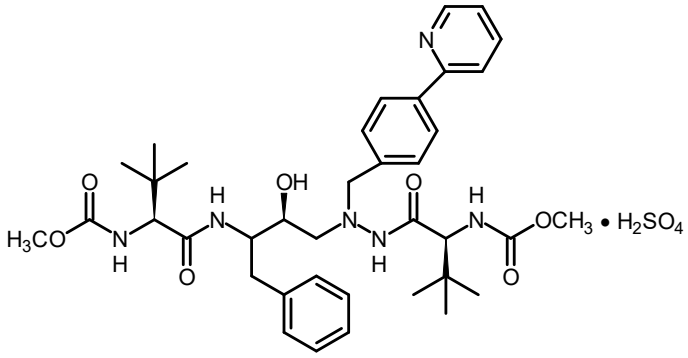
Atazanavir PK Fact Sheet

Details

Generic Name	Atazanavir
Trade Name	Reyataz®
Class	Protease Inhibitor
Molecular Weight	704.9 (free base), 802.9 (sulphate)
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	The pharmacokinetics of atazanavir exhibit a non-linear disposition.
Plasma half life	8.6 h (atazanavir/ritonavir 300/100 mg once daily) 6.5 h (400 mg once daily)
Cmax	4466 ng/ml (atazanavir/ritonavir 300/100 mg once daily) 2298 ng/ml (400 mg once daily)
Cmin	654 ng/ml (atazanavir/ritonavir 300/100 mg once daily) 120 ng/ml (400 mg once daily)
AUC	44185 ng.h/ml (atazanavir/ritonavir 300/100 mg once daily) 14874 ng.h/ml (400 mg once daily)
Bioavailability	~68%
Absorption	Atazanavir should be taken with food. Co-administration of atazanavir/ritonavir (300/100 mg single dose) with a light meal increased AUC by 33% and both Cmax and C24h by 40% relative to the fasting state. Co-administration with a high-fat meal did not affect atazanavir AUC relative to fasting conditions and Cmax was within 11% of fasting values. C24h following a high fat meal increased by ~33% due to delayed absorption; the median Tmax increased from 2.0 to 5.0 h. Administration of atazanavir/ritonavir with either a light or a high-fat meal decreased the coefficient of variation of AUC and Cmax by ~25% compared to the fasting state.
Protein Binding	~86%
Volume of Distribution	Not available
CSF:Plasma ratio	0.0021- 0.0226
Semen:Plasma ratio	0.11- 4.42
Renal Clearance	7% as unchanged drug
Renal Impairment	No pharmacokinetic data available on patients with renal insufficiency; the impact of renal impairment on atazanavir elimination is anticipated to be minimal.
Hepatic Impairment	Atazanavir with ritonavir should be used with caution in mild hepatic impairment and should not be used in patients with moderate to severe hepatic impairment.

Metabolism and Distribution

Metabolised by	CYP3A4
Inducer of	P-gp expression and function, MRP1 expression [1]
Inhibitor of	CYP3A4, UGT1A1, CYP2C8, BCRP(*in vitro*) [2], P-gp, MRPs [3], OATPs [4]
Transported by	P-gp, MRPs, BCRP [1]

References

Unless otherwise stated (see below), information is from:
Reyataz® Summary of Product Characteristics, Bristol-Myers Squibb Pharmaceuticals Ltd.
Reyataz® US Prescribing Information, Bristol-Myers Squibb Co.

1. .Bousquet,L, Roucairol, C *et al:* Comparison of ABC transporter modulation by atazanavir in lymphocytes and human brain endothelial cells: ABC transporters are involved in the atazanavir-limited passage across an in vitro human model of the blood–brain barrier. *AIDS Res Hum Retroviruses.* 2008, 24 (9): 1147-54.
2. 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.
3. Lucia MB, Golotta C, Rutella S, *et al.* Atazanavir inhibits P-glycoprotein and multidrug resistance-associated protein efflux activity. *J Acquir Immune Defic Syndr.* 2005; 39(5): 635–637.
4. 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.