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Sunlenca® (lenacapavir) Administration Outside the Dosing Window

This document is in response to your request for information regarding Sunlenca® (lenacapavir [LEN]) and administration outside the dosing window.

Gilead Sciences is unable to provide treatment recommendations. We recommend that you use your best clinical judgment in guiding therapy based on patient-specific therapeutic goals.

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The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.

Product Labeling[1]

Adherence to Treatment Regimen

Prior to starting LEN, healthcare providers should carefully select patients who agree to the required every 6 month injection dosing schedule and counsel patients about the importance of adherence to scheduled LEN dosing visits and concomitant oral antiretroviral therapy to help maintain viral suppression and reduce the risk of viral rebound and potential development of resistance with missed doses.

Recommended Dosage

LEN can be initiated using one of the two recommended dosage regimens (Table 1 and Table 2). Maintenance dosing is administered by subcutaneous injection every 6 months regardless of the initiation regimen. Healthcare providers should determine the appropriate initiation regimen for the patient. LEN oral tablets may be taken with or without food.

Table 1. Recommended Treatment Regimen for LEN Initiation and Maintenance, Option 1[1]

Treatment Time	
	Dosage of LEN: Initiation
Day 1	927 mg by subcutaneous injection (2 x 1.5 mL injections) 600 mg orally (2 x 300 mg tablets)
Day 2	600 mg orally (2 x 300 mg tablets)
	Dosage of LEN: Maintenance
Every 6 months (26 weeks)[a] +/- 2 weeks	927 mg by subcutaneous injection (2 x 1.5 mL injections)

[a]From the date of the last injection.

Table 2. Recommended Treatment Regimen for LEN Initiation and Maintenance, Option 2[1]

Treatment Time	
	Dosage of LEN: Initiation
Day 1	600 mg orally (2 x 300 mg tablets)
Day 2	600 mg orally (2 x 300 mg tablets)
Day 8	300 mg orally (1 x 300 mg tablet)
Day 15	927 mg by subcutaneous injection (2 x 1.5 mL injections)
	Dosage of LEN: Maintenance
Every 6 months (26 weeks)[a] +/- 2 weeks	927 mg by subcutaneous injection (2 x 1.5 mL injections)

[a]From the date of the last injection.

Recommended Dosing Schedule for Missed Dose[1]

Planned Missed Injections

During the maintenance period, if a patient plans to miss a scheduled 6-month injection visit by more than 2 weeks, LEN tablets may be taken for up to 6 months until injections resume (Table 3).

Table 3. Recommended Dosage after Planned Missed Injections: Weekly Oral Maintenance[1]

Time since Last Injection	Recommendation
26 to 28 weeks	Maintenance oral dosage of 300 mg taken once every 7 days for up to 6 months. Resume the maintenance injection dosage within 7 days after the last oral dose.

Unplanned Missed Injections

Patients who miss a scheduled injection visit should be clinically reassessed, including consideration of lenacapavir resistance testing, to ensure resumption of therapy remains appropriate. During the maintenance period, if more than 28 weeks have elapsed since the last injection and LEN tablets have not been taken, see Table 4 below for the recommended dosage after unplanned missed injections. Adherence to the injection dosing schedule is strongly recommended.

Table 4. Recommended Dosage after Unplanned Missed Injections[1]

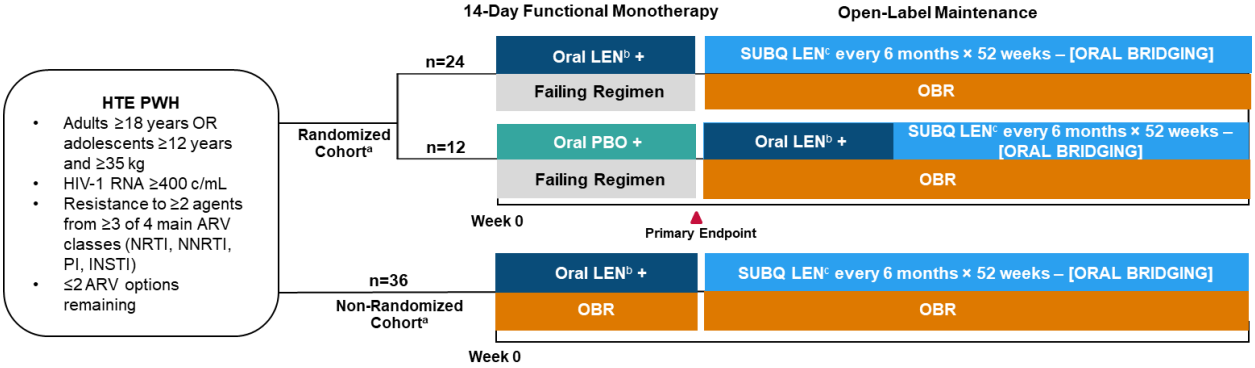
Time since Last Injection	Recommendation
More than 28 weeks	Reinitiate with Option 1 (Table 1) or Option 2 (Table 2) and then continue with maintenance injection dosing.

