Lenacapavir (oral) PK Fact Sheet

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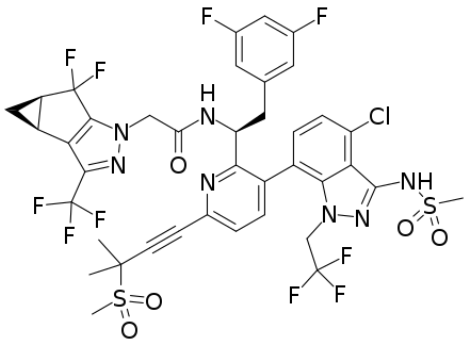
Details

Generic Name	Lenacapavir
Trade Name	Bixlenvo® (with bictegravir) Sunlenca® (as oral loading dose and supplemental dosing for sub-cutaneous administration)
Class	HIV-1 capsid inhibitor
Molecular Weight	968.3
Structure	

Summary of Key Pharmacokinetic Parameters

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.
Steady state	Not available
Plasma half life	10-12 days
Cmax	99.3 (171) ng/mL (mean (%CV) steady state exposures from population PK analyses in adults with HIV following oral administration of Bixlenvo)
Ctrough	96.6 (174) ng/mL (mean (%CV) steady state exposures from population PK analyses in adults with HIV following oral administration of Bixlenvo)
AUC	2360 (178) ng.h/mL (mean (%CV) steady state exposures from population PK analyses in adults with HIV following oral administration of Bixlenvo)
Bioavailability	Approximately 6-10%
Absorption	Lenacapavir AUC and Cmax decreased by 33% and 14% following administration Bixlenvo with a high fat (~1000 kcal, 50% fat) meal relative to fasted conditions. Bixlenvo and Sunlenca 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%

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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 Bixlenvo 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) for up to 4 weeks after the last oral dose of Bixlenvo. Not a clinically meaningful inhibitor of P-gp and BCRP. Does not inhibit OATP.
Transported by	P-gp

References

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

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