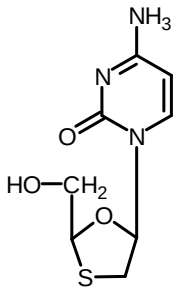
Lamivudine PK Fact Sheet

Details

Generic Name	Lamivudine (3TC)
Trade Name	Epivir®
Class	Nucleoside Reverse Transcriptase Inhibitor
Molecular Weight	229.3
Structure	

Summary of Key Pharmacokinetic Parameters

Lamivudine is metabolised intracellularly to the active moiety, lamivudine 5'-triphosphate.

Linearity/non-linearity	Lamivudine exhibits linear pharmacokinetics over the therapeutic dose range.
Plasma half life	5-7 h
Cmax	1.2 µg/ml (150 mg twice daily, healthy subjects); 2.0 µg/ml (300 mg once daily)
Cmin	0.09 µg/ml (150 mg twice daily, healthy subjects); 0.04 µg/ml (300 mg once daily)
AUC	4.7 µg.h/ml (150 mg twice daily, healthy subjects); 8.9 µg.h/m (300 mg once daily)
Bioavailability	80-85%
Absorption	Lamivudine may be administered with or without food. Co-administration with food delays Tmax and lowers Cmax (decreased by 47%). However, the extent (based on the AUC) of lamivudine absorbed is not influenced.
Protein Binding	<36%
Volume of Distribution	1.3 L/kg
CSF:Plasma ratio	~0.12
Semen:Plasma ratio	9.1 (2.3-16.1) [1]
Renal Clearance	>70%
Renal Impairment	Lamivudine concentrations are increased in patients with moderate - severe renal impairment due to decreased clearance. The dose should therefore be adjusted, using oral solution presentation, for patients whose creatinine clearance falls below 30 ml/min.
Hepatic Impairment	Data obtained in patients with moderate to severe hepatic impairment shows that lamivudine pharmacokinetics are not significantly affected by hepatic dysfunction.

Metabolism and Distribution

Metabolised by	Predominantly cleared unchanged by renal excretion. Hepatic metabolism is low (5-10%).
Inducer of	N/A
Inhibitor of	MRP1, MRP2, MRP3 [2]
Transported by	Possibly MRP4, MRP8 (*in vitro*) [3]

References

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

1. Pereira AS, Kashuba AD, Fiscus SA, *et al*. Nucleoside analogues achieve high concentrations in seminal plasma: relationship between drug concentration and virus burden. *J Infect Dis.* 1999; 180(6): 2039-2043.
2. 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.
3. Turriziani O, Schuetz JD, Focher F, *et al*, Impaired 2',3'-dideoxy-3'-thiacytidine accumulation in T-lymphoblastoid cells as a mechanism of acquired resistance independent of multidrug resistant protein 4 with a possible role for ATP-binding cassette C11. *Biochem J.* 2002; 368(Pt 1): 325-332