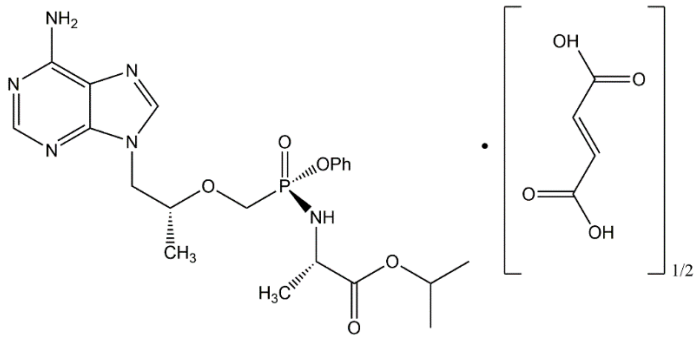
Tenofovir Alafenamide PK Fact Sheet

Details

Generic Name	Tenofovir alafenamide fumarate (TAF)
Trade Name	Vemlidy® (for hepatitis B)
Class	Nucleoside/nucleotide Reverse Transcription Inhibitor
Molecular Weight	534.5
Structure	

Summary of Key Pharmacokinetic Parameters

Tenofovir alafenamide is a phosphonamidate prodrug of tenofovir and is primarily hydrolyzed to form tenofovir. Intracellular tenofovir is subsequently phosphorylated to the pharmacologically active metabolite tenofovir diphosphate.

Linearity/non-linearity	Tenofovir alafenamide exposures are dose proportional over the dose range of 8 to 125 mg.
Steady state	Not reported
Plasma half-life	TAF 0.51 h; tenofovir 32.37 h (median).
Cmax	TAF 0.27 (63.3) µg/ml; tenofovir 0.03 (24.6) µg/ml (mean, CV%), from multiple dose administration in subjects with chronic hepatitis B.
Ctrough	TAF not applicable; tenofovir 0.01 (39.6) µg/ml (mean, CV%), from multiple dose administration in subjects with chronic hepatitis B.
AUC	TAF 0.27 (47.8) µg·h/ml; tenofovir 0.40 (35.2) µg·h/ml (mean, CV%), from multiple dose administration in subjects with chronic hepatitis B.
Bioavailability	Not reported
Absorption	Relative to fasting conditions, the administration of a single dose of Vemlidy with a high fat meal resulted in a 65% increase in tenofovir alafenamide exposure.
Protein Binding	TAF ~80%; tenofovir <0.7%
Volume of Distribution	Not reported
CSF:Plasma ratio	Not reported
Semen:Plasma ratio	Not reported
Renal Clearance	TAF - <1% renally excreted unchanged Tenofovir - renally eliminated by glomerular filtration and active tubular secretion
Renal Impairment	No dose adjustment is required in patients with CrCl ≥15 mL/min or in patients with CrCl <15 mL/min who are receiving haemodialysis (on haemodialysis days, Vemlidy should be administered after completion of haemodialysis treatment). No dosing recommendations can be given for patients with CrCl <15 mL/min who are not receiving haemodialysis.
Hepatic Impairment	No dosage adjustment is required in patients with mild hepatic impairment (Child-Pugh A). Vemlidy is not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

Metabolism and Distribution

Metabolised by	Carboxylesterase-1, cathepsin A, CYP3A (minimal)
Inducer of	None expected. Does not induce CYP3A in vivo.
Inhibitor of	None expected. Does not inhibit CYP3A in vivo. Does not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or UGT1A1 in vitro
Transported by	P-gp, BCRP, OATP1B1, OATP1B3,

References

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