GILEAD | Medical Information

Yeztugo® (lenacapavir) Use in Individuals Switching from Oral PrEP

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and its use in individuals switching from oral PrEP.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The use of FTC/TAF for prevention of HIV-1 in individuals at risk of HIV-1 from receptive vaginal sex is investigational and has not been approved by any regulatory authority. The full indication, important safety information, and boxed warning(s) are available at:
www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Summary

Product Labeling

LEN is indicated for PrEP to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating LEN.[1]

Severe acute exacerbations of HBV have been reported in individuals with HBV who have discontinued products containing FTC and/or TDF, and may occur with discontinuation of FTC/TAF. Hepatic function should be monitored closely in these individuals. If appropriate, anti-hepatitis B therapy may be warranted.[2]

Severe acute exacerbations of HBV have been reported in HBV-infected individuals who have discontinued FTC/TDF. Hepatic function should be monitored closely in these individuals who discontinue FTC/TDF. If appropriate anti-hepatitis B therapy may be warranted.[3]

Clinical Data

Once a healthcare professional has identified an individual for LEN, they can switch immediately.[4]

In the OLE phase of the PURPOSE 1 and PURPOSE 2 trials, there were no reported DDIs in participants on FTC/TDF and FTC/TAF who switched directly to LEN.[4]

LEN PK

Based on drug interaction studies conducted with LEN, no clinically significant drug interactions have been observed with tenofovir alafenamide.[1]

Product Labeling[1]

Warning: Risk of Drug Resistance with Use of LEN for HIV-1 PrEP in Undiagnosed HIV-1 Infection

Individuals must be tested for HIV-1 infection prior to initiating LEN, and with each subsequent injection of LEN, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of LEN by individuals with undiagnosed HIV-1 infection. Do not initiate LEN unless negative infection status is confirmed. Individuals who acquire HIV-1 while receiving LEN must transition to a complete HIV-1 treatment regimen.

Indications and Usage

LEN is indicated for PrEP to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating PrEP.

Recommended Dosage

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

Table 1. Dosing Schedule for LEN Initiation and Continuation in Adults and Adolescents Weighing ≥35 kg

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

[a] The complete initiation dosing schedule, consisting of subcutaneous 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.

Clinical Data

PURPOSE 1 is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN (n=2134) and once-daily oral FTC/TAF (n=2136) or FTC/TDF (active control; n=1068) for HIV-1 PrEP in 5338 cisgender women and adolescent

girls (16–25 years old) across South Africa and Uganda. Participants receiving PrEP in the 3 months prior to screening were excluded from the study.[5]

PURPOSE 2 is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN (n=2179) or once-daily oral FTC/TDF (n=1086) for HIV-1 PrEP in cisgender gay, bisexual, and other men, TGW, TGM, and GNB individuals in Argentina, Brazil, Mexico, Peru, South Africa, Thailand, and the US who have condomless receptive anal sex with partners assigned male at birth (N=3265). Participants receiving PrEP in the 3 months prior to screening were excluded from the study.[6]

Participants in both PURPOSE 1 and PURPOSE 2 were offered entry into the LEN OLE phase following the completion of the primary analysis, as LEN demonstrated acceptable efficacy and safety in the Randomized Blinded phase for each of the studies. Participants randomized to FTC/TAF or FTC/TDF switched directly to oral LEN 600 mg on OLE Days 1 and 2, and SUBQ LEN 927 mg on OLE Day 1 and every 26 weeks thereafter.[4,7,8]

In the OLE phase of the PURPOSE 1 and PURPOSE 2 trials, there were no reported DDIs in participants on FTC/TDF and FTC/TAF who switched directly to LEN.[4]

PK DDI Evaluation

Based on drug interaction studies conducted with LEN, no clinically significant drug interactions have been observed with tenofovir alafenamide (Table 2).[1]

Table 2. Effect of LEN on TFV[a,1]

Co-administered Drug	Dose of Co-administered Drug (mg)	Mean Ratio of Co-administered Drug PK Parameters (90% CI)[b]; No effect = 1.00	
		C_{max}	AUC
TAF (fed) (substrate of P-gp)	25 single dose	1.24 (0.98, 1.58)	1.32 (1.09, 1.59)
TFV[c] (substrate of P-gp)		1.23 (1.05, 1.44)	1.47 (1.27, 1.71)

[a] Following 600 mg twice daily for 2 days, single 600 mg doses of LEN were administered with each co-administered drug, resulting in LEN exposures similar to or higher than those at the usual LEN dosing schedule.
[b] All No Effect Boundaries are 70% to 143%.
[c] TAF is converted to TFV in vivo.

