Gilead Sciences, Inc. is providing this document to you, a US Healthcare Professional, in response to your unsolicited request for medical information.

GILEAD | Medical Information

Yeztugo® (lenacapavir) Adherence

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and adherence data.

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.

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 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]

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.

Please refer to Section 2.4 of the Prescribing Information for the dosing schedule for missed dose.

Clinical Data on Adherence to LEN

In PURPOSE 1, a phase 3 study comparing the efficacy and safety of twice-yearly SUBQ LEN with once-daily oral FTC/TAF or FTC/TDF for HIV-1 PrEP in CGW, adherence to LEN or placebo injections was 91.5% for the second injection at Week 26 and 92.8% for the third injection at Week 52.[2] At OLE Week 52, adherence was 96% in both the continuous LEN group and the LEN switch group at OLE Week 26 and in 97% of participants in both groups at OLE Week 52.[3]

In PURPOSE 2, a phase 3 study comparing the efficacy and safety of twice-yearly SUBQ LEN with those of once-daily oral FTC/TDF in CGM, TGW, TGM, and GNB individuals for HIV-1 PrEP, adherence to LEN or placebo injections was 91% at Week 26 and 92.8% at Week 52.[4] At OLE Week 52, adherence was 95% in the continuous LEN group and 96% in the LEN switch group at OLE Week 26 and 90% and 92%, respectively, at OLE Week 52.[5]

Gilead Sciences, Inc. is providing this document to you, a US Healthcare Professional, in response to your unsolicited request for medical information.

Clinical Data on Adherence to LEN

PURPOSE 1 Study in CGW

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 CGW 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. 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. The prespecified primary analysis was conducted when 50% of participants had completed ≥52 weeks of follow-up.

The primary efficacy endpoint was the incidence of HIV among randomized participants. A total of 5345 participants were randomly assigned and received ≥1 dose of study drug. Baseline characteristics at randomization among the three treatment groups were similar (Table 1).

Table 1. PURPOSE 1: Select Baseline Demographics and Clinical 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)
Black race,[a] n (%)		2135 (99.9)	2136 (>99.9)	1068 (99.8)
Education, n/N (%)	No primary school	17/2136 (0.8)	19/2134 (0.9)	3/1069 (0.3)
	Primary school	235/2136 (11)	223/2134 (10.4)	106/1069 (9.9)
	Secondary school	1701/2136 (79.6)	1694/2134 (79.4)	851/1069 (79.6)
	College or university	183/2136 (8.6)	198/2134 (9.3)	109/1069 (10.2)
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)
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)

[a]Race was reported by the participants. All non-Black participants were multiracial.

Adherence results

Primary analysis[2]

Adherence to LEN was defined as on-time injections (≤28 weeks after the last injection). Most participants received their injections (LEN and placebo LEN) on time at Weeks 26 (91.5%; 4545/4967) and 52 (92.8%; 2025/2181), and adherence to injections was similar across all groups receiving injections.

Adherence to FTC/TAF and FTC/TDF was evaluated at study visits using DBS analysis of TDF levels in 10% of participants, who were randomly preselected from each group. Adherence in the 10% sample of participants in the FTC/TAF and FTC/TDF groups was low and decreased over time. At Week 8, in the FTC/TAF and FTC/TDF groups, adherence was low (<2 doses/week) in 34% and 50% of participants, respectively; at Week 52, adherence was low in 84% and 93%. Among participants who acquired HIV and had data available, 34/37 participants in the FTC/TAF group and 13/14 participants in the FTC/TDF group had low or undetectable levels of TDF. In a matched case-control analysis to assess the association between adherence and efficacy in the FTC/TAF group, participants with medium (2 or 3 doses/week) or high (≥4 doses/week) adherence had lower odds of acquiring HIV than those with low adherence (odds ratio, 0.11; 95% CI: 0.01–0.49).

OLE Week 52 analysis[3]

Adherence to open-label LEN was high in both groups, with on-time injections (≤28 weeks after the last injection) in 96% of participants who received the second injection in the OLE phase at Week 26 in both the continuous LEN group (n=1660) and LEN switch group (n=2438) and in 97% of participants who received the third injection in the OLE at Week 52 in both the continuous LEN group (n=1018) and LEN switch group (n=2318).

