subjects must have been receiving a stable failing antiretroviral (ARV) regimen for >8 weeks before Screening and willing to continue the regimen until Day 1. Participants in Cohort 1 must also be willing to continue the failing regimen until completing the Functional Monotherapy Period (Day 1 to Day 14). This subject's failing ARV regimen was documented as Biktarvy, Pifeltro, and Trogarzo. This subject, who was randomized on (b) (6) into Cohort 1A and completed the initial 14-day Functional Monotherapy Period, did not adequately inform the site staff until (b) (6) that he had not been taking Trogarzo for a few months before randomization due to pharmacy issues. Dr. DeJesus consulted with the Gilead Medical Monitor during the trial, and the medical monitor approved the subject's continued participation in the trial, even though the subject did not continue his failing regimen to the end of the Functional Monotherapy Period (Day 14). This deviation for Subjects (b) (6) was reported to FDA in the listings of protocol deviations.

- Subject (b) (6), randomized to placebo: This subject was enrolled and randomized into Cohort 1B although he met exclusion criteria #16, which excludes subjects who are using or planning to use exclusionary medications as listed in the protocol. This subject took etravirine, a prohibited medication, for 13 days during the Functional Monotherapy Period. This deviation for Subjects (b) (6) was reported to FDA in the listings of protocol deviations.

Reviewer's comment: Although Subjects (b) (6) and (b) (6) did not continue all drugs that were part of their failing regimens from the screening period through the functional monotherapy period, both subjects met the primary efficacy endpoint by achieving a reduction in HIV-1 RNA of ≥ 0.5 log_{10} copies/mL from baseline to the end of the Functional Monotherapy Period. The protocol deviations for these subjects do not appear to have an impact on the overall study results.

For Subject (b) (6), while concomitant use of lenacapavir with some medications or herbal/natural supplements that are inhibitors and inducers of CYP3A, UGT1A1 or P-gp may result in increased or decreased exposure of lenacapavir, respectively, concomitant use of etravirine (a CYP3A inducer) in this subject would have no impact on exposure of the study drug because this subject was randomized to placebo.

A Form FDA 483 was issued at the end of the inspection for failure to conduct the clinical trial in accordance with the signed statement of investigator and investigational plan. Dr. DeJesus adequately responded to the inspection finding in a letter, dated 15 Oct 2021. He acknowledged the enrollment and other protocol deviations and has implemented a corrective action plan.

2. Peter J. Ruane, MD
   Site # 00407
   Ruane Clinical Research Group Inc.
   5901 W Olympic Blvd., Suite 420,
   Los Angeles, CA, 90036
   PDUFA Inspection Dates: 30 Aug to 2 Sep 2021

At this site, 10 subjects were screened and 3 were enrolled. Per the sponsor's BIMO data line listings, all 3 enrolled subjects were randomized into Cohort 1.

A full audit of the study records for the 3 enrolled subjects was conducted. Records reviewed during the inspection included, but were not limited to, the study protocol and amendments; IRB submissions, approvals, and correspondence; subject eligibility criteria; informed consent process and forms; source records, including medical records and other regulatory documentation (e.g., Form FDA 1572s); primary efficacy endpoint data related to the HIV-1 RNA test results at baseline (Day 1) and at the end of the Functional Monotherapy Period (Day 15); adverse event reporting; protocol deviations; drug accountability logs; and monitor logs and follow-up letters.

There was no evidence of under-reporting of adverse events. The source records documenting the HIV-1 RNA test results at baseline (Day 1) and at the end of the Functional Monotherapy Period (Day 15) were reviewed and verified against the sponsor's data line listings for the 3 enrolled subjects. No discrepancies were noted.

