GILEAD | Medical Information

Yeztugo® (lenacapavir) Use in Pediatric and Adolescent Individuals

This document is in response to your request for information regarding the use of Yeztugo® (lenacapavir [LEN]) in pediatric and adolescent individuals.

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]

LEN is indicated for PrEP to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing ≥35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating LEN. The safety, effectiveness, and pharmacokinetics of LEN in pediatric populations weighing <35 kg have not been established.

Clinical Data on LEN Use in Pediatric and Adolescent Individuals

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.[2]

- Zero HIV cases occurred in adolescent participants aged 16 and 17 years in the LEN, FTC/TAF, and FTC/TDF arms.[3]
- LEN was well tolerated and deemed safe in adolescents by study investigators. AEs were generally similar between adolescents and adults receiving LEN.[3]
- LEN plasma concentrations were similar between adolescents and adults.[3]

PURPOSE 2 is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN (n=1086) and once-daily oral FTC/TDF (n=2179) 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.[4] There were 2 incident cases of HIV-1 in the LEN group (1938 PY; incidence rate, 0.1 per 100 PY; 95% CI: 0.01–0.37); both cases occurred in participants aged 16 to 25 years.[4,5]

In a pooled analysis of the efficacy, safety, and PK of youth participants who received SUBQ LEN in PURPOSE 1 and PURPOSE 2, there were no incident cases of HIV in PURPOSE 1 and 2 incidences in PURPOSE 2 among youths in the LEN group. Overall, LEN was well tolerated, and AEs and lab abnormalities were similar between the two studies. Most ISRs in youths were mild in severity and were consistent with the overall rates reported in PURPOSE 1 and PUROSE 2. LEN plasma concentrations were generally comparable between youth and adults.[5]

Product Labeling[1]

Indications and Usage

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

Use in Specific Populations

Pediatric use

The safety and effectiveness of LEN for HIV-1 PrEP in adolescents weighing ≥35 kg who are at risk for HIV-1 acquisition is supported by two adequate and well-controlled trials, PURPOSE 1 and PURPOSE 2, that enrolled both adults and adolescents.

PURPOSE 1 and PURPOSE 2 enrolled a total of 128 adolescent participants. In the 59 adolescents who received LEN, the safety data were comparable to the safety data reported in adults receiving LEN.

HIV-1 testing should be conducted prior to initiating LEN, prior to each subsequent injection of LEN, and additionally, as clinically appropriate, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Adolescents may benefit from additional counseling and appointment reminders to support adherence to the dosing and testing schedule.

The safety, effectiveness, and pharmacokinetics of LEN in pediatric populations weighing <35 kg have not been established.

Clinical Data on LEN Use in Pediatric and Adolescent Individuals

PURPOSE 1 Study

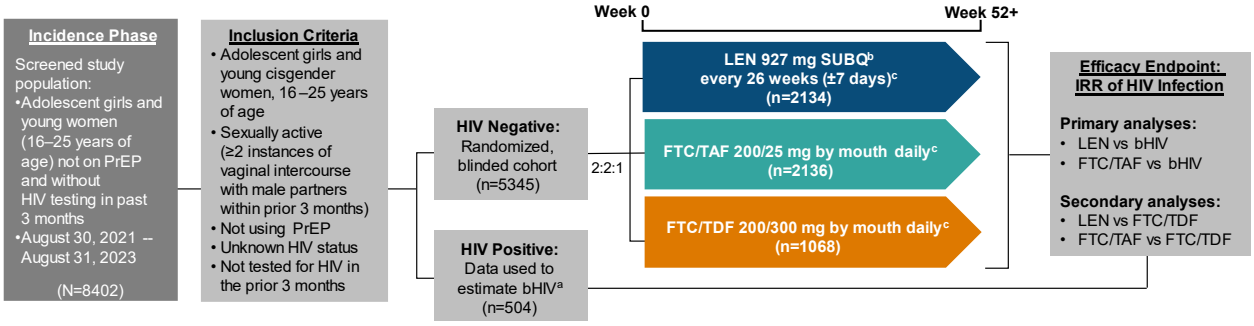
Study design and demographics[2]

PURPOSE 1 (NCT04994509) is an ongoing, phase 3, double-blind, randomized, active-controlled study evaluating the efficacy and safety of twice-yearly SUBQ LEN and once-daily oral FTC/TAF for HIV-1 PrEP in cisgender women and adolescent girls across South Africa and Uganda. Additionally, a third group was assigned once-daily oral FTC/TDF, which served as the active control. Eligible women and adolescent girls were tested for HIV

at screening, and those who tested negative were randomly assigned in a 2:2:1 ratio to receive LEN 927 mg SUBQ every 26 weeks, FTC/TAF 200/25 mg orally daily, or FTC/TDF 200/300 mg orally daily, respectively (Figure 1).