PURPOSE 2 Study in CGM, TGW, TGM, and GNB Individuals

Study design and demographics

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 + daily oral FTC/TDF placebo (n=2179) or SUBQ LEN placebo every 26 weeks + 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.[6]

The primary efficacy endpoint was the incidence of HIV among randomized participants. A total of 3271 participants were randomly assigned and received ≥1 dose of study drug; 6 participants were diagnosed with HIV on Day 1 and were excluded from the efficacy analysis (modified ITT, n=3265). Baseline demographics were balanced between randomized groups (Table 2).[4]

Table 2. PURPOSE 2: Select Baseline Demographics and Disease Characteristics[4]

Key Demographics and Characteristics		LEN (n=2183)	FTC/TDF (n=1088)
Age	Median (range), years	28 (17–74)	29 (17–73)
	16 to ≤25 years, n (%)	752 (34.4)	344 (31.6)
Country, n (%)	Brazil	769 (35.2)	396 (36.4)
	United States	440 (20.2)	235 (21.6)
	Peru	309 (14.2)	138 (12.7)
	Thailand	250 (11.5)	139 (12.8)
	South Africa	246 (11.3)	112 (10.3)
	Argentina	161 (7.4)	64 (5.9)
	Mexico	8 (0.4)	4 (0.4)
Race or ethnicity, n/N (%)	Hispanic or Latine	1378/2182 (63.2)	675/1088 (62)
	Black[a]	811/2175 (37.3)	420/1086 (38.7)
	White	722/2175 (33.2)	344/1086 (31.7)
	Indigenous or Indigenous ancestry[b]	341/2175 (15.7)	156/1086 (14.4)
	Asian	269/2175 (12.4)	144/1086 (13.3)
	Other and other multiracial[c]	32/2175 (1.5)	22/1086 (2)
Gender identity, n (%)	CGM	1697 (77.7)	846 (77.8)
	TGW	315 (14.4)	161 (14.8)
	GNB[d]	136 (6.2)	63 (5.8)
	TGM	29 (1.3)	14 (1.3)
	Other[e]	6 (0.3)	4 (0.4)
Sexually transmitted infections,[f] n (%)	*Chlamydia trachomatis*	253 (11.6)	126 (11.6)
	Neisseria gonorrhea	193 (8.8)	115 (10.6)
	Syphilis	84 (3.8)	43 (4)
No history of HIV test, n (%)		597 (27.3)	306 (28.1)
Any history of PrEP use, n (%)		515 (23.6)	249 (22.9)
Self-reported use of stimulants with sex in last 12 weeks, n (%)		491 (22.5)	271 (24.9)

[a]Included all participants who identified as Black/of Black ancestry: Black, Black/White, Black/Pardo (a specific racial category in Brazil), Black/Brown (Brazil), Black/Colored (a specific racial category in South Africa), Black/American Indian or Alaskan Native, Black/Asian, and Black/Native Hawaiian or Pacific Islander.
[b]Included all participants who identified as American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Asian/Native Hawaiian or Pacific Islander, White/Native Hawaiian or Pacific Islander, and White/American Indian or Alaskan Native.
[c]Included all participants who identified as Asian/White, Colored (South Africa), Pardo (Brazil), White/Brown (Brazil), multiracial any other, and not multiracial other.
[d]Included 122 participants (89.7%) in the LEN group and 53 participants (84.1%) in the FTC/TDF group assigned male at birth.
[e]Included individuals who identified as Travesti (LEN, n=3; FTC/TDF, n=3) or as an "Other" gender (LEN, n=3; FTC/TDF, n=1).
[f]*Chlamydia trachomatis* and *Neisseria gonorrhea* were diagnosed based on testing of pharyngeal, rectal, and urethral (urine) samples by central and local laboratories. Syphilis was diagnosed by testing blood and was performed locally by local testing protocols.

