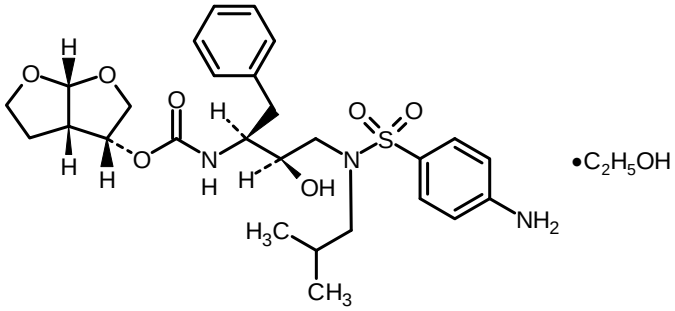
Darunavir PK Fact Sheet

Details

Generic Name	Darunavir
Trade Name	Prezista®
Class	Protease Inhibitor
Molecular Weight	547.7
Structure	

Summary of Key Pharmacokinetic Parameters

Plasma half life	15 h (with ritonavir)
Cmax	~6500 ng/ml (darunavir/ritonavir 600/100 mg twice daily) [1]
Cmin	3578 ± 1151 ng/ml
AUC	62349 ± 16143 ng.h/ml
Bioavailability	~37% (darunavir alone, 600 mg single dose) ~82% (with ritonavir 100 mg single dose)
Absorption	When administered without food, the relative bioavailability of darunavir in the presence of low dose ritonavir is 30% lower as compared to intake with food. Therefore, darunavir tablets should be taken with ritonavir and with food. The type of food does not affect exposure to darunavir.
Protein Binding	~95%
Volume of Distribution	88.1 ± 59.0 L (darunavir alone) 131 ± 49.9 L (with ritonavir 100 mg twice daily)
CSF:Plasma ratio	Unknown
Semen:Plasma ratio	Unknown
Renal Clearance	1.2% as unchanged drug; 7.7% when co-administered with ritonavir [2]
Renal Impairment	Darunavir is predominantly metabolised by the liver. No dose adjustment is required in patients with renal impairment.
Hepatic Impairment	No dose adjustment is recommended in mild or moderate (Child Pugh Class A,B) hepatic impairment, however, it should be used with caution. No pharmacokinetic data are available in patients with severe hepatic impairment; darunavir should not be used in patients with severe hepatic impairment (Child Pugh Class C).

Metabolism and Distribution

Metabolised by	CYP3A4
Inducer of	CYP2C9, CYP2C19 (with darunavir/ritonavir, possibly ritonavir effect), CYP2C8(in vitro, darunavir/ritonavir)
Inhibitor of	CYP3A4, CYP2D6 (2D6 observed with darunavir/ritonavir, possibly ritonavir effect), P-glycoprotein (with ritonavir); OATPs [3]
Transported by	P-glycoprotein (in vitro) *[1]*

References

Unless otherwise stated (see below), information is from:
Prezista® Summary of Product Characteristics, Janssen-Cilag Ltd.
Prezista® Prescribing Information, Janssen Therapeutics.

1. Rittweger M, Arasteh K. Clinical pharmacokinetics of darunavir, *Clin Pharmacokinet.* 2007; 46(9):739-756.
2. Back D, Sekar V, Hoetelmans R. Darunavir: pharmacokinetics and drug interactions. *Antivir Ther.* 2008; 13(1): 1-13.
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.