GILEAD | Medical Information

# Yeztugo® (lenacapavir) Use in Renal Impairment

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and use in individuals with renal impairment.

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**The full indication, important safety information, and boxed warning are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.**

## Product Labeling[1]

### Renal Impairment

No dosage adjustment of LEN is recommended in individuals with mild, moderate, or severe renal impairment (estimated CrCl ≥15 mL/min). LEN has not been studied in patients with end-stage renal disease (estimated CrCl <15 mL/min).

### Pharmacokinetics

#### Specific populations

There were no clinically significant differences in the PK of LEN based on severe renal impairment (CrCl of 15 to <30 mL/min, estimated by Cockcroft-Gault method). The effect of end-stage renal disease (including dialysis) on the PK of LEN is unknown. As LEN is >98.5% protein bound, dialysis is not expected to alter exposures of LEN.

## Clinical Data on the Use of LEN in Participants With Severe Renal Impairment

### PK Study in Participants With Severe Renal Impairment[2]

#### Study design and demographics

A phase 1, open-label, parallel-group, single-dose study evaluated the PK and safety of oral LEN in participants with severe renal impairment (CrCl 15–29 mL/min). Participants with stable, severe renal impairment (n=10) who were not dependent or expected to become dependent on dialysis were matched to healthy volunteers (n=10) with normal renal function (CrCl ≥90 mL/min) according to age (±10 years), sex, and BMI (±20%). Safety assessments

included monitoring of vital signs, physical examinations, ECGs, clinical laboratory tests, and incidence of AEs.

**Figure 1. PK Study Design (Jogiraju et al)[2]**

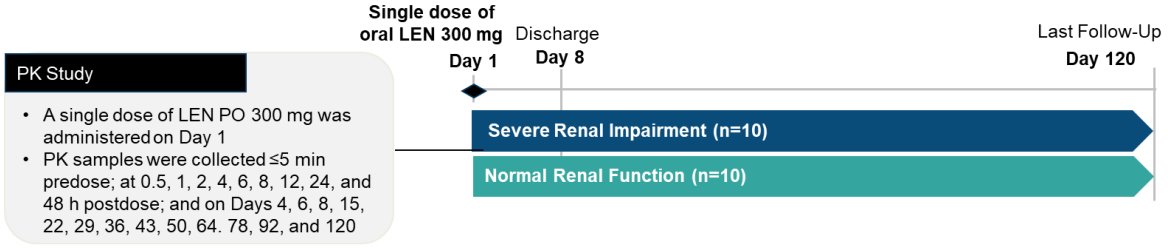


**Table 1. Baseline Demographics and Disease Characteristics (Jogiraju et al)[2]**

| Key Demographics and Characteristics | Severe Renal Impairment (n=10) | Normal Renal Function (n=10) |
|---|---|---|
| Age, median (range), years | 69 (18–77) | 63 (21–73) |
| Male, n (%) | 7 (70) | 7 (70) |
| Race, White/Black, n (%) | 9 (90)/1 (10) | 10 (100)/0 |
| Hispanic/Latinx, n (%) | 7 (70) | 5 (50) |
| BMI, median (range), kg/m$^2$ | 26.6 (19.7–33.2) | 26.6 (23.7–30.5) |
| SCr, median (range), mg/dL | 3.24 (1.81–5.03) | 0.83 (0.51–1.05) |
| CrCl, median (range), mL/min | 21.9 (15.8–30.8) | 98.4 (90–130) |

## PK results

After a single oral dose of LEN 300 mg, the LEN $AUC_{inf}$ GMR was 1.84-fold higher and the $C_{max}$ GMR was 2.62-fold higher in participants with severe renal impairment than in healthy volunteers with normal renal function (Table 2). No significant relationship between LEN exposure (AUC and $C_{max}$) and CrCl was observed in exploratory analyses. The authors described the difference in exposure to LEN between groups as modest and not clinically significant. Plasma protein binding of LEN was >99% overall and did not differ between groups.

**Table 2. Summary of PK Parameters (Jogiraju et al)[2]**

| PK Parameter | Severe Renal Impairment (n=10) | Normal Renal Function (n=10) | GMR (90% CI) |
|---|---|---|---|
| $AUC_{inf}$, GM (range), h·ng/mL | 12,100 (1430–63,000) | 6590 (2660–13,200) | 1.84 (0.936–3.6) |
| $AUC_{last}$, GM (range), h·ng/mL | 11,500 (1310–62,400) | 6050 (2420–12,300) | 1.89 (0.952–3.77) |
| $C_{max}$, GM (range), ng/mL | 51.5 (6.8–427) | 19.7 (5.9–34.4) | 2.62 (1.12–6.14) |
| CL/F, GM (range), L/h | 24.8 (4.76–210) | 45.5 (22.6–113) | – |
| $T_{max}$, median (range), h | 8 (4–48) | 6 (4–48) | – |
| $t_{1/2}$, median (range), days | 9.73 (5.69–16.6) | 13.3 (11–17) | – |
| Vz/F, GM (range), L | 8560 (1690–46,000) | 20,900 (10,000–52,300) | – |

Abbreviations: $AUC_{last}$=area under the concentration-time curve from time zero to last quantifiable plasma concentration; CL/F=apparent oral clearance; GM=geometric mean; $t_{1/2}$=terminal half-life; $T_{max}$=time to maximum drug concentration; Vz/F=apparent volume of distribution.

## Safety results

A single oral dose of LEN 300 mg was generally well tolerated in participants with severe renal impairment (Table 3). Most treatment-emergent AEs were Grade 1 or 2 in severity,

and none was Grade 4 or led to study discontinuation. No deaths were reported, and no AEs in the participants with severe renal impairment were considered related to LEN.

**Table 3. Summary of Safety Parameters (Jogiraju et al)[3]**

| Safety Outcomes, n (%) | Severe Renal Impairment (n=10) | Normal Renal Function (n=10) |
|---|---|---|
| Any AE | 4 (40) | 1 (10) |
| Diarrhea | 1 (10) | 0 |
| Hypertension | 1 (10) | 0 |
| Infusion site extravasation | 1 (10) | 0 |
| Melena[a] | 1 (10) | 0 |
| Pain in extremity | 1 (10) | 0 |
| Prehypertension | 1 (10) | 0 |
| Hyperglycemia | 0 | 1 (10) |
| Grade 3 AEs | 1 (10)[b] | 0 |
| Serious AEs[a] | 1 (10) | 0 |
| LEN-related AEs | 0 | 1 (10)[c] |
| Study procedure-related AEs | 1 (10) | 0 |

[a] Melena was considered serious and not LEN related.
[b] Hypertension; not considered LEN related.
[c] Grade 2.

The authors noted that the results did not indicate a safety risk or warrant a dose adjustment of LEN in patients with severe renal impairment.

# 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, Weber E, Hindman J, et al. Pharmacokinetics of long-acting lenacapavir in participants with hepatic or renal impairment. *Antimicrob Agents Chemother.* 2024;68(4):e0134423.
3. Jogiraju V, Weber E, Hindman J, et al. Pharmacokinetics of long-acting lenacapavir in participants with hepatic or renal impairment. [Supplementary Tables]. *Antimicrob Agents Chemother.* 2024;68(4):e0134423.

# Abbreviations

AE=adverse event
AUC=area under the concentration-time curve
$AUC_{inf}$=area under the concentration-time curve from 0 to infinity
$C_{max}$=maximum plasma concentration
GMR=geometric least-squares mean ratio
LEN=lenacapavir
PK=pharmacokinetic(s)

## 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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