GILEAD | Medical Information

Sunlenca® (lenacapavir) Use in Hepatic Impairment

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

Use in Specific Populations

Hepatic impairment

No dosage adjustment of LEN is recommended in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. LEN has not been studied in patients with severe hepatic impairment (Child-Pugh Class C).

Clinical Pharmacology

PK

Specific populations

There were no clinically significant differences in the PK of LEN based on moderate hepatic impairment (Child-Pugh Class B). The effect of severe hepatic impairment (Child-Pugh Class C) on the PK of LEN is unknown.

Clinical Data on the Use of LEN in Participants With Hepatic Impairment

PK Study in Participants With Moderate Hepatic 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 moderate hepatic impairment (CPT Class B score, 7–9). Participants with stable, moderate hepatic impairment for >6 months (n=10) were matched

to healthy volunteers (n=10) according to age (±10 years), sex, race, and BMI (±20%). Safety assessments included physical examinations, ECGs, clinical laboratory tests, and incidence of AEs.

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

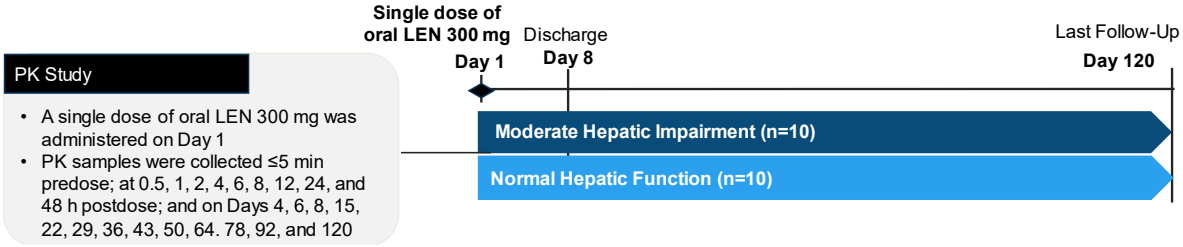

Table 1. Baseline Demographics and Disease Characteristics (Jogiraju et al)[2]

Key Demographics and Characteristics		Oral LEN 300 mg	
		Moderate Hepatic Impairment (n=10)	Normal Hepatic Function (n=10)
Age, median (range), years		56 (39–71)	55 (31–69)
Male, n (%)		7 (70)	7 (70)
White, n (%)		10 (100)	10 (100)
Hispanic/Latinx, n (%)		7 (70)	5 (50)
ALT/AST, median (range), U/L		23 (11–312)/33 (14–129)	17 (8–32)/17 (11–19)
BMI, median (range), kg/m^2		31.9 (23.5–37.8)	29.5 (25–36.1)
CPT score, n (%)	7	7 (70)	–
	8	3 (30)	–

PK results

After a single oral dose of LEN 300 mg, the AUC_{inf} GMR was 1.47-fold higher and the C_{max} GMR was 2.61-fold higher in participants with moderate hepatic impairment than in healthy volunteers with normal hepatic function (Table 2). The authors described the difference in exposure to LEN between groups as modest and not clinically significant. No significant relationships between LEN exposure (AUC and C_{max}) and additional hepatic function measures (CPT score, albumin and total bilirubin levels, prothrombin time, and INR) were observed. 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	Moderate Hepatic Impairment (n=10)	Normal Hepatic Function (n=10)	GMR (90% CI)
AUC_{inf}, GM (range), h·ng/mL	12,000 (4990–29,600)	8180 (3150–20,700)	1.47 (0.947–2.27)
AUC_{last}, GM (range), h·ng/mL	11,900 (4940–29,200)	7590 (3050–20,500)	1.57 (1.01–2.43)
C_{max}, GM (range), ng/mL	61.1 (21–229)	23.4 (9.7–55.2)	2.61 (1.51–4.52)
CL/F, GM (range), L/h	25 (10.1–60.2)	36.6 (14.5–95.3)	–
T_{max}, median (range), h	6 (2–48)	4 (4–12)	–
$t_{1/2}$, median (range), days	12.6 (9.74–17.1)	13.1 (10.7–17)	–
Vz/F, GM (range), L	10,800 (4060–23,000)	17,000 (6970–49,800)	–

Abbreviations: AUC_{last}=area under the 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 peak concentration; Vz/F=apparent volume of distribution.

Safety results

A single oral dose of LEN 300 mg was generally well tolerated in participants with moderate hepatic impairment (Table 3). All treatment-emergent AEs were Grade 1 or 2 in severity and were resolved during the study. There were no serious AEs, and no AEs led to study discontinuation. No deaths were reported.

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

Safety Outcomes, n (%)	Moderate Hepatic Impairment (n=10)	Normal Hepatic Function (n=10)
Any AE	3 (30)	3 (30)
Headache	2 (20)	1 (10)
Anxiety	1 (10)	0
Dizziness	1 (10)	0
Hyponatremia	1 (10)	0
Malaise	1 (10)	0
Skin abrasion	1 (10)	0
Type 2 diabetes mellitus	1 (10)	0
Constipation	0	1 (10)
Hyperglycemia	0	1 (10)
Any drug-related AE	1[a] (10)	1[b] (10)

[a]Grade 2. [b]Grade 1.

The authors noted that the results did not indicate a safety risk or warrant dose adjustment of LEN in patients with moderate hepatic 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 time 0 to infinity
C_{max}=peak concentration
CPT=Child-Pugh-Turcotte
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 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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