PHARMACOKINETIC DRUG INTERACTIONS
WITH TENOFOVIR ALAFENAMIDE (TAF)

	Interaction	**Dosing Recommendation**
Usual Dose	25 mg once daily with food.	Take with food.
Kinetic Characteristics	Tenofovir alafenamide (TAF) is a prodrug of tenofovir. Tenofovir alafenamide 25 mg provides enhanced delivery of tenofovir to lymphatic tissues, resulting in ~5-fold higher tenofovir diphosphate concentrations in peripheral blood mononuclear cells and ~90% lower circulating tenofovir compared to tenofovir disoproxil 300 mg. TAF is a Pgp substrate and weak inhibitor of OCT1 and MATE1.	
Effect of renal impairment	The kinetics of single dose TAF 25 mg was assessed in 14 subjects with severe renal impairment (eGFR 15-29 mL/min) and 13 controls (eGFR ≥90 mL/min). TAF exposures were moderately higher (92% increase AUCinf and 83% increase in Cmax) in severe renal impairment compared to controls. Less than 1% of TAF was eliminated in urine. Tenofovir AUCinf and Cmax were 5.8-fold and 2.8-fold higher, respectively in severe renal impairment compared to controls.[1]	Longterm evaluation of standard dose TAF (as part of elvitegravir/ cobicistat/emtricitabine /TAF single tablet regimen) in patients with renal impairment is underway.
Effect of hepatic impairment	The kinetics of single dose TAF 25 mg was assessed in subjects with stable mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment versus healthy controls. In subjects with mild hepatic impairment, TAF AUC decreased 7% and Cmax decreased 11% and tenofovir AUC decreased 11% and Cmax decreased 3% compared to controls. In subjects with moderate hepatic impairment, TAF AUC increased 13% and Cmax increased 19% and tenofovir AUC decreased 3% and Cmax decreased 12% compared to controls. These changes are not considered clinically relevant.[2]	No dose adjustment of TAF is necessary in mild to moderate hepatic impairment.
Atazanavir	When TAF 10 mg/emtricitabine 200 mg was coadministered with atazanavir 300/ritonavir 100 mg once daily, TAF AUC increased 91%, Cmax increased 77% and tenofovir AUC increased 162% and Cmax increased 112%, compared to TAF 10 mg/emtricitabine 200 mg administered alone. Atazanavir pharmacokinetics were not significantly altered in the presence of TAF/emtricitabine.[3]	Use tenofovir alafenamide 10 mg with boosted PIs.
Darunavir	When TAF 10 mg/emtricitabine 200 mg was coadministered with darunavir 800/ritonavir 100 mg once daily, TAF AUC increased 5%, Cmax increased 42% and tenofovir AUC increased 105% and Cmax increased 142%, compared to TAF 10 mg/emtricitabine 200 mg administered alone. Darunavir pharmacokinetics were not significantly altered in the presence of TAF/emtricitabine.[3]	Use tenofovir alafenamide 10 mg with boosted PIs.
Dolutegravir	When TAF 10 mg/emtricitabine 200 mg was coadministered with dolutegravir 50 mg once daily, TAF AUC increased 18%,	Use tenofovir alafenamide 25 mg

	Interaction	Dosing Recommendation
	Cmax increased 24% and tenofovir AUC increased 25% and Cmax increased 10%, compared to TAF 10 mg/emtricitabine 200 mg administered alone. Dolutegravir pharmacokinetics were not significantly altered in the presence of TAF/emtricitabine.[3]	with integrase inhibitors.
Lopinavir/ ritonavir	When TAF 10 mg/emtricitabine 200 mg was coadministered with lopinavir 800/ritonavir 200 mg once daily, TAF AUC increased 47%, Cmax increased 119% and tenofovir AUC increased 316% and Cmax increased 275%, compared to TAF 10 mg/emtricitabine 200 mg administered alone. Lopinavir pharmacokinetics were not significantly altered in the presence of TAF/emtricitabine.[3]	Use tenofovir alafenamide 10 mg with boosted PIs.
Rilpivirine	When TAF 25 mg was coadministered with rilpivirine 25 mg once daily, TAF AUC decreased 4%, Cmax increased 1% and tenofovir AUC increased 9% and Cmax increased 18%, compared to TAF 25 mg administered alone. Atazanavir pharmacokinetics were not significantly altered in the presence of TAF.[3]	Use tenofovir alafenamide 25 mg with NNRTIs.

Please note: This chart summarizes some of the major drug interactions identified to date, based on current available data; other drug interactions may exist. Please use caution whenever adding/modifying therapy. The information in this table is intended for use by experienced physicians and pharmacists. It is not intended to replace sound professional judgment in individual situations, and should be used in conjunction with other reliable sources of information. Due to the rapidly changing nature of information about HIV treatment and therapies, users are advised to recheck the information contained herein with the original source before applying it to patient care.

References:

1. Ramanathan S, Custodio J, Fordyce M, et al. Tenofovir alafenamide pharmacokinetics in renal impairment: Potential for administration without dose adjustment [abstract 529]. 20th Conference on Retroviruses and Opportunistic Infections (CROI), March 3-6, 2013, Atlanta, GA.

2. Begley R, Martin H, Lawson EB, et al. Pharmacokinetics and safety of tenofovir alafenamide in subjects with mild or moderate hepatic impairment [abstract P_39]. 15th International Workshop on Clinical Pharmacology of HIV and Hepatitis Therapy, May 19-21, 2014, Washington, DC.

3. Lawson EB, Martin H, McCallister S, et al. Drug interactions between tenofovir alafenamide and HIV antiretroviral agents [abstract H-1012]. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), September 5-9, 2014, Washington, DC.