Adherence results

Primary analysis

Adherence was high, and injections were administered on time (≤28 weeks of prior injection) in 91% of participants (2606/2864) at Week 26 and in 92.8% of participants (1016/1095) at Week 52. In the FTC/TDF group, TFV-DP concentrations in DBS consistent with high adherence (≥4 pills per week) were observed in 82% at Week 8, 67% at Week 26, and 62% at Week 52 (Table 3).[4]

Table 3. PURPOSE 2: Adherence to LEN and Placebo LEN Injections[7]

Parameter, n or n (%)	LEN	Placebo Injections
Expected to receive second LEN injection at Week 26[a]	1912	952
On-time SUBQ injections ≤14 days	1729 (90.4)	877 (92.1)
< -14 days	2 (0.1)	4 (0.4)
-14 to -8 days	12 (0.6)	9 (0.9)
-7 to 7 days	1643 (85.9)	826 (86.8)
8 to 14 days	72 (3.8)	38 (4)
>14 days (late injection)	81 (4.2)	40 (4.2)
Did not receive injection	102 (5.3)	35 (3.7)
Expected to receive third LEN injection at Week 52[a]	727	368
On-time SUBQ injections ≤14 days	678 (93.3)	338 (91.8)
< -14 days	4 (0.6)	4 (1.1)
-14 to -8 days	13 (1.8)	4 (1.1)
-7 to 7 days	615 (84.6)	305 (82.9)
8 to 14 days	46 (6.3)	25 (6.8)
>14 days (late injection)	32 (4.4)	16 (4.3)
Did not receive injection	17 (2.3)	14 (3.8)

[a]Projected SUBQ LEN or placebo injection visit date is the previous injection visit date plus 26 weeks (182 days). Expected to receive an SUBQ injection includes participants with the potential to be followed up on or beyond the upper limit of the clinical injection visit window (previous SUBQ injection date +189 days [26+1 weeks]) and did not permanently discontinue randomized blinded phase prior to upper limit of the protocol clinical injection visit window. Participants with an SUBQ injection at a visit also counted as expected at the visit. Injections are considered received if any injection dose is administered, including partial or incomplete injections.

OLE Week 52 analysis[5]

Adherence to open-label LEN was high in both groups, with on-time injections (≤28 weeks after the last injection) in 95% of participants in the continuous LEN group and 96% of those in the LEN switch group who received the second OLE injection at OLE Week 26 (n=1536 and n=801, respectively). Of the participants who received the third OLE injection at OLE Week 52 in the continuous LEN (n=1477) and LEN switch groups (n=767), 90% and 92%, respectively, had on-time injections.

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):1179-1192.
3. Kiwanuka N, Malahleha M, Nair G, et al. Zero HIV Acquisitions With Twice-Yearly Subcutaneous Lenacapavir for PrEP During 52 Weeks of Open-Label Extension in PURPOSE 1 [Presentation]. Paper presented at: The 26th International AIDS Conference (AIDS); July 26-31, 2026; Rio de Janeiro, Brazil.
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. Losso M, Santos B, Lama JR, et al. High Efficacy of Twice-Yearly Subcutaneous Lenacapavir for PrEP Through 52 Weeks of Open-Label Extension in PURPOSE 2 [Presentation]. Paper presented at: The 26th International AIDS Conference (AIDS); July 26-31, 2026; Rio de Janeiro, Brazil.
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.* 2025;392(13):1261-1276.

7. Kelley CF, Acevedo-Quinones M, Agwu AL, et al. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons [Supplementary Appendix]. *N Engl J Med.* 2024.

Abbreviations

bHIV=background HIV incidence
CGM=cisgender men
CGW=cisgender women
DBS=dried blood spot
FTC=emtricitabine
GNB=gender nonbinary
LEN=lenacapavir
OLE=open-label extension
PrEP=pre-exposure prophylaxis
SUBQ=subcutaneous(ly)
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TFV-DP=tenofovir diphosphate
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

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact gilead.privacy@gilead.com.

YEZTUGO, DESCOVY, DESCOVY for PrEP, TRUVADA, TRUVADA for PrEP, GILEAD, and the GILEAD logo are registered trademarks of Gilead Sciences, Inc., or its related companies.
© 2026 Gilead Sciences, Inc.