GILEAD | Medical Information

Yeztugo® (lenacapavir) Tail-Phase Pharmacokinetics

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and its tail-phase pharmacokinetics.

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 are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.

Available Data

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]

There are currently no data regarding the duration of the protective effect conferred by LEN after administration. There are no data regarding the potential for resistance development upon drug discontinuation.

Product Labeling[1]

Warnings and Precautions

Potential Risk of Resistance with LEN

There is a potential risk of developing resistance to LEN if an individual acquires HIV-1 either before or when receiving LEN, or following discontinuation of LEN. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection who are taking only LEN, because LEN alone does not constitute a complete regimen for HIV-1 treatment.

To minimize this risk, it is essential to test before each injection and additionally as clinically appropriate (e.g., upon diagnosis of other STIs or if clinical symptoms consistent with acute HIV-1 infection are present) to confirm HIV-1 negative status using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Individuals who are confirmed to have HIV-1 must immediately begin a complete HIV-1 treatment regimen to reduce the risk of developing resistance.

In addition, due to the long-acting properties of LEN, alternative forms of PrEP should be considered following discontinuation of LEN for those individuals with HIV-1 negative status who are at continuing risk of HIV-1 acquisition and initiated within 28 weeks of the last LEN injection.

Long-Acting Properties and Potential Associated Risks with LEN

Healthcare providers should take the long-acting properties of LEN into consideration when LEN is prescribed. Residual concentrations of LEN may remain in the systemic circulation of individuals for prolonged periods (up to 12 months or longer after the last subcutaneous dose).

It is important to select individuals who agree to the required injection dosing schedule because non-adherence to every-6-monthly injections or missed doses could lead to HIV-1 acquisition and development of resistance.

LEN, a moderate CYP3A inhibitor, may increase the exposure to, and therefore potential risk of adverse reactions from, drugs primarily metabolized by CYP3A initiated within 9 months after the last subcutaneous dose of LEN.

Literature Search

A literature search was conducted in Ovid MEDLINE and Embase databases for studies published between 1946 and June 18, 2025 using search terms that included Yeztugo, lenacapavir, tail-phase, clearance, elimination 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.

Abbreviations

LEN=lenacapavir

PrEP=pre-exposure prophylaxis

STI=sexually transmitted infection

Product Label

For the full indication, important safety information, and boxed warning, please refer to the Yeztugo US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_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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