{See appended electronic signature page}

Cheryl Grandinetti, Pharm.D.
Clinical Pharmacologist
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
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cc:
Central Doc. Rm. NDAs 215973 and 215974
DAV/Project Manager/Kevin Allen
DAV/Medical Reviewer/Benjamin Lorenz
DAV/Medical Team Leader/Sarah Connelly
OSI/DCCE/Branch Chief/Kassa Ayalew
OSI/DCCE/Team Leader/Phillip Kronstein
OSI/DCCE/GCP Reviewer/Cheryl Grandinetti
OSI/ GCP Program Analysts/Yolanda Patague
OSI/Database Project Manager/Dana Walters

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/s/

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KASSA AYALEW
12/16/2021 10:50:21 AM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	October 29, 2021
Requesting Office or Division:	Division of Antivirals (DAV)
Application Type and Number:	NDA 215973 NDA 215974
Product Name and Strength:	Sunlenca (lencapavir) Injection: 463.5 mg/1.5 mL (309 mg/mL) Tablet: 300 mg
Applicant/Sponsor Name:	Gilead Sciences, Inc.
OSE RCM #:	2021-1278-2
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph
DMEPA 1 Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS

1 PURPOSE OF MEMORANDUM

On October 26, 2021 the Applicant requested further clarification to a recommendation that we made during a previous label and labeling review dated October 21, 2021.[a] The Division of Antivirals (DAV) requested that we provide a response.

2 DISCUSSION AND CONCLUSION

Upon further consideration of the Applicants rationale provided in the October 18, 2021 submission of revised labels and labeling, we consider the proposed changes to the instruction for use (IFU) acceptable with additional recommendations to add a statement to remove air bubbles prior to priming and specify the IFU is for healthcare use only. We provide specific recommendations to Gilead in section 3 below.

[a] Fanari, M. Label and Labeling Review for Sunlenca (NDA 215973). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2021 Oct 21. RCM No.: 2021-1278-1.

3 RECOMMENDATIONS FOR GILEAD SCIENCES, INC.

Based on your email request dated October 26, 2021, we have reconsidered your rationale and revised IFU as outlined in your October 18, 2021 submission and find your proposed revisions to the IFU acceptable with the following recommendations:

1-Step 5 should be revised to read 'Attach injection needle, expel air bubbles and prime to 1.5 mL.'

2-Add the following statement to the top portion of the IFU: 'The following information is intended for medical or healthcare professionals only'.

APPENDIX A. LABELING RECEIVED ON OCTOBER 18, 2021

- Instruction for use (IFU): available in EDR at: //cdsesub1/evsprod/NDA215973/0011/m1/us/114-labeling/draft/carton-and-container/draft-carton-container-label-ifu.pdf

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SEVAN H KOLEJIAN
10/29/2021 02:57:15 PM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	October 21, 2021
Requesting Office or Division:	Division of Antivirals (DAV)
Application Type and Number:	NDA 215973 NDA 215974
Product Name and Strength:	Sunlenca (lencapavir) Injection: 463.5 mg/1.5 mL (309 mg/mL) Tablet: 300 mg
Applicant/Sponsor Name:	Gilead Sciences, Inc.
OSE RCM #:	2021-1278-1
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph
DMEPA 1 Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling and instruction for use (IFU) received on October 18, 2021 for Sunlenca. The Division of Antivirals (DAV) requested that we review the revised IFU, container labels and carton labeling for Sunlenca (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The revised container labels and carton labeling are acceptable from medication error perspective. However, the revised IFU is unacceptable from a medication error perspective. The below recommendation previously provided to Gilead has not been addressed.

[a] Fanari, M. Label and Labeling Review for Sunlenca (NDA 215973). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2021 Oct 1. RCM No.: 2021-1278.

IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Step 3 indicates to withdraw all contents of vial.	Minimize wrong dose medication errors.	Revise step 3 to instruct HCPs to withdraw 1.5 mL from vial.

3 RECOMMENDATIONS FOR GILEAD SCIENCES, INC.

We recommend the following be implemented prior to approval of this NDA:

A. We note the below recommendation previously provided had not been addressed. A revised IFU should be submitted to address this comment.

IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Step 3 indicates to withdraw all contents of vial.	Minimize wrong dose medication errors.	Revise step 3 to instruct HCPs to withdraw 1.5 mL from vial.

