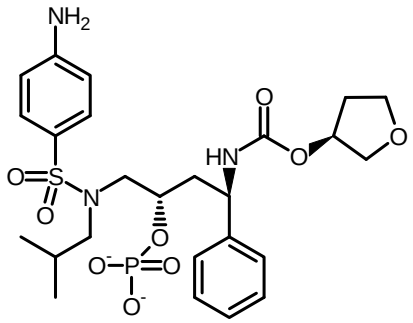
Fosamprenavir PK Fact Sheet

Details

Generic Name	Fosamprenavir
Trade Name	Telzir®, Lexiva®
Class	Protease Inhibitor
Molecular Weight	625.7
Structure	

Summary of Key Pharmacokinetic Parameters

Pharmacokinetic parameters refer to amprenavir. Fosamprenavir is rapidly and almost completely hydrolysed to amprenavir and inorganic phosphate as it is absorbed through the gut epithelium, following oral administration.

Plasma half life	7.7 h (fosamprenavir alone) 15-23 h (with ritonavir)
Cmax	6.08 (5.38-6.86) µg/ml (700 mg with ritonavir 100 mg twice daily)
Cmin	2.12 (1.77-2.54) µg/ml (700 mg with ritonavir 100 mg twice daily)
AUC	39.6 (34.5–45.3) µg/ml.h (700 mg with ritonavir 100 mg twice daily)
Bioavailability	Not available
Absorption	Administration of the fosamprenavir tablet formulation in the fed state (standardised high fat meal: 967 kcal, 67 g fat, 33 g protein, 58 g carbohydrate) did not alter plasma amprenavir pharmacokinetics (Cmax, Tmax or AUC) compared to the administration of this formulation in the fasted state. Fosamprenavir tablets may be taken without regard to food intake.
Protein Binding	~90% *in vitro*
Volume of Distribution	~ 430 L (6 L/kg assuming a 70 kg body weight)
CSF:Plasma ratio	Negligible in humans
Semen:Plasma ratio	Amprenavir appears to penetrate into semen, though semen concentrations are lower than plasma concentrations.
Renal Clearance	<1%
Renal Impairment	The impact of renal impairment on amprenavir and ritonavir elimination is expected to be minimal.
Hepatic Impairment	Fosamprenavir with ritonavir should be used with caution and at reduced doses in adults with mild or moderate hepatic impairment and is contraindicated in patients with severe hepatic impairment.

Metabolism and Distribution

Metabolised by	Primarily CYP3A4
Inducer of	Possibly CYP3A4 (net inhibition when administered with ritonavir)
Inhibitor of	CYP3A4, BCRP(*in vitro*) [1]; P-gp, MRP1 [2], OATPs[3]
Transported by	P-glycoprotein

References

Unless otherwise stated (see below), information is from:
Telzir® Summary of Product Characteristics, ViiV Healthcare UK Ltd.
Lexiva® US Prescribing Information, ViiV Healthcare.

1. Weiss J, Rose J, Storch CH, *et al.* Modulation of human BCRP (ABCG2) activity by anti-HIV drugs. *J Antimicrob Chemother.* 2007; 59(2): 238-245.
2. Janneh,O, Jones,E, Chandler B, *et al*: Inhibition of P-glycoprotein and multidrug resistance-associated proteins modulates the intracellular concentration of lopinavir in cultured CD4 T cells and primary human lymphocytes. *J Antimicrob Chemother.* 2007; 60(5): 987-993.
3. Ye Z, Augustijns P, Annaert P. Cellular accumulation of cholyl-glycylamido-fluorescein in sandwich-cultured rat hepatocytes: kinetic characterization, transport mechanisms, and effect of human immunodeficiency virus protease inhibitors. *Drug Metab Dispos.* 2008 36(7): 1315-1321.