Tenofovir PK Fact Sheet

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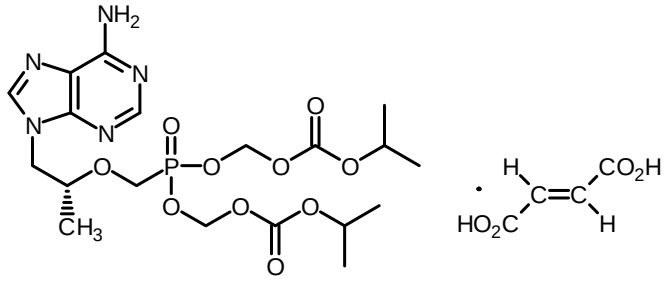
Details

Generic Name	Tenofovir disoproxil fumarate (TDF)
Trade Name	Viread®
Class	Nucleotide Reverse Transcriptase Inhibitor
Molecular Weight	305.2 (as free base)
Structure	

Summary of Key Pharmacokinetic Parameters

Tenofovir disoproxil fumarate is a prodrug which is rapidly converted in vivo to tenofovir and formaldehyde. Tenofovir is converted intracellularly to tenofovir monophosphate and to the active component, tenofovir diphosphate.

Linearity/non-linearity	The pharmacokinetics of tenofovir were independent of dose over the dose range 75-600 mg.
Plasma half life	~12-18 h
Cmax	326 ng/ml (HIV infected patients)
Cmin	64.4 ng/ml (HIV infected patients)
AUC	3324 ng.h/ml (HIV infected patients)
Bioavailability	~25% (fasting)
Absorption	Tenofovir can be taken without regard to food. Administration of tenofovir disoproxil fumarate with a high fat meal increased tenofovir AUC by approximately 40% and Cmax by approximately 14%. However, administration with a light meal did not have a significant effect on the pharmacokinetics of tenofovir.
Protein Binding	<0.7%
Volume of Distribution	~0.8 L/kg
CSF:Plasma ratio	Believed to be low due to anionic charge of the molecule at physiological pH[1].
Semen:Plasma ratio	Found to accumulate in semen at higher concentrations than plasma[2].
Renal Clearance	70-80% as unchanged drug over 72 h following IV administration. 32 ± 10% of administered dose over 24 h following multiple oral dosing with food.
Renal Impairment	Elimination is primarily by renal excretion; exposure to tenofovir increases in patients with renal dysfunction. It is recommended that the dosing interval is modified in patients with creatinine clearance <50 ml/min or in patients who already have ESRD and require dialysis.
Hepatic Impairment	Tenofovir pharmacokinetics were not substantially altered in subjects with hepatic impairment suggesting that no dose adjustment is required.

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Metabolism and Distribution

Metabolised by	No P450 involvement; 70-80% of an IV dose is excreted unchanged.
Inducer of	N/A
Inhibitor of	MRP1, MRP2, MRP3[3]. May also compete with other drugs for tubular secretion[1].
Transported by	Renal transport proteins hOAT 1 and 3, MRP4

References

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

1. Kearney B, Flaherty J, Shah J; Tenofovir disoproxil fumarate: clinical pharmacology and pharmacokinetics. *Clin Pharmacokinet*. 2004; 43(9): 595-612.
2. Ghosn J, Chaix ML, Peytavin G, *et al*. Penetration of enfuvirtide, tenofovir, efavirenz, and protease inhibitors in the genital tract of HIV-1-infected men. *AIDS.* 2004; 18(14): 1958-1961.
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.

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