APPENDIX A. IMAGES OF LABEL AND LABELING RECEIVED ON OCTOBER 18, 2021

- Instruction for use (IFU): available in EDR at: //cdsesub1/evsprod/NDA215973/0011/m1/us/114-labeling/draft/carton-and-container/draft-carton-container-label-ifu.pdf

- Container label(s)

Injection

Tablet

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M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 10/4/2021

TO: Division of Antivirals (DAV)
Office of Infectious Diseases (OID)

FROM: Division of New Drug Study Integrity (DNDSI)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to conduct an on-site inspection**

RE: NDA 215973
NDA 215974

The Division of New Drug Study Integrity (DNDSI) within the Office of Study Integrity and Surveillance (OSIS) determined that inspections are not warranted at this time for the sites listed below. The rationale for this decision is noted below.

Rationale

Quotient, Miami: The Office of Regulatory Affairs (ORA) inspected the site in May 2019, which falls within the surveillance interval. The inspection was conducted under the following submission: NDA Non Responsive .

The final classification for the inspection was No Action Indicated (NAI).

(b) (4): OSIS inspected the site in August 2018, which falls within the surveillance interval. The inspection was conducted under the following submissions: NDA Non Responsive and ANDAs Non Responsive and Non Responsive .

The final classification for the inspection was Voluntary Action Indicated (VAI) for the following observation:

- The site did not follow established criteria for run acceptance. Specifically, the chromatographic results from one run were initially accepted, but then rejected without justification. Only results from the re-chromatographed samples from the run were reported.

After review of the inspectional findings and the written response from the site, OSIS recommended that all study data be accepted for Agency review. (OSIS Final EIR Review – Oct 2018).

Therefore, based on the rationale described above, inspections are not warranted at this time.

Inspection Sites

Facility Type	Facility Name	Facility Address
Clinical	Quotient Sciences – Miami	3898 Northwest 7th Street, Miami, FL
Analytical		(b) (4)

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/s/

JAMES J LUMALCURI
10/04/2021 09:28:32 AM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	October 1, 2021
Requesting Office or Division:	Division of Antivirals (DAV)
Application Type and Number:	NDA 215973 NDA 215974
Product Name and Strength:	Sunlenca (lenacapavir) Injection: 463.5 mg/1.5 mL (309 mg/mL) Tablet: 300 mg
Product Type:	Combination Product and Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Gilead Sciences, Inc. (Gilead)
FDA Received Date:	June 28, 2021
OSE RCM #:	2021-1278
DMEPA 1 Safety Evaluator:	Melina Fanari, R.Ph
DMEPA 1 Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS

1 REASON FOR REVIEW

As part of the approval process for Sunlenca (lenacapavir) injection and tablet, the Division of Antivirals (DAV) requested that we review the proposed Sunlenca prescribing information (PI), instruction for use (IFU), patient prescribing information (PPI), container labels and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

DMEPA previously reviewed a human factors (HF) validation study protocol submitted under IND 136260 for Sunlenca injection[a]. Sunlenca injection is a combination product packaged in a kit containing injection vials, syringes, vial access devices and injection needles that is intended to be administered by healthcare professionals. Our review of the use-related risk analysis did not identify any new, differing, or unique risks as compared to other approved vials, syringes, vial access devices, and injection needles intended for use by HCPs. Thus, we determined that the results of a HF validation study were not needed to support the NDA submission. The proposed product packaging configuration and components for the Sunlenca injection (NDA 215973) are the same as previously reviewed under IND 136260.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B-N/A
ISMP Newsletters*	C-N/A
FDA Adverse Event Reporting System (FAERS)*	D-N/A
Other	E-N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 CONCLUSION AND RECOMMENDATIONS

We note based on feedback from the Office of Product Quality (OPQ) that the Sunlenca injection vial presentation contains a significant overfill with an extractable volume for the