Relevant PK Data for LEN, FTC/TAF and FTC/TDF are presented in Table 3, Table 4, and Table 5 below.

Table 3. LEN DDI Potential[1,9]

DDI Mechanism		LEN
Drug Transporters	OCT2	NA
	MATE1	NA
	P-gp	Substrate[a], and Weak Inhibitor
	BCRP	Weak Inhibitor
	OATP1B1	NA
	OATP1B3	NA
Drug Metabolizing Enzymes	CYP3A	Substrate[a,b], and Moderate inhibitor
	UGT1A1	Substrate[a]

[a] Combined P gp, UGT1A1, and strong CYP3A inhibitors may significantly increase plasma concentrations of LEN. Concomitant administration of LEN with these inhibitors is not recommended.
[b] Drugs that are strong or moderate inducers of CYP3A may significantly decrease plasma concentrations of LEN, which may result in reduced effectiveness of LEN. Therefore, dosage modifications (supplemental doses) of LEN are recommended when initiating strong or moderate CYP3A inducers. Please refer to Section 2.5, *Dosage Modifications for Co-administration with Strong or Moderate CYP3A Inducers*, of the Yeztugo US Prescribing Information for more information.

Table 4. FTC/TAF DDI Potential[2]

DDI Mechanism		FTC	TAF
Drug Transporters	P-gp/BCRP	N/A	Substrate
	OATP1B1	N/A	Substrate
	OATP1B3	N/A	Substrate
Drug Metabolizing Enzymes	CYP3A	N/A	Minor Substrate

Table 5. FTC/TDF DDI Potential[3]

DDI Mechanism		FTC	TDF
Drug Transporters	P-gp/BCRP	N/A	Substrate

Literature Search

A literature search was conducted in Ovid MEDLINE and Embase databases for studies published between 1946 and September 2, 2025 using search terms that included Yeztugo, lenacapavir, PrEP, switch, Descovy, Truvada, emtricitabine, tenofovir alafenamide, tenofovir disoproxil fumarate and related search terms. No relevant citations were found.

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. Enclosed. Gilead Sciences Inc, DESCOVY® (emtricitabine and tenofovir alafenamide) tablets, for oral use. U. S. Prescribing Information. Foster City, CA.
3. Enclosed. Gilead Sciences Inc, TRUVADA® (emtricitabine/tenofovir disoproxil fumarate) tablets, for oral use. U.S. Prescribing Information. Foster City, CA.
4. Gilead Sciences Inc. Data on File.

5. Bekker LG, Das M, Abdool Karim Q, et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. *N Engl J Med.* 2024;391(13):1179-1192.
6. Kelley CF, Acevedo-Quinones M, Agwu AL, et al. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons. *N Engl J Med.* 2024.
7. ClinicalTrials.gov. Study to Assess Safety and Efficacy of Lenacapavir and Emtricitabine/Tenofovir Alafenamide for Pre-Exposure Prophylaxis in Adolescent Girls and Young Women at Risk of HIV Infection (PURPOSE 1). ClinicalTrials.gov Identifier: NCT04994509. Available at: https://clinicaltrials.gov/ct2/show/NCT04994509. Accessed: 22 December. Last Updated: 19 December. 2022.
8. ClinicalTrials.gov. Study to Assess the Effectiveness and Safety of Lenacapavir for Human Immunodeficiency Virus (HIV) Pre-Exposure Prophylaxis (PURPOSE 2). ClinicalTrials.gov Identifier: NCT04925752. Available at: https://clinicaltrials.gov/ct2/show/NCT04925752. Accessed: 22 December. Last Updated: 21 December. 2022.
9. Lutz J. CLINICAL EVALUATION OF DRUG INTERACTIONS WITH ORAL LENACAPAVIR AND PROBE DRUGS [Presentation]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); March 6-10, 2021; Virtual.

Abbreviations

AUC=area under the curve
BCRP=breast cancer resistance protein
C_{max}=maximum concentration
DDI=drug-drug interaction
FTC=emtricitabine
GNB=gender nonbinary
LEN=lenacapavir
MATE=multidrug and toxin extrusion protein
NA=not applicable
OATP=organic anion transporting polypeptide
OCT=organic cation transporter
OLE=open-label extension
P-gp=P-glycoprotein
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
SUBQ=subcutaneous
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV=tenofovir
TGM=transgender men
TGW=transgender women

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Yeztugo, Descovy, and Truvada US Prescribing Information available at:
www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_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

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 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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