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GILEAD | Medical Information

Sunlenca® (lenacapavir) Use in Severe Renal Impairment

This document is in response to your request for information regarding the use of Sunlenca® (lenacapavir [LEN]) in patients with severe renal impairment.

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The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.

Product Labeling[1]

Renal Impairment

No dosage adjustment of LEN is recommended in patients 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.

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

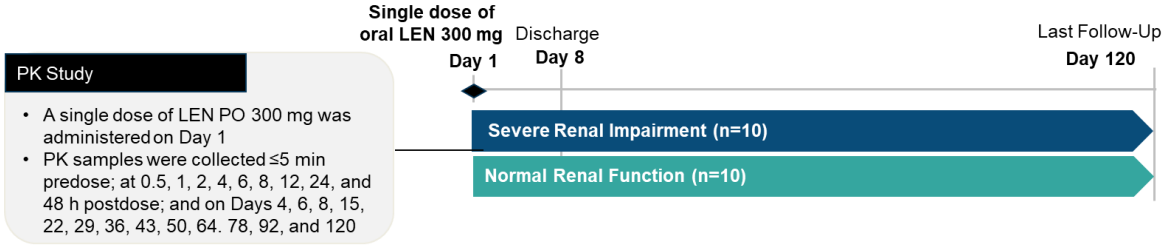


Table 1. Baseline Demographics and Disease Characteristics (Jogiraju et al)[2]

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. SUNLENCA, Gilead Sciences Inc. SUNLENCA® (lenacapavir) tablets, for oral use. SUNLENCA® (lenacapavir) injection, for subcutaneous use. US 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(s), please refer to the Sunlenca US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_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 https://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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