[a] Bhalodia, A., Human Factors Validation Study Protocol Review for Sunlenca (IND 136260). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Feb 9. Panorama No.: 2020-2621

registration batches ranging from (b) (4) to (b) (4) mL. There is a potential for wrong dose medication errors if a provider were to misinterpret the entire vial as a single dose and administer the contents of two entire vials (approximately 1200) instead of the recommended dose of two 1.5 mL injections (927 mg). This concern was shared with the clinical team in DAV. The clinical team stated that the clinical impact of a patient receiving a wrong dose (i.e. contents of two entire vials) is not clinically serious or life threatening. Thus, we determined that the residual risk association with potential wrong dose medication errors associated with the design of this product is minimal. Furthermore, we note that the residual risk can be further mitigated through appropriate labeling of the product (see section 4 and 5). In addition, OPQ has issued a request (IR) to Gilead to reduce the overfill amount contained in the Sunlenca vial. We note that at the time of this review, OPQ's IR was outstanding.

The proposed PI, PPI, container label and carton labeling may be improved to promote the safe use of this product from a medication error perspective. Below we provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication errors in Section 4 for the Division and in Section 5 for Gilead Sciences, Inc.

4 RECOMMEDATIONS FOR DIVISION OF ANTIVIRALS (DAV)

Table 2. Identified Issues and Recommendations for Division of Antivirals (DAV)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information – General Issues			
1.	Dose is expressed as 927 mg by subcutaneous injection (2 x 1.5 mL injections).	Expressing dose in mixed units (mL vs mg) can be confusing and lead to wrong dose medication errors.	Revise all instances of the recommended injection dose (in Highlights and section 2) to read as follows: 927 mg by subcutaneous injection (2 injections of 463.5 mg/1.5 mL)
2.	Oral tablet dosing is missing tablet strength.	Minimize wrong dose errors.	Revise all instances of the recommended tablet dose (in Highlights and section 2) to read as follows: 600 mg (2 tablets of 300 mg)
3.	Use of confusing symbols (e.g., "+" and "-").	These symbols may be mistaken as opposite of intended.	Replace all instances of the symbols "+" and "-" in Highlights and section 2) with their intended meanings to prevent

Table 2. Identified Issues and Recommendations for Division of Antivirals (DAV)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			misinterpretation and confusion.
Highlights of Prescribing Information			
1.	Day 1 and 2 dosing (b) (4) .	Improve readability.	Each day and corresponding dose (e.g. Day 1 and Day 2) should be (b) (4) separately.

5 RECOMMENDATIONS FOR GILEAD SCIENCES, INC.

Table 3. Identified Issues and Recommendations for Gilead Sciences, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
All Container Labels and Carton Labeling			
	As currently presented the tradename is missing on labels.	Unable to review the tradename placement on the labels.	Place the conditionally acceptable proprietary name "Sunlenca" on all labels and labeling and submit for our review.
Container Label (vial)			
1.	Discard Unused Portion statement is missing.	Minimize risk of entire contents of vial being given as a single dose.	The statement "Single-Dose Vial" should be revised to read "Single-Dose Vial – Discard Unused Portion".
2.	Barcode is in horizontal position.	Barcodes placed in a horizontal position may not scan due to vial curvature.	Reorient the linear barcode to a vertical position to improve the scannability of the barcode.
3.	Usual dose statement requires revisions.	Per 21 CFR 201.55	To ensure consistency with the Prescribing Information, revise the statement, "(b) (4) " to read "Recommended Dosage: See prescribing information."

Table 3. Identified Issues and Recommendations for Gilead Sciences, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			This revision should be made to all product labels and labeling (injection and tablet).
Container Label (blister card)			
1.	Product strength per single unit statement is missing.	To avoid wrong dose errors and to clarify the designated strength is per unit.	Revise the strength presentation statement on the blister card as follows: "300 mg per tablet"
2.	Dose (i.e tablet quantity) under each Day designation is not included.	Minimize wrong dose errors.	Consider adding the following statements after each day designation as follows: Day 1- Take 2 tablets Day 2- Take 2 tablets
Carton Labeling			
1.	The recommended dose is 927 mg, but the product strength is 463.5 mg/1.5 mL (309 mg/mL). Two 1.5 mL injections (2 vials) are needed to make one dose.	The product strength in a manner that is incongruent with the recommended dose which complicates the calculating of dosage and has led to dosing errors.	Add on principal display panel the following statement: "Both 463.5 mg/1.5 mL (2 single dose vials) must be administered together to receive the 927 mg dose"
2.	Kits contents require revisions.	Improve readability.	Revise the statements related to kit contents as follows: <u>Contents</u> -2 lencapavir single dose vials -2 vial access devices -2 syringes -2 injection needles (22 gauge, ½ inch) -Prescribing Information -Instruction for Use -Patient Information