Those who tested positive for HIV at screening were referred for care at a local center, and their samples underwent additional testing to determine the recency of HIV; these data were used to estimate the bHIV that would be expected without PrEP. Participants who discontinued blinded study drug were given the option to take open-label FTC/TDF. Testing for HIV in the randomized cohort was conducted at Weeks 4, 8, and 13 and every 13 weeks thereafter.

Figure 1. PURPOSE 1: Study Design[2]



[a]The bHIV was determined based on a cross-sectional incidence estimate derived from rates of recent HIV in 8094 screened participants; these participants were not followed longitudinally.
[b]All participants randomly assigned to receive LEN received an initial loading dose of LEN, which consisted of 600 mg (two 300-mg tablets) administered on Days 1 and 2.
[c]Participants in the LEN SUBQ group also received placebo FTC/TAF or placebo FTC/TDF (2:1), and participants in the FTC/TAF and FTC/TDF groups also received placebo LEN oral loading doses and placebo LEN SUBQ.

A total of 5345 participants were randomly assigned and received ≥1 dose of study drug. Baseline HIV was identified in 7 participants after having received ≥1 dose of study drug. Baseline characteristics at randomization among the three groups were similar (Table 1). Overall retention in the study was high and similar across groups, with 4855/5020 participants (96.7%) completing 26 weeks of follow-up, 2439/2612 participants (93.4%) completing 52 weeks, and 39/43 participants (91%) completing 104 weeks.

An independent committee determined that the planned interim efficacy analysis (when 50% of participants had completed ≥52 weeks of follow-up; data cutoff for clinical data, May 28, 2024, and data cutoff for laboratory data, May 29, 2024) met the prespecified criteria for stopping the randomized, blinded portion of the trial. Starting July 8, 2024, all participants were offered open-label LEN.

Table 1. PURPOSE 1: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		LEN (n=2138)	FTC/TAF (n=2137)	FTC/TDF (n=1070)
Age	Median (range), years	21 (16–25)	21 (16–26)	21 (16–25)
	16 or 17 years of age, n (%)	56 (2.6)	45 (2.1)	23 (2.1)
Black race, n (%)		2135 (99.9)	2136 (>99.9)	1068 (99.8)
Living with primary partner, n/N (%)		148/2136 (6.9)	132/2134 (6.2)	73/1069 (6.8)
Previous use of PrEP, n (%)		143 (6.7)	121 (5.7)	71 (6.6)
Previously tested for HIV, n (%)		1713 (80.1)	1731 (81)	860 (80.4)
Time since last HIV test, median (IQR), months		6.8 (4.7–11.5)	6.6 (4.8–11)	6.5 (4.6–11)

Key Demographics and Characteristics		LEN (n=2138)	FTC/TAF (n=2137)	FTC/TDF (n=1070)
Sexually transmitted infections, n (%)	*Chlamydia trachomatis*	520 (24.3)	562 (26.3)	263 (24.6)
	Neisseria gonorrhoeae	197 (9.2)	178 (8.3)	90 (8.4)
	Trichomonas vaginalis	154 (7.2)	165 (7.7)	82 (7.7)
	Syphilis	57 (2.7)	63 (2.9)	29 (2.7)
Country, n (%)	South Africa	1809 (84.6)	1790 (83.8)	909 (85)
	Uganda	329 (15.4)	347 (16.2)	161 (15)

Efficacy and safety

A total of 55 incident HIV cases occurred in the overall randomized cohort; no participants in the LEN group acquired HIV (1939 PY; incidence rate, 0 per 100 PY; 95% CI: 0–0.19), 39 HIV cases occurred in the FTC/TAF group (1932 PY; incidence rate, 2.02 per 100 PY; 95% CI: 1.44–2.76), and 16 occurred in the FTC/TDF group (949 PY; incidence rate, 1.69 per 100 PY; 95% CI: 0.96–2.74). The bHIV in the screened population was 2.41 per 100 PY.[2]

Zero HIV cases occurred in adolescent participants aged 16 to 17 years in any treatment group (Table 2).[3]

Table 2. PURPOSE 1: Incident HIV Cases Among Adolescent Participants[3]

	LEN (n=56)	FTC/TAF (n=45)	FTC/TDF (n=23)
Incidence rate	0 cases per 42 PY	0 cases per 33 PY	0 cases per 18 PY

LEN was well tolerated and was deemed safe in adolescents by study investigators. Adverse events were generally similar between adolescents and adults receiving LEN (Table 3).[3]

