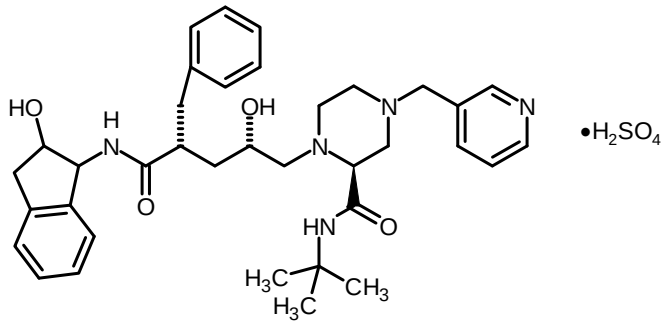
Indinavir PK Fact Sheet

Details

Generic Name	Indinavir
Trade Name	Crixivan®
Class	Protease Inhibitor
Molecular Weight	711.88 (as sulphate)
Structure	

Summary of Key Pharmacokinetic Parameters

Plasma half life	1.8 ± 0.4 h
Cmax	8.97 ± 2.87 µg/ml (800 mg every 8 hours)
Cmin	0.146 µg/ml (800 mg every 8 hours)
AUC	21.82 ± 8.11 µg/ml.h (800 mg every 8 hours)
Bioavailability	Approx 65%
Absorption	Administration of indinavir with a meal high in calories, fat, and protein resulted in a blunted and reduced absorption with an approximate 80 % reduction in AUC and an 86 % reduction in Cmax. Administration with light meals (e.g., dry toast with jam or fruit conserve, apple juice, and coffee with skimmed or fat–free milk and sugar or corn flakes, skimmed or fat–free milk and sugar) resulted in plasma concentrations comparable to the corresponding fasted values.
Protein Binding	~60%
Volume of Distribution	~1.74 L/kg [1]
CSF:Plasma ratio	0.14 [2]
Semen:Plasma ratio	1.9 [2]
Renal Clearance	<20% as unchanged drug
Renal Impairment	Safety in patients with impaired renal function has not been studied; less than 20% of indinavir is excreted in the urine as unchanged drug or metabolites.
Hepatic Impairment	Safety and efficacy of indinavir has not been established in patients with significant underlying liver disorders and should be used with caution.

Metabolism and Distribution

Metabolised by	CYP3A4
Inducer of	N/A
Inhibitor of	CYP3A4, P-glycoprotein [3], MRP1 [4], OATP-C [5]
Transported by	P-glycoprotein [3], MRP1 [4]

References

Unless otherwise stated (see below), information is from:
Crixivan® Summary of Product Characteristics, Merck Sharp & Dohme Ltd.
Crixivan® US Prescribing Information, Merck & Co Inc.

1. Zhou J, Havlir DV, Richman DD, *et al*. Plasma population pharmacokinetics and penetration into cerebrospinal fluid of indinavir in combination with zidovudine and lamivudine in HIV-1-infected patients. *AIDS.* 2000; 14(18): 2869-2876.
2. Lafeuillade A, Solas C, Halfon P, *et al.* Differences in the detection of three HIV-1 protease inhibitors in non-blood compartments: clinical correlations. *HIV Clin Trials.* 2002; 3(1): 27-35.
3. Lee C, Gottesman M, Cardarelli CO, *et al*. HIV-1 protease inhibitors are substrates for the MDR1 multidrug transporter. *Biochemistry.* 1998; 37(11): 3594-3601.
4. Srinivas R, Middlemas D, Flynn P, Fridland A. Human immunodeficiency virus protease inhibitors serve as substrates for multidrug transporter proteins MDR1 and MRP1 but retain antiviral efficacy in cell lines expressing these transporters. *Antimicrob Agents Chemother.* 1998; 42(12): 3157-3162.
5. Tirona R, Leake B, Wolkoff AW, Kim RB. Human organic anion transporting polypeptide-C (SLC21A6) is a major determinant of rifampicin mediated pregnane X receptor activation. *J Pharmacol Exp Ther.* 2003; 304(1): 223-228.