GILEAD | Medical Information

Yeztugo® (lenacapavir) Missed Dose

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and management of a missed dose.

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

Summary

Product Labeling[1]

It is important to follow the required oral initiation and continuation injection dosing schedule because non-adherence to every 6-month injections or missed doses could lead to HIV-1 acquisition and development of resistance.

- If an individual misses the Day 2 oral initiation dose (LEN 600 mg), they should take it as soon as possible. They should not take Day 1 and Day 2 oral initiation doses on the same day.
- If the scheduled 6-month injection is anticipated to be delayed by more than 2 weeks, LEN tablets may be taken on an interim basis (for up to 6 months if needed), until injections resume. Dosing schedule for delayed injection is LEN 300 mg orally taken once every 7 days. Resume the continuation injection dosage within 7 days after the last oral dose.
- If more than 28 weeks have elapsed since the last injection and LEN tablets have not been taken, they will need to reinitiate with the initiation dosing schedule from Days 1 and 2, if clinically appropriate, and then continue with continuation injection dosing.

Pharmacokinetic Data on Missed Doses

- According to a population PK analysis of pooled data from participants across 13 phase 1 to phase 3 studies, simulations showed that without oral loading doses on Day 1 and Day 2, the mean plasma LEN concentration thought to be associated with antiretroviral activity, IQ4 (15.5 ng/mL), would be reached by Day 22. With the oral loading dose (LEN 600 mg orally on Day 1 and Day 2), concentrations exceeded the IQ4 earlier (within the first day) and were maintained above this threshold on Day 2 and thereafter, following the administration of the second oral loading dose. This PK data supports taking the missed oral loading doses as soon as possible to achieve target concentrations.[2]
- PK simulations also showed that twice-yearly SUBQ LEN consistently maintained the C_{trough} above the IQ4 threshold of 15.5 ng/mL, as well as for at least 2 weeks following a missed SUBQ dose.[2]
- Missing the Day 1 and 2 doses is predicted to result in LEN plasma concentrations below IQ4, which could persist for several weeks until the SUBQ dose takes effect.[3]

Product Labeling[1]

Adherence

Prior to starting LEN, healthcare providers should select individuals who agree to the required testing and every 6-month injection dosing schedule, and counsel individuals about the importance of adherence to scheduled LEN dosing visits to help reduce the chance of acquiring HIV-1 and development of resistance.

It is important to select individuals who agree to the required injection dosing schedule because non-adherence to every-6-month injections or missed doses could lead to HIV-1 acquisition and development of resistance. In the event of a missed injection, please refer to Section 2.4 of the Prescribing Information for the appropriate dosing schedule.

Dosing Schedule

The LEN dosing schedule in adults and adolescents weighing at least 35 kg consists of a required initiation dosing (SUBQ injections and oral tablets) followed by once every 6-months continuation dosing (SUBQ injections; Table 1). LEN oral tablets may be taken with or without food.

Table 1. LEN Initiation and Continuation Dosing Schedule[1]

Regimen	Frequency	Dosage of LEN
Initiation[a]	Day 1	927 mg by SUBQ injection (2 × 1.5 mL injections) and 600 mg orally (2 × 300 mg tablets)
	Day 2	600 mg orally (2 × 300 mg tablets)
Continuation	Every 6-months (26 weeks)[b] ± 2 weeks	927 mg by SUBQ injection (2 × 1.5 mL injections)

[a] The complete initiation dosing schedule, consisting of SUBQ injections and oral tablets, is required; the efficacy of LEN has only been established with this dosing schedule.
[b] From the date of the last injection.

Dosing Schedule for Missed Dose

Missed Oral Initiation Dose

If the Day 2 oral initiation dose is missed, take it as soon as possible. Do not take Day 1 and Day 2 oral initiation doses on the same day.

Anticipated Delayed Injection

During continuation dosing, if the scheduled 6-month injection is anticipated to be delayed by more than 2 weeks, LEN tablets may be taken on an interim basis (for up to 6 months if needed), until injections resume. Refer to Table 2 below for the dosing schedule for delayed injections.

Table 2. Dosing Schedule for Anticipated Delayed Injections: Weekly Oral Dosage[1]

Time since Last Injection	Dosage of LEN
26 to 28 weeks	Oral dosage of 300 mg taken once every 7 days.[a] Resume the continuation injection dosage within 7 days after the last oral dose.

[a] Use on an interim basis only (for up to 6 months if needed).

Missed Injection

Individuals who miss a scheduled injection visit should be clinically reassessed to ensure resumption of LEN remains appropriate and that the individual remains HIV-1 negative. During continuation dosing, if more than 28 weeks have elapsed since the last injection and LEN tablets have not been taken, see Table 3 below for the dosing schedule after missed injections. Adherence to the injection dosing schedule is strongly recommended.

Table 3. Dosing Schedule after Missed Injections[1]

Time since Last Injection	Dosage of LEN
More than 28 weeks	Reinitiate with initiation dosing schedule from Day 1 (Table 1) and then continue with continuation injection dosing.

Clinical Data on Missed Doses

PK Analysis[2,3]

In a population PK analysis of pooled data from participants across 13 phase 1 to phase 3 studies (N=1337 participants; N=14,648 samples), LEN exposures were characterized following a stepwise modeling approach of SUBQ, oral, and IV administration. Simulations were conducted to support dosing recommendations, which were based on ensuring the 90% CI of mean LEN concentrations remained above the IQ4 (15.5 ng/mL), which is thought to be associated with significant antiviral activity. Based on model simulations of twice-yearly SUBQ LEN in people who want or need PrEP, the lower bound of the 90% CI of mean trough concentration (C_{trough}) was consistently above the IQ4 threshold of 15.5 ng/mL, as well as for at least 2 weeks following a missed SUBQ dose.

Simulations of SUBQ LEN (927 mg) without oral loading showed that the C_{trough} reached the IQ4 of 15.5 ng/mL by Day 22. With the oral loading regimen (600 mg oral on Day 1 and Day 2), concentrations exceeded this threshold earlier (within the first day) and were maintained above IQ4 on Day 2 and thereafter, following the administration of the second oral loading dose. This PK data supports taking the missed oral loading doses as soon as possible to achieve target concentrations.

References

1. Enclosed, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA.
2. Imperial M, Hughes E, Panchia R, et al. Population Pharmacokinetic Analysis of Lenacapavir in People Who Want or Need Pre-Exposure Prophylaxisfor HIV [Poster I-109]. Paper presented at: Population Approach Group Europe (PAGE); 4–6 June, 2025; Thessaloniki, Greece.

3. Begley R, Lutz J, Rhee M, et al. Lenacapavir Sustained Delivery Formulation Supports 6-Month Dosing Interval [Poster PEB0265]. Paper presented at: AIDS 2020: 23rd International AIDS Conference Virtual; 06-10 July, 2020.

Abbreviations

IQ=inhibitory quotient
LEN=lenacapavir
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
SUBQ=subcutaneous(ly)

Product Label

For the full indication, important safety information, and boxed warning, please refer to the Yeztugo US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_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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🖱 www.gilead.com/utility/contact/report-an-adverse-event

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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