

Tenofovir Alafenamide PK Fact Sheet

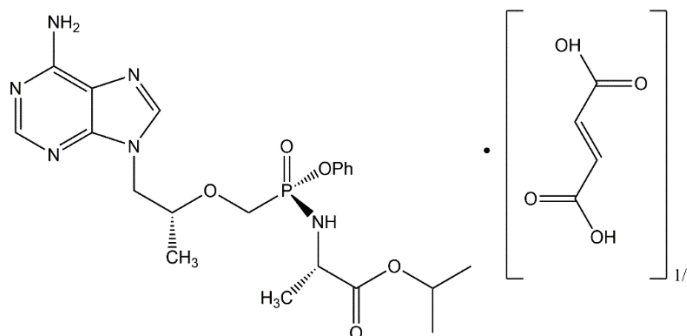
Prepared July 2022

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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).
C_{max}	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.
C_{trough}	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.

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Metabolism and Distribution

<i>Metabolised by</i>	Carboxylesterase-1, cathepsin A, CYP3A (minimal)
<i>Inducer of</i>	None expected. Does not induce CYP3A in vivo.
<i>Inhibitor of</i>	None expected. Does not inhibit CYP3A in vivo. Does not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or UGT1A1 in vitro
<i>Transported by</i>	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.