Oral Bridging With Once Weekly LEN 300 mg

Study design and demographics

A post hoc analysis was conducted to assess the efficacy and safety of oral bridging with LEN 300 mg once weekly among participants enrolled in the CAPELLA (highly treatment-experienced PWH with multidrug resistance) and CALIBRATE (ARV-naïve PWH) studies whose LEN SUBQ dosing was interrupted from December 2021 to May 2022.[2] PK model simulations were used to predict that an oral LEN 300-mg once-weekly dosing schedule would maintain the lower bounds of the 90% CI for the mean trough concentrations above the IQ4 of 15.5 ng/mL during the oral bridging period.[3] Oral bridging was initiated within 2 weeks of the next scheduled SUBQ injection, and participants were given oral LEN to administer at home. See Figure 1 and Figure 2 for the modified CAPELLA and CALIBRATE study designs.[2]

Figure 1. CAPELLA: Study Design[2,4,5]



Abbreviations: HTE=highly treatment-experienced; INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor; NRTI=nucleos(t)ide reverse transcriptase inhibitor; PBO=placebo; PI=protease inhibitor.

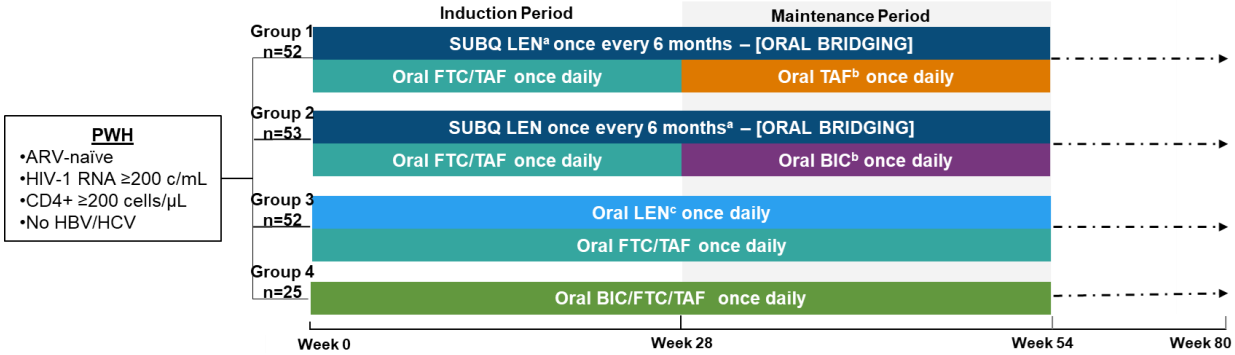
[a]Participants with <0.5 $\log_{10}$ decline in HIV-1 RNA and HIV-1 RNA ≥400 c/mL were enrolled in the randomized cohort; participants were enrolled in the nonrandomized cohort if they had ≥0.5 $\log_{10}$ decline in HIV-1 RNA and/or had HIV-1 RNA <400 c/mL or were enrolled after the randomized cohort was fully recruited.

[b]Oral LEN dosing schedule: Day 1, 600 mg; Day 2, 600 mg; and Day 8, 300 mg.

[c]SUBQ LEN dosing schedule: 927 mg (2× 1.5 mL) on Day 15 and then every 6 months.

Note: ATV, ATV/cobicistat, ATV/ritonavir, efavirenz, etravirine, nevirapine, and tipranavir were not permitted for use in the OBR.

Figure 2. CALIBRATE: Study Design[2,6]



[a]The LEN dosing schedule included an oral lead-in phase (Day 1, 600 mg; Day 2, 600 mg; Day 8, 300 mg), followed by SUBQ LEN 927 mg (2 × 1.5 mL) on Day 15 and every 6 months (26 weeks) thereafter.

[b]Participants needed to have HIV-1 RNA <50 c/mL at Weeks 16 and 22 to initiate treatment with a two-agent regimen at Week 28. Those with HIV-1 RNA ≥50 c/mL discontinued the study at Week 28.

[c]The oral LEN dosing schedule consisted of the following: 600 mg on Day 1, 600 mg on Day 2, and 50 mg on Day 3 and thereafter.

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Note: The following doses were used: FTC/TAF, 200/25 mg; TAF, 25 mg; BIC, 75 mg; and BIC/FTC/TAF, 50/200/25 mg.

Baseline demographics and characteristics for the participants who received oral bridging in either study are presented in Table 5.

