Tenofovir Disoproxil Fumarate (TDF) and Tenofovir Alafenamide (TAF) Interactions
(also see drug package inserts)

Class or Drug	Mechanism of Action	Clinical Comments
Adefovir [Jafari, et al. 2014]	• Similar mechanisms of action and elimination, and thus, similar adverse event profiles. • Competitive inhibition of elimination results in additive adverse events.	Avoid concomitant use to avoid increased risk of hepatic steatosis and lactic acidosis.
Other nephrotoxic agents [Jafari, et al. 2014]	Competitive inhibition of elimination results in additive adverse events.	• Avoid concomitant use or use the lowest effective dose of other drug to avoid renal impairment and kidney dysfunction. • May be preferable to use TAF in these instances because TAF is less nephrotoxic.
Sofosbuvir/velpatasvir/ voxilaprevir [brand name Vosevi] [Garrison, et al. 2017]	• TDF and TAF are substrates for BCRP and P-gP. • Voxilaprevir is a BCRP inhibitor. • Velpatasvir inhibits BCRP and P-gP.	• Avoid concomitant use if possible to avoid TDF-associated adverse events. • May be preferable to use TAF in these instances.
Potent CYP3A4 or P-gP inducers (phenytoin, rifampin, carbamazepine, St. John's wort, etc.) [Gibson, et al. 2016]	• CYP3A4 is a minor metabolic pathway for TAF, and as such, potent inducers of this enzyme may modestly reduce concentrations. • TAF is also a substrate of P-gP, and inducers may decrease TAF concentrations.	Avoid coadministration of TAF with potent inducers of CYP3A4 or P-gP
Zonisamide	TDF may increase concentration of zonisamide.	Monitor for adverse events of zonisamide with TDF.
Topiramate	No significant interactions noted.	Monitor renal function when coadministered (topiramate may cause kidney stones; TDF is associated with renal toxicity).

Abbreviations: BCRP, breast cancer resistance protein; CYP, cytochrome P450; P-gP, P-glycoprotein.
No significant interactions/no dose adjustments necessary: Common oral antibiotics; drugs used as antihypertensive medicines; anticoagulants; antiplatelet drugs; statins; antidiabetic drugs; acid-reducing agents; polyvalent cations; asthma and allergy medications; long-acting beta agonists; inhaled and injected corticosteroids; antidepressants; benzodiazepines; sleep medications; antipsychotics; non-opioid pain medications; opioid analgesics and tramadol; hormonal contraceptives; erectile and sexual dysfunction drugs; tobacco and smoking cessation products; alcohol, disulfiram, and acamprosate; methadone, buprenorphine, naloxone, and naltrexone; immunosuppressants.

References

Garrison KL, Mogalian E, Zhang H, et al. Evaluation of drug-drug interactions between sofosbuvir/velpatasvir/voxilapevir and boosted or unboosted HIV antiretroviral regimens. 18th International Workshop on Clinical Pharmacology of Antiviral Therapy; 2017 Jun 14-17; Chicago, IL. http://www.natap.org/2017/Pharm/Pharm_19.htm

Gibson AK, Shah BM, Nambiar PH, et al. Tenofovir alafenamide: A review of its use in the treatment of HIV-1 infection. *Ann Pharmacother* 2016;50(11):942-952. [PMID: 27465879] https://www.ncbi.nlm.nih.gov/pubmed/27465879

Jafari A, Khalili H, Dashti-Khavidaki S. Tenofovir-induced nephrotoxicity: incidence, mechanism, risk factors, prognosis and proposed agents for prevention. *Eur J Clin Pharmacol* 2014;70(9):1029-1040. [PMID: 24958564] https://www.ncbi.nlm.nih.gov/pubmed/24958564