GILEAD | Medical Information

Yeztugo® (lenacapavir) Coadministration with Gender-Affirming Hormone Therapy

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and coadministration with gender-affirming hormone therapy.

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[1]

There is no information in the LEN product labeling about the coadministration of LEN and gender-affirming hormone therapy.

Clinical Data from PURPOSE 1 and PURPOSE 2[2]

At present, there are no subgroup analyses evaluating the efficacy and safety outcomes of LEN in PURPOSE 1 and PURPOSE 2 participants receiving hormones.

Pharmacokinetic Data[3]

In a population PK analysis of pooled data from participants across 13 phase 1 to phase 3 studies, simulations showed that the use of gender-affirming hormone therapy had no impact on LEN exposures.

Product Labeling[1]

There is no information in the LEN product labeling about the coadministration of LEN and gender-affirming hormone therapy.

Clinical Data on Coadministration of LEN and GAHT

PURPOSE 1

PURPOSE 1 is an ongoing, phase 3, double-blind, randomized, active-controlled study evaluating the efficacy and safety of twice-yearly, SUBQ LEN (n=2134) and once-daily oral FTC/TAF (n=2136) for HIV-1 PrEP in cisgender women and adolescent girls (16–25 years old) across South Africa and Uganda. Additionally, a third group was assigned once-daily oral FTC/TDF (n=1068), which served as the active control. The primary efficacy endpoint was the incidence of HIV among randomized participants.[2]

At present, there are no subgroup analyses evaluating the efficacy and safety outcomes of LEN in participants receiving hormones.

PURPOSE 2

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 aged ≥16 years 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). The primary efficacy endpoint was the incidence of HIV among randomized participants.[4]

The use of gender-affirming hormone therapy was reported in 253 (11.6%) participants in the LEN group (n=2183) and 131 (12%) participants in the FTC/TDF group (n=1088).[4]

At present, there are no subgroup analyses evaluating the efficacy and safety outcomes of LEN in participants receiving gender-affirming hormone therapy.

PK Analysis

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. Subgroups of interest which were modeled in graphical evaluations with PK parameters included participants in PURPOSE 1 on long-acting contraceptives and who became pregnant, and in PURPOSE 2 included participants on gender-affirming hormone therapy.

A total of 534 participants in PURPOSE 2 were evaluated on gender-affirming hormone therapy. From the PK analysis, the use of gender-affirming hormone therapy did not have an impact on LEN exposures.[3]

PK DDI Evaluation

Relevant LEN PK Data is presented in Table 1 below. For more information about the specific hormone therapy of interest, please refer to its product labeling.

LEN PK

Table 1. LEN DDI Potential[1,5]

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.

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. 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):1179-92.
3. 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]. 2025:
4. 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;
5. Lutz J. CLINICAL EVALUATION OF DRUG INTERACTIONS WITH ORAL LENACAPAVIR AND PROBE DRUGS [Presentation]. 2021

Abbreviations

BCRP=breast cancer resistance protein
DDI=drug-drug interaction
FTC=emtricitabine
GNB=gender non-binary
LEN=lenacapavir
MATE=multidrug and toxin extrusion protein
NA=not applicable
OATP=organic anion transporting polypeptide
OCT=organic cation transporter
P-gp=P-glycoprotein
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
SUBQ=subcutaneous(ly)
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TGM=transgender men
TGW=transgender women
UGT=uridine 5'-diphospho-glucuronosyltransferase

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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