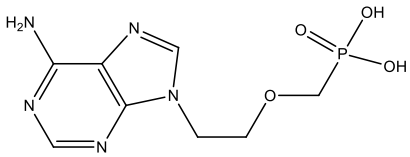
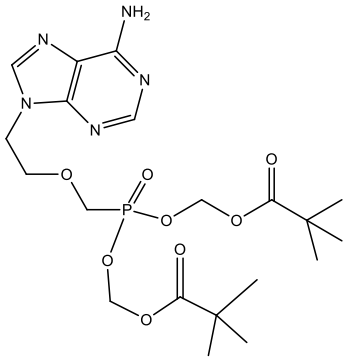
Adefovir PK Fact Sheet

Details

Generic Name	Adefovir dipivoxil, a dipivaloyloxymethyl ester prodrug of the active substance adefovir
Trade Name	Hepsera®
Class	Acyclic nucleotide analog of adenosine, with antiviral activity against HBV polymerases
Molecular Weight	273.2 (adefovir), 501.48 (adefovir dipivoxil prodrug)
Structure	*Adefovir*  *Adefovir Dipivoxil (prodrug)* 

Summary of Key Pharmacokinetic Parameters

Following oral administration, adefovir dipivoxil is rapidly converted to adefovir which is phosphorylated by cellular kinases to active adefovir diphosphate. The intracellular half life of adefovir diphosphate is 12-36 h in activated and resting lymphocytes.

Linearity/non-linearity	The pharmacokinetics of adefovir are dose proportional over an adefovir dipivoxil dose range of 10 to 60 mg and are not affected by repeat dosing.
Steady state	Data unavailable
Plasma half life	Terminal elimination half-life 7.22 h (4.72-10.70)
Cmax	16.70 (9.66-30.56) ng/ml (10 mg single dose adefovir dipivoxil)
Cmin	Data unavailable
AUC	204.40 (109.75-356.05) ng.h/ml (10 mg single dose adefovir dipivoxil)
Bioavailability	Oral bioavailability of adefovir from 10 mg adefovir dipivoxil is 59%
Absorption	Absorption may be delayed but is not reduced when given with food. Adefovir may therefore be taken without regard to food.
Protein Binding	≤4% in vitro
Volume of Distribution	392 ± 75 ml/kg (1.0 mg/kg/day IV, steady state) 352 ± 9 ml/kg (3.0 mg/kg/day IV, steady state)
CSF:Plasma ratio	Data unavailable
Semen:Plasma ratio	Data unavailable
Renal Clearance	Predominant mode of clearance. Undergoes glomerular filtration and active tubular secretion. With repeated administration of 10 mg adefovir dipivoxil, 45% of the dose is recovered as adefovir in the urine over 24 hours.
Renal Impairment	The manufacturer advises adjustment of dosing interval in patients with creatinine clearance <50 ml/min or on dialysis. Use of adefovir is not recommended with creatinine clearance <30 ml/min and should only be considered if potential benefits outweigh potential risks. A 4-hour period of haemodialysis removed approximately 35% of the adefovir dose. The effect of peritoneal dialysis on adefovir removal has not been evaluated.

Hepatic Impairment	Pharmacokinetic properties were similar in patients with moderate and severe hepatic impairment compared to healthy volunteers. No dose adjustment is required in patients with hepatic impairment.

Metabolism and Distribution

Metabolised by	No CYP450 involvement in vitro
Inducer of	Potential for adefovir to induce CYP450 enzymes is unknown
Inhibitor of	No inhibition of CYP450 in vitro
Transported by	hOAT1, MRP2,4,5 [1,2]

References

Unless otherwise stated (see below), information is from:
Hepsera® Summary of Product Characteristics, Gilead Sciences Ltd.
Hepsera® US Prescribing Information, Gilead Sciences Inc.

1. Imaoka T, Kusuhara H, Adachi M et al. Functional involvement of multidrug resistance-associated protein 4 (MRP4/ABCC4) in the renal elimination of the antiviral drugs adefovir and tenofovir. *Mol Pharmacol* 2007; **71**: 619-27.
2. Servais A, Lechat P, Zahr N et al. Tubular transporters and clearance of adefovir. *Eur J Pharmacol* 2006; **540**: 168-74.