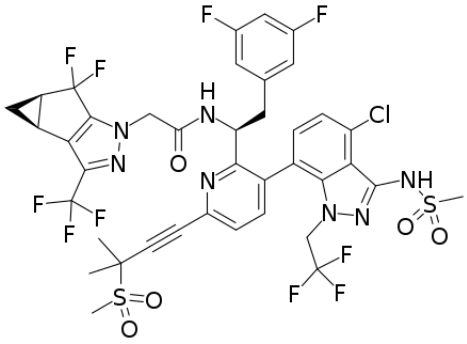
Lenacapavir PK Fact Sheet

Details

Generic Name	Lenacapavir (formerly GS-6207)
Trade Name	Sunlenca®
Class	HIV-1 capsid inhibitor
Molecular Weight	968.3
Structure	

Summary of Key Pharmacokinetic Parameters

Initiation of treatment with lenacapavir requires tablets to be taken as oral loading prior to administration of a long-acting sub-cutaneous injection which is then administered every 6 months.

Linearity/non-linearity	Single dose pharmacokinetics of lenacapavir after oral administration are non-linear and less than dose proportional over the dose range of 50 to 1800 mg. Single dose pharmacokinetics of lenacapavir after subcutaneous injection (309 mg/mL) are dose proportional over the dose range of 309 to 927 mg.
Steady state	Not available
Plasma half life	10-12 days (oral) 8-12 weeks (subcutaneous)
Cmax	97.2 (70.3) ng/mL (mean (%CV) at steady state following subcutaneous administration) Cmax following subcutaneous administration occurs ~84 days post dose.
Ctau	36.2 (90.6) ng/mL (mean (%CV) at steady state following subcutaneous administration)
AUC	300,000 (68.5) h.ng/mL (mean (%CV) at steady state following subcutaneous administration)
Bioavailability	Approximately 6-10% following oral administration
Absorption	Oral tablets can be taken with or without food.
Protein Binding	~99.8%
Volume of Distribution	976 L
CSF:Plasma ratio	Not available
Semen:Plasma ratio	Not available
Renal Clearance	<1%

Dosing in Renal and Hepatic Impairment

Renal Impairment	No dose adjustment of lenacapavir is required in patients with mild, moderate, or severe renal impairment (CrCl ≥15 mL/min). The pharmacokinetics of oral lenacapavir (300 mg single dose) were evaluated in a dedicated study in subjects with severe renal impairment (estimated CrCl ≥15 and <30 mL/minute). Lenacapavir AUC and Cmax increased by 84% and 162% in subjects with severe renal impairment compared with subjects with normal renal function; however, the increase was not considered clinically relevant. Lenacapavir has not been studied in patients with end stage renal disease (CrCl <15 mL/min or on renal replacement therapy), therefore lenacapavir should be used with caution in these patients. As lenacapavir is approximately 99.8% protein bound, dialysis is not expected to alter exposures of lenacapavir.
Hepatic Impairment	No dose adjustment of lenacapavir is required in patients with mild or moderate hepatic impairment (Child-Pugh Class A or B). The pharmacokinetics of oral lenacapavir (300 mg single dose) were evaluated in a dedicated Phase 1 trial in subjects with moderate hepatic impairment (Child-Pugh Class B). Lenacapavir mean AUC and Cmax (total and unbound) were 1.47- to 2.84-fold and 2.61- to 5.03-fold higher in patients with moderate hepatic impairment compared to subjects with normal hepatic function. However, this increase is not considered clinically relevant based on lenacapavir exposure-response. Lenacapavir has not been studied in patients with severe hepatic impairment (Child-Pugh Class C), therefore lenacapavir should be used with caution in these patients.

Metabolism and Distribution

Metabolised by	CYP3A, UGT1A1
Inducer of	Does not induce CYP3A in vivo
Inhibitor of	CYP3A (moderate). If lenacapavir is discontinued, residual concentrations of lenacapavir may remain in the systemic circulation for prolonged periods. These concentrations may affect the exposures of other medicinal products (i.e. sensitive CYP3A substrates) that are initiated within 9 months after the last subcutaneous dose of lenacapavir. Not a clinically meaningful inhibitor of P-gp and BCRP. Does not inhibit OATP.
Transported by	P-gp

References

Information is from:
Sunlenca® Summary of Product Characteristics, Gilead Sciences Ltd.