Table 5. CAPELLA (Combined Cohorts) and CALIBRATE: Baseline Demographics and Characteristics: Oral Bridging Analysis Set[2][a]

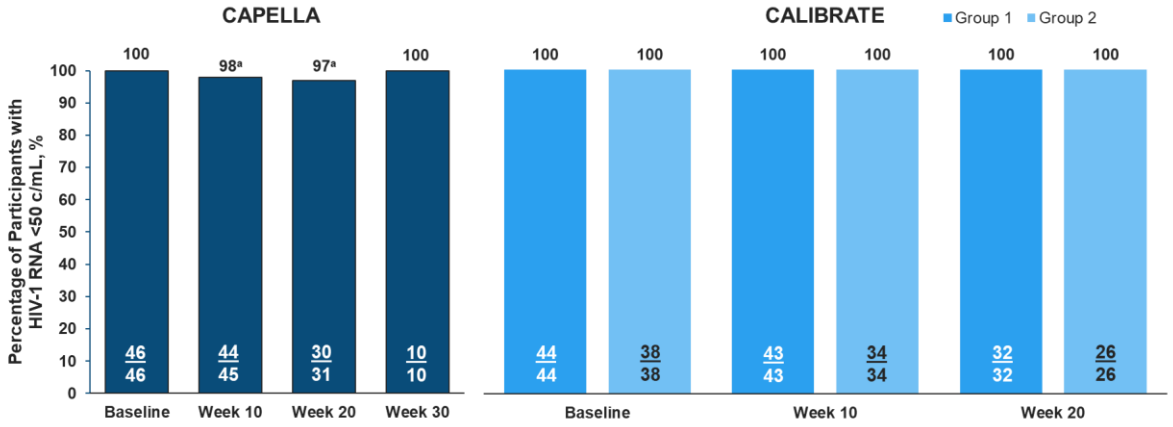
Key Demographics and Characteristics		CAPELLA N=57	CALIBRATE	
			Group 1 n=44	Group 2 n=38
Age, mean (SD), years		50 (13.2)	35 (9.9)	33 (8.9)
Male sex at birth, n (%)		45 (78.9)	39 (88.6)	37 (97.4)
Race, n (%)	Asian	15 (26.8)	0	0
	Black	16 (28.6)	21 (47.7)	16 (42.1)
	White	25 (44.6)	20 (45.5)	21 (55.3)
	Other	1 (1.8)	3 (6.9)	1 (2.6)
BMI, mean (SD), kg/m^2		26.7 (5.82)	29.3 (8.59)	27.8 (6.36)
HIV-1 RNA <50 c/mL at oral bridging baseline, n (%)		46 (80.7)	44 (100)	38 (100)

[a]Comprised all participants with ≥1 dose of LEN 300 mg oral bridging.

Efficacy[2]

In the CAPELLA and CALIBRATE studies, the median duration of LEN oral bridging was 18 weeks; the mean (SD) exposure to oral LEN was 17.8 (7.66) weeks in CAPELLA, 18.1 (5.27) weeks in CALIBRATE Group 1, and 18.2 (5.18) weeks in CALIBRATE Group 2. The mean adherence to oral LEN per pill count was 96.9% in CAPELLA, 94.8% in CALIBRATE Group 1, and 96.7% in CALIBRATE Group 2. Among participants who were virologically suppressed when oral bridging began, CD4 counts remained stable throughout the oral bridging period. Of the 11 participants who were viremic at the oral bridging baseline, 27% (3/11) of participants achieved virologic suppression at Week 10, and 50% (2/4) of participants achieved virologic suppression at Week 20. Efficacy of LEN 300 mg during oral bridging among participants who were virologically suppressed when oral bridging began is presented in Figure 3.

Figure 3. CAPELLA (Combined Cohorts) and CALIBRATE: Efficacy During Oral Bridging (Missing=Excluded Analysis)[2]



[a]One participant did not maintain HIV-1 RNA <50 c/mL during the oral bridging period at Week 10 and 20; the participant developed a LEN resistance-associated mutation (ie, N74D) and had missed two nonconsecutive

oral doses prior to developing elevated HIV-1 RNA levels. After the oral bridging period, the participant achieved virologic suppression without changing regimens.

PK data[3]

PK samples were collected from participants in both studies at the beginning of the oral bridging period and every 10 to 12 weeks thereafter until SUBQ LEN was resumed. In both studies, the mean LEN plasma concentrations and lower bounds of the 90% CI were above IQ4 (15.5 ng/mL) at Day 1, Weeks 10, 20, and 30, and at the SUBQ LEN resumption visit.

