GILEAD | Medical Information

Yeztugo® (lenacapavir) Time to Protection

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

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.

Summary

PK Data

- The time from initiation of LEN to maximal protection against HIV-1 is unknown.[1]
- PK data are available from a small Phase 1 study in healthy participants which were used as the basis for dosing in the PURPOSE 1 and PURPOSE 2 studies. PK can vary among individuals and in this study, 14 individuals who completed the full initiation dosing had a mean plasma LEN concentration thought to be associated with antiretroviral activity two hours after the second oral dose on Day 2. These PK data are not correlative of efficacy.[2]
- The full initiation dosing of LEN should be followed and consists of taking 2 tablets and 2 injections on Day 1, and 2 tablets on Day 2.[1]

PK Data

Pharmacokinetic Surrogates

Since direct measurement of time to protection is infeasible, estimates of time to protection come from pharmacokinetic surrogates (ie, how long it takes for relevant drug concentrations to reach target levels thought to be protective). The target IQ4 concentration is thought to be a threshold trough for HIV treatment, but the levels required for HIV prevention remain unknown.[3]

The time for LEN to reach target IQ4 for antiretroviral activity is based on PK surrogates reported from dose-response relationship of LEN and mean concentrations predicted to provide near maximal antiretroviral activity.[3] In the case of LEN, the target drug concentration of IQ4 (15.5 ng/mL) is based on the observation that this concentration conferred potent antiretroviral activity as monotherapy in people living with HIV in a phase 1b study and based on the observation of high rates of virologic suppression in phase 2/3 studies in people living with HIV when LEN was dosed targeting trough concentrations ≥IQ4.[2]

Please note: While IQ4 is considered a measure associated with antiretroviral activity, it is not a validated threshold and is it not the only factor in determining antiretroviral or prophylactic activity.[3]

Phase 1 PK Study in Healthy Volunteers

The LEN regimen consisting of concurrent dosing of SUBQ LEN 927 mg and oral LEN 600 mg on Day 1 and oral LEN 600 mg on Day 2 followed by SUBQ LEN every 6 months thereafter was characterized in a Phase 1, single-center, open-label study. Among 14 healthy participants following LEN administration, mean plasma LEN concentration and its lower 90% confidence interval bound exceeded the target IQ4 (15.5 ng/mL) from 2 hours post-dose on Day 2 and was consistently maintained above the target IQ4 during the dosing interval. These PK data are not correlative of efficacy. Overall, LEN was well tolerated, and there were no serious adverse events. Injection site reactions were the most common AEs and no deaths were reported.[2]

Following the full initiation dosing consisting of SUBQ injections and oral tablets is required.[1] The complete oral loading dose on Days 1 and 2 must be taken for LEN to achieve adequate concentrations in a timely manner.[4]

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. Jogiraju V, Graham H, West S, et al. Pharmacokinetics of a Simplified Subcutaneous Lenacapavir Regimen Versus Phase 2/3 Regimen [Poster PESUB22]. Paper presented at: AIDS 2022; 29 July-2 August, 2022; Montreal, Quebec, Canada.
3. Daar E, McDonald C, Crofoot G, et al. Dose-response Relationship of Subcutaneous Long-Acting HIV Capsid Inhibitor GS-6207 [Presentation]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 08-11 March, 2020; Boston, MA.
4. Begley R, Lutz J, Rhee M, et al. Lenacapavir Sustained Delivery Formulation Supports 6-Month Dosing Interval [Poster PEB0265]. Paper presented at: AIDS 2020: 23rd International AIDS Conference Virtual; 06-10 July, 2020.

Abbreviations

AE=adverse event
IQ=inhibitory quotient
LEN=lenacapavir
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
SUBQ=subcutaneous(ly)

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

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 privacy@gilead.com.