Table 3. PURPOSE 1: Safety Outcomes of Participants in the LEN Group[3]

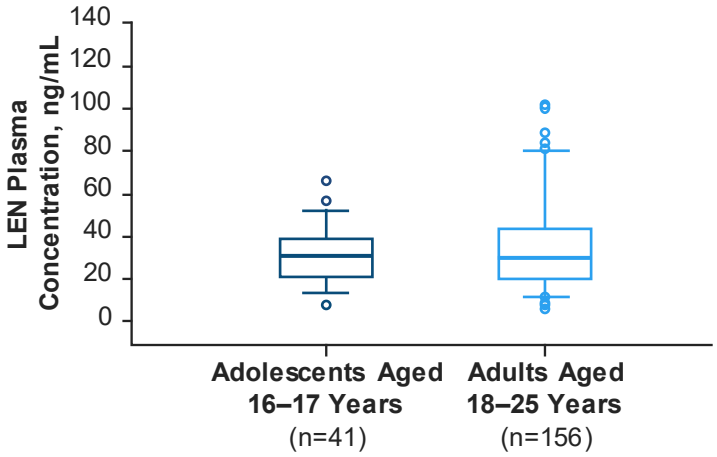
AEs,[a] n or n (%)		Adolescent Participants Aged 16–17 Years (n=56)	Adult Participants Aged 18–25 Years (n=2084)
Any AE		53 (94.6)	1840 (88.3)
AE related to study drug		40 (71.4)	1337 (64.2)
SAEs		1 (1.8)[b]	58 (2.8)
AEs that led to study drug discontinuation		0	5 (0.2)[c]
ISR and non-ISR AEs occurring in ≥10% of participants in the adolescent group	Injection-site nodule	42 (75.0)	1323 (63.5)
	Injection-site pain	18 (32.1)	651 (31.2)
	Headache	9 (16.1)	276 (13.2)
	Genitourinary chlamydia infection	7 (12.5)	293 (14.1)
Laboratory abnormalities,[d] n		55	2073
Any grade ≥1		49 (89.1)	1881 (90.7)
Grade ≥3		6 (10.9)[e]	110 (5.3)

[a]AEs were treatment emergent in participants who received ≥1 dose of study drug. AEs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) Version 27.0.
[b]SAE of pyelonephritis.
[c]AEs that led to study drug discontinuation were nausea, decreased creatinine renal clearance, increased hepatic enzymes, spontaneous miscarriage, and suicide attempt/major depression (each, n=1).
[d]Included data from participants with ≥1 post-baseline result. Severity grades were defined by DAIDS Table for Grading the Severity of Adult and Pediatric AEs, Version 2.1.
[e]Included decreased creatinine clearance (n=2), decreased Hgb (n=2), increased creatinine kinase (n=1), and decreased creatinine clearance and proteinuria (n=1).

PK analysis[3]

Median LEN plasma concentrations were similar between adolescents aged 16 to 17 years (31.1 ng/mL) and adults aged 18–25 years (29.8 ng/mL; Figure 2).

Figure 2. PURPOSE 1: LEN Plasma Concentrations in Adolescents and Adults at Week 26 (C_{trough})[3a,b]



[a]Excluded participants who became pregnant and those who received oral LEN bridging.
[b]Values below the limit of quantitation were treated as zero.
Note: Box represents Q1 and Q3, the horizonal line inside the box represents the median, and the whiskers represent the 5th and 95th percentiles.

PURPOSE 2 Study

PURPOSE 2 (NCT04925752) is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN and once-daily oral FTC/TDF 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). Eligible participants were tested for HIV at screening, and those who tested negative were randomly assigned in a 2:1 ratio to SUBQ LEN every 26 weeks plus daily oral FTC/TDF placebo (n=2179) or SUBQ LEN placebo every 26 weeks plus daily oral FTC/TDF (n=1086). Additional testing was performed with samples from participants who tested positive for HIV at screening to determine the recency of the HIV infection, and these data were used to estimate the bHIV that would be expected without PrEP. The primary efficacy endpoint was the incidence of HIV among randomized participants.[4]

In total, there were 11 incident HIV cases: 2 in the LEN group (1938 PY; incidence rate, 0.1 per 100 PY; 95% CI: 0.01–0.37) and 9 in the FTC/TDF group (967 PY; incidence rate, 0.93 per 100 PY; 95% CI: 0.43–1.77). The bHIV in the screened population was 2.37 per 100 PY (95% CI: 1.65–3.42).[4]

Both cases of HIV acquisition in the LEN group occurred in youths aged 15 to 24 years.[5]

Pooled Analysis: PURPOSE 1 and PURPOSE 2[5]

The efficacy, safety, and PK of SUBQ LEN in youth participants in PURPOSE 1 (aged 16 to <18 years vs ≥18 to 25 years) and PURPOSE 2 (aged 16 to ≤25 years vs >25 years) were

assessed in a pooled analysis. There were no incident cases of HIV in PURPOSE 1 and 2 incidences in PURPOSE 2 among participants who received LEN.

