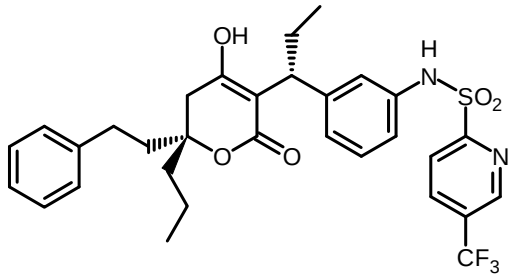
Tipranavir PK Fact Sheet

Details

Generic Name	Tipranavir
Trade Name	Aptivus®
Class	Protease Inhibitor
Molecular Weight	602.7
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	Tipranavir, with low dose ritonavir, exhibits linear pharmacokinetics at steady state.
Steady state	Steady-state is attained in most subjects after 7 days of dosing.
Plasma half life	5.5 h (female); 6.0 h (male)
Cmax	57.2 ± 13.7 µg/ml (female),46.8 ± 10.0 µg/ml (male), 500/200 mg tipranavir/ritonavir twice daily
Cmin	25.1 ± 14.7 µg/ml (female), 21.5±10.1 µg/ml (male), 500/200 mg tipranavir/ritonavir twice daily
AUC	513 ± 186 µg/ml.h (female), 428 ± 125 µg/ml.h (male), for above regimen
Bioavailability	Not available
Absorption	Food improves the tolerability of tipranavir with ritonavir. Therefore tipranavir, co-administered with low dose ritonavir, should be given with food.
Protein Binding	>99.9%
Volume of Distribution	Not available
CSF:Plasma ratio	Not available
Semen:Plasma ratio	Not available
Renal Clearance	<5% (mainly as glucuronide conjugate, 0.5% as unchanged drug)
Renal Impairment	Since the renal clearance of tipranavir is negligible, increased plasma concentrations are not expected in patients with renal impairment. No dosage adjustment is required.
Hepatic Impairment	Tipranavir should be used with caution, and with increased monitoring frequency in mild hepatic impairment (Child-Pugh Class A) and should not be used in moderate or severe hepatic impairment (Child-Pugh Class B or C).

Metabolism and Distribution

Metabolised by	Predominantly CYP3A
Inducer of	CYP3A & P-glycoprotein (when co-administered with ritonavir, net induction is observed over time) Modest inhibition of CYP2C19 has been observed at first dose, but there was marked induction at steady state.
Inhibitor of	CYP3A (when co-administered with ritonavir, net inhibition is observed). Potent inhibition of CYP2D6 and both hepatic and intestinal CYP3A4/5 activities were observed after first dose and steady state. P-glycoprotein. BCRP(*in vitro*) [1]
Transported by	P-glycoprotein

References

Unless otherwise stated (see below), information is from:
Aptivus Summary of Product Characteristics, Boehringer Ingelheim Ltd.
Aptivus US Prescribing Information, Boehringer Ingelheim Pharmaceuticals Inc.

1. 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.