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GILEAD | Medical Information

Yeztugo® (lenacapavir) Body Mass Index

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and data in individuals with different body mass index (BMI).

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.

Product Labeling

There were no clinically significant differences in the PK of LEN based on body weight.[1]

There are no dosage modifications or precautions for use of LEN in high BMI individuals. There is no upper weight limit or BMI limitation stated. Individuals of any higher weight are eligible if they meet the minimum weight threshold of 35 kg.[1]

It is recommended to administer LEN using the injection safety needle for subcutaneous injection (22-gauge, ½ inch) provided in the dosing kit, regardless of BMI. No recommendations are given to vary needle size based on weight, BMI, or body habitus.[1]

Clinical Data on LEN and BMI

PURPOSE 1 and 2

Study Design and Demographics

PURPOSE 1 (NCT04994509) is an ongoing, phase 3, double-blind, randomized, active-controlled study evaluating the efficacy and safety of twice-yearly SUBQ LEN, once-daily oral FTC/TAF, and once-daily oral FTC/TDF for HIV-1 PrEP in cisgender women and adolescent girls across South Africa and Uganda.[2]

Median BMI at screening for the 5368 participants who were randomized was 25.2 kg/m^2 (range: 14.6–62.7 kg/m^2).[2]

PURPOSE 2 (NCT04925752) is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN or once-daily oral FTC/TDF 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.[3]

Median BMI at screening for the 3291 participants who were randomized as 25.1 kg/m^2 (range: 14.4–89.3 kg/m^2).[3]

The clinical trials (PURPOSE 1 and 2) did not mention reduced efficacy in people with higher BMI. Efficacy outcomes were also not reported separately for participants with lower BMI. There was no sub-analysis of efficacy and safety in participants by baseline BMI classification or by baseline weight.[4,5]

Pharmacokinetics

Available PK analysis of LEN in individuals who want or need PrEP assessed weight as a covariate for its impact on LEN exposures. The population PK analysis consisted 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. Despite some inter-individual variability in absorption rates and lag times, model diagnostics indicated that body weight was a statistically significant covariate; however, the effect on LEN exposure was not considered clinically relevant.[6]

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 [Supplementary Appendix]. *N Engl J Med.* 2024:1-69.
3. 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.
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. 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. 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.

Abbreviations

BMI=body mass index
FTC=emtricitabine
GNB=gender non-binary
LEN=lenacapavir
PK=pharmacokinetics
PrEP=pre-exposure prophylaxis
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, 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:
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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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