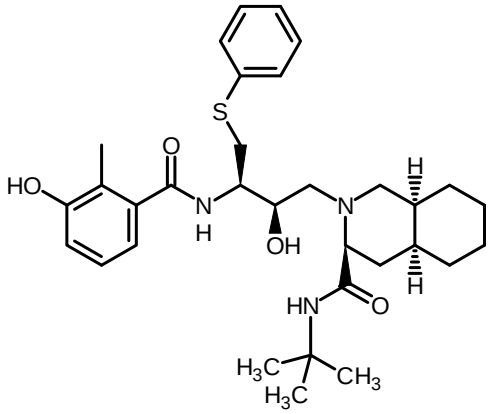
Nelfinavir PK Fact Sheet

Details

Generic Name	Nelfinavir
Trade Name	Viracept®
Class	Protease Inhibitor
Molecular Weight	663.90
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	A greater than dose-proportional increase in nelfinavir plasma concentrations was observed after single doses; however, this was not observed after multiple dosing.
Plasma half life	3.5-5 h
Cmax	3-4 µg/ml (750 mg three times daily), 4.0 ± 0.8 µg/ml (1250 mg twice daily)
Cmin	1-3 µg/ml (750 mg three times daily), 0.7-2.2 µg/ml (1250 mg twice daily)
AUC	43.6 ± 17.8 µg/ml.h (750 mg three times daily), 52.8 ± 15.7 µg/ml.h (1250 mg twice daily)
Bioavailability	70-80%, with food [1]
Absorption	Nelfinavir should always be ingested with food as it increases nelfinavir exposure and decreases nelfinavir pharmacokinetic variability relative to the fasted state. Nelfinavir exposure increases with increasing calorie or fat content of meals.
Protein Binding	>98%
Volume of Distribution	2-7 L/kg
CSF:Plasma ratio	Consistently undetectable [2]
Semen:Plasma ratio	0.07 [2]
Renal Clearance	1-2% as unchanged drug
Renal Impairment	No special precautions or dose adjustments are required in renal impairment.
Hepatic Impairment	An increase in nelfinavir AUC has been observed in hepatically impaired patients. Specific dose recommendations for nelfinavir cannot be made.

Metabolism and Distribution

Metabolised by	CYP3A, CYP2C19, also CYP2C9 and CYP2D6
Inducer of	N/A
Inhibitor of	CYP3A, MRP1 [3], BCRP(*in vitro*) [4], OATP-C [5]
Transported by	P-gp [5], MRP1 [3,6], MRP2 [6]

References

Unless otherwise stated (see below), information is from:
Viracept® Summary of Product Characteristics, Roche Products Ltd.
Viracept®US Prescribing Information, ViiV Healthcare Co.

1. Bardsley-Elliot A, Plosker GL. Nelfinavir: an update on its use in HIV infection. *Drugs.* 2000; 59(3): 581-620.
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. 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.
4. 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.
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.
6. Chandler B, Detsika M, Owen A, *et al*, Effect of transporter modulation on the emergence of nelfinavir resistance in vitro. *Antivir Ther.* 2007; 12(5): 831-834.