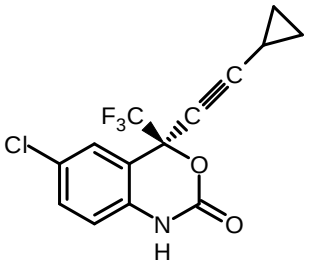
Efavirenz PK Fact Sheet

Details

Generic Name	Efavirenz
Trade Name	Sustiva®, Stocrin®
Class	Non-Nucleoside Reverse Transcriptase Inhibitor
Molecular Weight	315.68
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	Dose related increases in Cmax and AUC were seen for doses up to 1600 mg; the increases were less than proportional suggesting diminished absorption at higher doses.
Steady state	Steady-state plasma concentrations were reached in 6-7 days.
Plasma half life	40-55 h after multiple doses
Cmax	4.07 µg/ml
Cmin	1.76 µg/ml
AUC	57.9 µg/ml.h
Bioavailability	Not available
Absorption	It is recommended that efavirenz be taken on an empty stomach, preferably at bedtime. The AUC and Cmax of a single 600 mg dose of efavirenz film-coated tablets in uninfected volunteers was increased by 28% (90% CI: 22-33%) and 79% (90% CI: 58-102%), respectively, when given with a high fat meal, relative to when given under fasted conditions.
Protein Binding	>99%
Volume of Distribution	~252 L [1]
CSF:Plasma ratio	0.69% (range 0.26-1.19%) of corresponding plasma concentrations.
Semen:Plasma ratio	0.09 (0.03-0.43) [2]
Renal Clearance	<1% as unchanged drug
Renal Impairment	Pharmacokinetics of efavirenz have not been studied in renal insufficiency. Less than 1% of a dose is excreted unchanged in the urine; impact of renal impairment on efavirenz elimination should be minimal.
Hepatic Impairment	Because of extensive CYP450 mediated metabolism and limited clinical experience, caution is recommended in patients with mild/moderate liver disease. Safety and efficacy of efavirenz has not been established in patients with significant underlying liver disorders. It is contraindicated in patients with severe hepatic impairment.

Metabolism and Distribution

Metabolised by	CYP3A4, CYP2B6 (*in vitro*)
Inducer of	CYP3A4
Inhibitor of	CYP2C9, CYP2C19, CYP3A4; BCRP(*in vitro*) [3]; MRP1, MRP2, MRP3 [4]
Transported by	Unknown

References

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

1. Csajka C, Marzolini C, Fattinger K, *et al*. Population pharmacokinetics and effects of efavirenz in patients with human immunodeficiency virus infection. *Clin Pharmacol Ther*. 2003; 73(1): 20-30.
2. Taylor S, Reynolds H, Sabin CA, *et al.* Penetration of efavirenz into the male genital tract: drug concentrations and antiviral activity in semen and blood of HIV-1-infected men. *AIDS.* 2001; 15(15): 2051-2053.
3. 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.
4. Weiss J, Theile D, Ketabi-Kiyanvash N, *et al.* Inhibition of MRP1/ABCC1, MRP2/ABCC2 and MRP3/ABCC3 by nucleoside, nucleotide and non-nucleoside reverse transcriptase inhibitors. *Drug Metab Dispos.* 2007; 35(3): 340-344.