Safety[2]

Oral LEN 300-mg bridging was generally well tolerated across both studies and had a safety profile consistent with SUBQ LEN in the primary analysis, aside from injection site reactions (Table 6). No serious or Grade ≥3 TEAEs were deemed to be related to LEN, and no TEAE led to study discontinuation. One participant in the CAPELLA study with a history of alcoholic hepatitis died of an unknown cause during the oral bridging period; the death was not considered by the investigator to be related to LEN treatment.

Table 6. CAPELLA and CALIBRATE: Safety Summary (Oral Bridging Analysis Set)[2]

TEAE, n (%)	CAPELLA N=57	CALIBRATE	
		Group 1 n=44	Group 2 n=38
Any-grade	28 (49.1)	28 (63.6)	25 (65.8)
Gastrointestinal disorders	7 (12.3)	4 (9.1)	7 (18.4)
Treatment-related	2 (3.5)	1 (2.3)	2 (5.3)
Grade ≥3	1 (1.8)	2 (4.5)	1 (2.6)
Serious	1 (1.8)	1 (2.3)	1 (2.6)
Select adverse events[a]	Cough: 5.3 Diarrhea: 5.3 URTI: 5.3	Nasopharyngitis: 4.9 Syphilis: 4.9 Oropharyngeal pain: 4.9	

[a]CAPELLA, COVID-19 (7%); CALIBRATE, influenza (8.5%), COVID-19 (4.9%).

Simulations for Missed Oral LEN Loading Doses[7]

Study design

A two-compartment population-PK model was used to simulate plasma LEN concentration-time profiles for various missed-dose scenarios of the Day 2 and Day 8 oral loading doses of the CAPELLA phase 2/3 regimen. These scenarios were evaluated at the start and restart of treatment (when a SUBQ LEN dose was missed by >2 weeks, treatment was restarted on Day 1 of the regimen). Simulated scenarios consisted of the following: missed Day 2 oral dose by <6 days or ≥6 days and missed Day 8 oral dose by <6 days or ≥6 days.

Results

Based on simulated scenarios, therapeutic LEN plasma concentrations were maintained by the following actions after a missed dose for either the start or restart of treatment (Table 7).

Table 7. Summary of Missed LEN Oral Loading Doses Scenarios in Phase 2/3 Regimen for the Start and Restart of Treatment[7]

Loading Dose Day	Missed Dose Scenario	Conditions to Maintain Therapeutic LEN Plasma Concentrations[a] ≥IQ4[b]
Day 2 (600 mg)	Day 2 oral dose missed by <6 days	• Oral LEN 600 mg dose as soon as possible • Oral LEN 300 mg dose on Day 8
	Day 2 oral dose missed by ≥6 days	• Oral LEN 600 mg dose as soon as possible • Oral LEN 300 mg dose on Day 15 + regularly scheduled SUBQ LEN dose
Day 8 (300 mg)	Day 8 oral dose missed by <6 days	• Oral LEN 300 mg dose as soon as possible
	Day 8 oral dose missed by ≥6 days	• Oral LEN 300 mg dose on Day 15 + regularly scheduled SUBQ LEN dose

[a]Therapeutic LEN plasma concentrations=mean (90% CI) LEN plasma concentrations (ng/mL).
[b]Current data indicate maximal antiviral activity was achieved at a mean trough concentration of 15.5 ng/mL.

Early Dosing

A literature search was conducted in Ovid MEDLINE and Embase databases for studies published between 1946 and August 19, 2025, using the search terms of Sunlenca, lenacapavir, early dosing, and other related search terms. No relevant citations were identified.

References

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2. Ogbuagu O, Avihingsanon A, Segal-Maurer S, et al. Lenacapavir Oral Bridging (300 mg QW) Maintains Efficacy with a Similar Safety Profile When SC LEN Cannot Be Administered. [Abstract Oral OAB0205]. Paper presented at: 12th IAS Conference on HIV Science; July 23-26, 2023; Brisbane, Australia.
3. Jogiraju V, Shelton M, Shaik N, et al. Pharmacokinetic Bridging with Oral Lenacapavir for Missed Subcutaneous Q6M Dosing. [Poster TUPEB07]. Paper presented at: 12th IAS Conference on HIV Science; July 23-26, 2023; Brisbane, Australia.
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Abbreviations

ARV=antiretroviral
ATV=atazanavir
BIC=bictegravir
c/mL=copies/mL
CD4=cluster of differentiation 4
FTC=emtricitabine
IQ4=inhibitory quotient 4
LEN=lenacapavir
OBR=optimized background regimen
PK=pharmacokinetic
PWH=people with HIV
SUBQ=subcutaneous(ly)
TAF=tenofovir alafenamide
TEAE=treatment emergent adverse events

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Sunlenca US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or www.askgileadmedical.com

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or www.accessdata.fda.gov/scripts/medwatch

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