# Adefovir PK Fact Sheet





## Details

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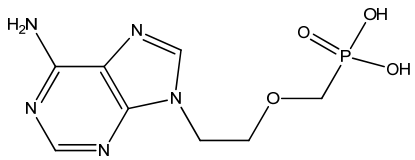
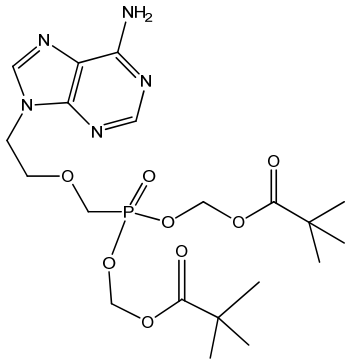
| *Generic Name* | Adefovir dipivoxil, a dipivaloyloxymethyl ester prodrug of the active substance adefovir |
| *Trade Name* | Hepsera® |
| *Class* | Acyclic nucleotide analog of adenosine, with antiviral activity against HBV polymerases |
| *Molecular Weight* | 273.2 (adefovir), 501.48 (adefovir dipivoxil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

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| *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)<br>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. |

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| *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

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| *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.