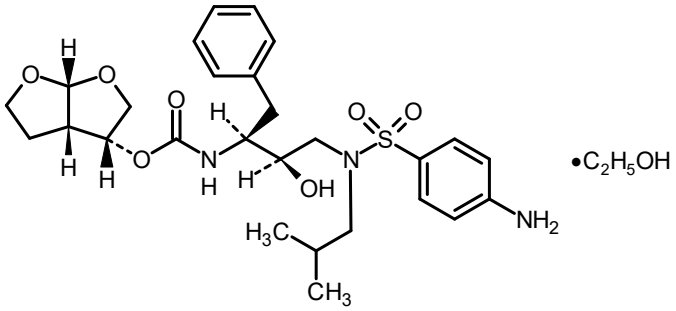
Darunavir PK Fact Sheet

Details

Generic Name	Darunavir
Trade Name	Prezista® Rezolsta®, Prezcobix® (with cobicistat) Symtuza® (with cobicistat, emtricitabine, tenofovir alafenamide)
Class	Protease Inhibitor
Molecular Weight	547.7
Structure	

Summary of Key Pharmacokinetic Parameters

Plasma half life	15 h (with ritonavir) 9.4 h (with cobicistat, as Symtuza®)
Cmax	~6500 ng/ml (darunavir/ritonavir 600/100 mg twice daily) [1] 8826 (33.3) ng/ml (darunavir/cobicistat 800/150 mg once daily as Symtuza®)
Cmin	3490±1401, 3386±1372, 3578±1154 ng/ml (darunavir/ritonavir 600/100 mg twice daily, population PK estimates from three clinical trials) 2282±1168, 2160±1201 ng/ml (darunavir/ritonavir 800/100 mg once daily, population PK estimates from two clinical trials) 2043±1257 ng/ml (darunavir/cobicistat 800/150 mg once daily, population PK estimates from one clinical trial) 1899 (759), 1813 (859) ng/ml (darunavir/cobicistat 800/150 mg once daily as Symtuza®, population PK estimates from two clinical trials)
AUC	116796±33594, 114302±32681, 124698±32286 ng.h/ml (darunavir/ritonavir 600/100 mg twice daily, population PK estimates from three clinical trials) 93026±27050, 93334±28626 ng.h/ml (darunavir/ritonavir 800/100 mg once daily, population PK estimates from two clinical trials) 100152±32042 ng.h/ml (darunavir/cobicistat 800/150 mg once daily, population PK estimates from one clinical trial) 87909 (20232), 85972 (22413) ng.h/ml (darunavir/cobicistat 800/150 mg once daily as Symtuza®, population PK estimates from two clinical trials)
Bioavailability	~37% (darunavir alone, 600 mg single dose) ~82% (with ritonavir 100 mg twice daily)
Absorption	When administered without food, the relative bioavailability of darunavir is lower with cobicistat (30-45% decrease seen with Symtuza®) or ritonavir (30% decrease) as compared to intake with food. Therefore, darunavir should be taken with cobicistat or 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	13.9% (7.7% as unchanged drug) when administered with ritonavir
Renal Impairment	No dose adjustment for darunavir/ritonavir is required in patients with renal impairment. Cobicistat as a pharmacokinetic enhancer of darunavir should not be initiated in patients with CrCL <70 ml/min if any co-administered agent requires dose adjustment based on creatinine clearance. Cobicistat has not been studied in patients receiving dialysis, and, therefore, no recommendation can be made for the use of darunavir/cobicistat in these patients. Symtuza® should not be initiated in patients with CrCL <30 mL/min, as there are no data available regarding the use of Symtuza® in this population
Hepatic Impairment	No dose adjustment is recommended in mild or moderate (Child Pugh Class A or 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 (CYP2D6 observed with ritonavir or cobicistat), P-glycoprotein; BCRP, MATE1, OATP1B1, OATP1B3 (with cobicistat); OATPs [2]
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.
Rezolsta® Summary of Product Characteristics, Janssen-Cilag Ltd.
Prezcobix® Prescribing Information, Janssen Therapeutics.
Symtuza® Summary of Product Characteristics, Janssen-Cilag Ltd.
Symtuza® Prescribing Information, Janssen Therapeutics.

1. Rittweger M, Arasteh K. Clinical pharmacokinetics of darunavir, *Clin Pharmacokinet.* 2007; 46(9):739-756.
2. 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.