Table 3. Identified Issues and Recommendations for Gilead Sciences, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
3.	The healthcare professional administration only statement is missing.	Ensure proper product use.	Add the following statement to the principal display panel (PDP): "For Healthcare Professional administration only"
Instruction for Use			
1.	Missing picture of how to attach syringe onto vial access device.	Ensure proper attachment of fill syringe to access device.	Add a step and photo in the proper sequence describing how to attach the syringe to the vial access device.
2.	Step 3 indicates to withdraw all contents of vial.	Minimize wrong dose medication errors.	Revise step 3 to instruct HCPs to withdraw 1.5 mL from vial.
3.	Step 5 does not state which direction to attach needle to syringe.	Ensure proper attachment of injection needle.	Include the direction (e.g. clockwise or counterclockwise) for needle attachment.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 4 presents relevant product information for Sunlenca injection and tablet that Gilead Sciences, Inc. submitted on June 28, 2021.

<table>
<tr><th colspan="2">Table 4. Relevant Product Information for Sunlenca</th></tr>
<tr><td>Initial Approval Date</td><td>N/A</td></tr>
<tr><td>Active Ingredient</td><td>lenacapavir</td></tr>
<tr><td>Indication</td><td>Treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults (b) (4) with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations</td></tr>
<tr><td>Route of Administration</td><td>Subcutaneous, Oral</td></tr>
<tr><td>Dosage Form</td><td>Injection, Tablet</td></tr>
<tr><td>Strength</td><td>Injection: 463.5 mg/1.5 mL (309 mg/mL); Tablet: 300 mg</td></tr>
<tr><td>Dose and Frequency</td><td>
<table>
<tr><td>Treatment Time</td><td></td></tr>
<tr><td colspan="2">Dosage: Initiation</td></tr>
<tr><td>Day 1</td><td>927 mg subcutaneous injection (2 x 1.5 mL injections)
600 mg orally (2 x 300 mg tablets)</td></tr>
<tr><td>Day 2</td><td>600 mg orally (2 x 300 mg tablets)</td></tr>
<tr><td colspan="2">Dosage: Maintenance</td></tr>
<tr><td>Every 6 Months (26 weeks) +/-2 weeks</td><td>927 mg subcutaneous injection (2 x 1.5 mL injections)</td></tr>
</table>
</td></tr>
<tr><td>How Supplied</td><td>Injection: packaged in a dosing kit containing:
- 2 single-dose clear glass vials, each containing sufficient volume to allow withdrawal of 463.5 mg/1.5 mL (309 mg/mL) of lenacapavir. Vials are sealed with a stopper and aluminium overseal with flip-off cap.
- 2 vial access devices, 2 disposable syringes, and 2 injection safety needles for subcutaneous injection (22-gauge, ½ inch).</td></tr>
</table>

	Tablets: packaged in a blister pack containing 4 tablets. Each tablet contains 300 mg of lenacapavir.
Storage	Both formulations (oral loading dose and subcutaneous injection) of this product should be stored below 30°C (86 °F).

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[b] along with postmarket medication error data, we reviewed the following Sunlenca injection and tablet labels and labeling submitted by Gilead Sciences, Inc.

- Container label(s) received on June 28, 2021
- Carton labeling received on June 28, 2021
- Instructions for Use, Prescribing Information and Patient Prescribing Information (Images not shown) received on June 28, 2021, available from \\CDSESUB1\evsprod\NDA215973\0001\m1\us\114-labeling\draft and \\CDSESUB1\evsprod\NDA215974\0001\m1\us\114-labeling\draft\labeling

F.2 Label and Labeling Images

Container label(s)

Injection

[b] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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