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GILEAD | Medical Information

Sunlenca® (lenacapavir) Use in Patients With Severe Renal Impairment and Hemodialysis

This document is in response to your request for information regarding the use of Sunlenca® (lenacapavir [LEN]) in patients with severe renal impairment (eGFR <30 mL/min), including those requiring hemodialysis (HD).

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 warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.

Product Labeling[1]

Use in Specific Populations

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 ESRD (estimated CrCl <15 mL/min).

Clinical Pharmacology

PK

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 ESRD (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.

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Clinical Data on LEN Use 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]

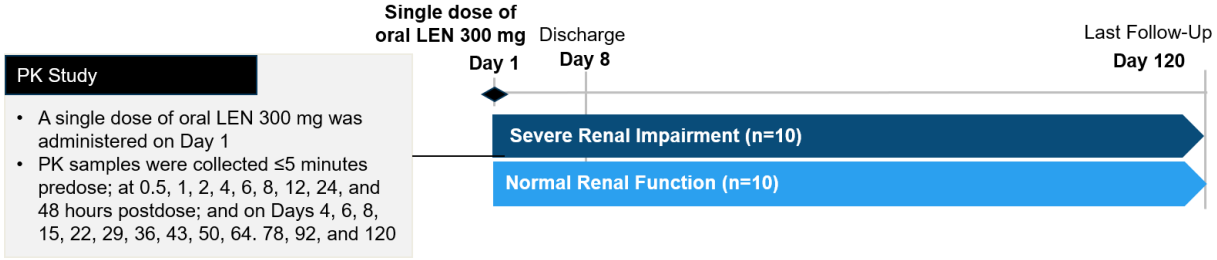

Table 1. Baseline Demographics and Disease Characteristics (Jogiraju et al)[2]

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
Ethnicity, Hispanic or 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 dose of oral 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)

PK Parameter	Severe Renal Impairment (n=10)	Normal Renal Function (n=10)	GMR (90% CI)
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 dose of oral 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 were 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 AEs	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 related to LEN.
[b]Hypertension; not considered related to LEN.
[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.

Case Report

There are limitations in the interpretation of case reports. Case reports cannot be generalized. Unlike controlled clinical trials, causality cannot be inferred based on uncontrolled observational data. In addition, incidence or prevalence cannot be estimated due to the lack of a representative population sample. Other limitations of case reports include the retrospective design and publication bias.[4]

LEN use in a patient with ESRD requiring HD[5]

A 35-year-old female patient with vertically acquired HIV-1 presented with esophageal candidiasis and disseminated tuberculosis. The patient had developed treatment failure and resistance to multiple ARVs due to periods of medical nonadherence. She had developed HIV-associated nephropathy with ESRD that required peritoneal dialysis in 2016 and HD in

2020. In 2022, she was switched from a multi-tablet regimen of MVC, 3TC, a high dose of DRV/r, and a high dose of DTG to LEN (oral loading dose over 8 days, followed by LEN subcutaneous injections twice yearly) with FTR 600 mg twice daily and 3TC 75 mg once daily. The patient maintained virologic suppression (HIV-1 RNA <20 copies/mL) on the ARV combination of LEN + FTR + 3TC until she underwent renal transplantation in 2023. No clinical or biological drug-related side effects were reported, and no significant changes in glucose, lipid, or liver enzyme levels were observed.

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.
4. Nissen T, Wynn R. The Clinical Case Report: A Review of Its Merits and Limitations. *BMC Res Notes.* 2014;7:264. https://www.ncbi.nlm.nih.gov/pubmed/24758689
5. Bigirimana F, Van den Wijngaert S, Fosso C, et al. Lenacapavir with Fostemsavir in a Multidrug-Resistant HIV-Infected Hemodialysis Patient. *Case Rep Infect Dis.* 2023;2023:8865265.

Abbreviations

3TC=lamivudine
AE=adverse event
ARV=antiretroviral
AUC=area under the concentration-time curve
AUC_{inf}=area under the concentration-time curve from 0 to infinity
C_{max}=maximum plasma concentration
DRV/r=darunavir boosted with ritonavir
DTG=dolutegravir
ESRD=end-stage renal disease
FTR=fostemsavir
GMR=geometric least squares mean ratio
HD=hemodialysis
LEN=lenacapavir
MVC=maraviroc
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

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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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