Overall, LEN was well tolerated, and AEs and lab abnormalities were similar among youth participants in the LEN groups of PURPOSE 1 and PURPOSE 2 (Table 4). Most ISRs in youths were mild in severity and were consistent with the overall rates reported in PURPOSE 1 and PUROSE 2.

Table 4. Pooled Analysis: Safety Outcomes in Youths in the LEN Groups in PURPOSE 1 and PURPOSE 2[5]

AEs,[a] n or n (%)		LEN in PURPOSE 1		LEN in PURPOSE 2	
		Aged 16 to <18 Years (n=56)	Aged ≥18 to 25 Years (n=2084)	Aged 16 to ≤25 Years (n=752)	Aged >25 Years (n=1431)
Any AE		41 (73.2)	1590 (76.3)	537 (71.4)	1070 (74.8)
Grade ≥2		19 (33.9)	1092 (52.4)	403 (53.6)	770 (53.8)
Grade ≥3		4 (7.1)	84 (4)	28 (3.7)	63 (4.4)
SAEs		1 (1.8)	58 (2.8)	22 (2.9)	49 (3.4)
AEs related to LEN		9 (16.1)	489 (23.5)	79 (10.5)	184 (12.9)
AEs that led to LEN discontinuation		0	5 (0.2)	5 (0.7)	2 (0.1)
Laboratory abnormalities		55	2073	739	1414
Any grade		49 (89.1)	1881 (90.7)	597 (80.8)	1225 (86.6)
Grade 3		6 (10.9)	90 (4.3)	39 (5.3)	145 (10.3)
Grade 4		0	20 (1)	24 (3.2)	35 (2.5)
Non-ISR AEs in ≥10% of participants in any arm	Headache	9 (16.1)	276 (13.2)	36 (4.8)	83 (5.8)
	Genitourinary chlamydia	7 (12.5)	293 (14.1)	-	-
	Upper respiratory infection	2 (3.6)	269 (12.9)	48 (6.4)	100 (7)
	Urinary tract infection	1 (1.8)	306 (14.7)	-	-
	Anal chlamydia infection	-	-	118 (15.7)	171 (11.9)
	Anal gonococcal infection	-	-	114 (15.2)	119 (8.3)
	Oropharyngeal gonococcal infection	-	-	109 (14.5)	174 (12.2)
Any-grade ISRs		44 (78.6)	1428 (68.5)	619 (82.3)	1197 (83.6)
Grade 1		35 (62.5)	1027 (49.3)	485 (64.5)	956 (66.8)
Grade 2		9 (16.1)	397 (19)	130 (17.3)	231 (16.1)
Grade 3		0	4 (0.2)	4 (0.5)	10 (0.7)
Serious ISRs		0	0	0	0
ISRs that led to LEN discontinuation		0	4 (0.2)	7 (0.9)	19 (1.3)

[a]AEs were treatment emergent in participants who received ≥1 dose of study drug. AEs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) Version 27.0, and the severity of grades were defined by DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1.

LEN plasma concentrations at Week 26 were generally comparable between youths aged ≤25 years in PURPOSE 1 and PURPOSE 2 (n=285) and adults aged >25 years in PURPOSE 2 (n=181).

References

1. YEZTUGO®, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA. Revised: June. 2025.
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):1179-1192.

3. Gill K, Ndlovu N, Brumskine W, et al. Lenacapavir Efficacy, Safety, and Pharmacokinetics in Adolescents and Adults in PURPOSE 1 [Presentation]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); March 9-12, 2025; San Francisco, CA.
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.* 2025.
5. Gill K, Karim QA, Anugulruengkitt S, et al. Efficacy, Safety, and Pharmacokinetics of Twice-Yearly Subcutaneous Lenacapavir for PrEP Among Adolescents and Young People in the Phase 3 Trials PURPOSE 1 and PURPOSE 2. [Presentation]. Paper presented at: 13th International AIDS Society (IAS) Conference on HIV Science; July 13–17, 2025; Kigali, Rwanda.

Abbreviations

AE=adverse events
bHIV=background HIV incidence
DAIDS=Division of AIDS
FTC=emtricitabine
GNB=gender non-binary
LEN=lenacapavir
ISR=injection site reaction
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
PY=person-years
Q=quarter
SAE=serious adverse event
SUBQ=subcutaneous
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
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

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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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