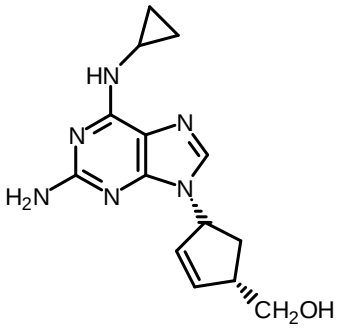
Abacavir PK Fact Sheet

Details

Generic Name	Abacavir (ABC)
Trade Name	Ziagen®
Class	Nucleoside Reverse Transcriptase Inhibitor
Molecular Weight	670.76 (as sulphate)
Structure	

Summary of Key Pharmacokinetic Parameters

Abacavir is metabolised intracellularly to the active moiety, carbovir 5'- triphosphate.

Plasma half life	1.5 h
Cmax	3.0 ± 0.89 µg/ml (300 mg bd dosing); 4.26 ± 1.19 µg/ml (600 mg once daily).
Cmin	0.01 µg/ml (300 mg twice daily).
AUC	6.02 ± 1.73 µg/ml.hr (300 mg bd dosing); 11.95 ± 2.51 µg/ml.hr (600 mg once daily).
Bioavailability	83%
Absorption	Food delayed absorption and decreased Cmax but did not affect AUC. Therefore abacavir can be taken with or without food.
Protein Binding	~49%
Volume of Distribution	0.86 ± 0.15 L/kg
CSF:Plasma ratio	30-44%
Semen:Plasma ratio	Good penetration into the male genital tract has been observed [1].
Renal Clearance	Minor route (<2%)
Renal Impairment	No dosage adjustment required, but should be avoided in those with end-stage renal disease.
Hepatic Impairment	Abacavir is primarily metabolised by the liver. The manufacturer makes no dose recommendation for mild hepatic impairment. No data are available in patients with moderate hepatic impairment; the use of abacavir is not recommended unless judged necessary. Use in severe hepatic impairment is contraindicated.

Metabolism and Distribution

Metabolised by	P450 does not play a major role in abacavir metabolism. Primary pathways of metabolism in man are by alcohol dehydrogenase and by glucuronidation.
Inducer of	Induction of hepatic metabolism has not been observed in clinical studies.
Inhibitor of	BCRP(*in vitro*) [2]; MRP1, MRP2 [3]. Does not inhibit CYP3A4, CYP2C9 or CYP2D6 at clinically relevant concentrations.
Transported by	P-gp [4], BCRP1 [5]

References

Unless otherwise stated (see below), information is from:
Ziagen® Summary of Product Characteristics, ViiV Healthcare UK.
Ziagen® US Prescribing Information, ViiV Healthcare.

1. van Praag R, van Heeswijk R, Jurriaans S, *et al*. Penetration of the nucleoside analogue abacavir into the genital tract of men infected with human immunodeficiency virus type 1. *Clin Infect Dis*. 2001; 33(8): e91-92.
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. 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.
4. Shaik N, Giri N, Pan G, Elmquist WF. P-glycoprotein-mediated active efflux of the anti-HIV1 nucleoside abacavir limits cellular accumulation and brain distribution. *Drug Metab Dispos.* 2007; 35(11): 2076-2085.
5. Pan G, Giri N, Elmquist W. Abcg2/Bcrp1 mediates the polarized transport of antiretroviral nucleosides abacavir and zidovudine. *Drug Metab Dispos.* 2007; 35(7): 1165-1173.