Resource: ART Drug-Drug Interactions

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Table 15: 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]	• Adefovir and tenofovir have similar mechanisms of action and elimination as well as overlapping adverse effect profiles. • Competitive inhibition of elimination results in additive adverse effects.	Avoid concomitant use to avoid increased risk of hepatic steatosis, lactic acidosis, and potential renal failure.
Other nephrotoxic agents [Jafari, et al. 2014]	Competitive inhibition of elimination results in additive adverse effects.	• **TDF:** Avoid concomitant use or use the lowest effective dose of another medication to avoid renal impairment and kidney dysfunction. • **TAF:** Using TAF in these instances may be preferable 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.	• **TDF:** Avoid concomitant use if possible to avoid TDF-associated adverse effects. • **TAF:** Using TAF in these instances may be preferable.
Potent CYP3A4 or P-gP inducers (phenytoin, 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 P-gP substrate, and inducers may decrease TAF concentrations.	**TAF:** Avoid coadministration of TAF with potent inducers of CYP3A4 or P-gP.
Rifampin, rifabutin, rifapentine	• **Rifabutin:** CYP3A and P-gP induction is expected to decrease TAF levels. • **Rifampin, rifapentine:** CYP3A induction may reduce TAF concentrations. • **Rifampin, rifabutin, rifapentine**: No clinically significant interactions with TDF are expected.	• **TAF:** – **Rifampin:** Do not coadminister with TAF; consider TDF as alternative. – **Rifabutin, rifapentine:** Do not coadminister with TAF unless benefit outweighs risk; monitor closely for virologic response. • **TDF + rifampin, rifabutin, rifapentine**: No dose adjustments are necessary.
Zonisamide	TDF may increase concentration of zonisamide.	**TDF:** When using with TDF, monitor for adverse effects.
Topiramate	No significant interactions reported.	**TDF:** When using with TDF, monitor renal function (topiramate may cause kidney stones; TDF is associated with renal toxicity).
Mpox treatments	**Cidofovir** is eliminated via glomerular filtration and active renal secretion by OAT1 and OAT3.	**Cidofovir:** Avoid coadministration with nephrotoxic agents. Consider use of TAF in place of TDF and monitor for renal-related adverse effects.

Table 15: Tenofovir Disoproxil Fumarate (TDF) and Tenofovir Alafenamide (TAF) Interactions (also see drug package inserts)
Abbreviations: BCRP, breast cancer resistance protein; CYP, cytochrome P450; OAT, organic anion transporter; P-gP, P-glycoprotein; VIGIV, vaccinia immune globulin intravenous.
No significant interactions/no dose adjustments necessary (see guideline section Drug-Drug Interactions by Common Medication Class)**:** Common oral antibiotics; antihypertensive medications; anticoagulants; antiplatelet medications; statins; antidiabetic medications; acid-reducing agents; polyvalent cations; asthma and allergy medications; long-acting beta agonists; inhaled and injected corticosteroids; antidepressants; benzodiazepines; sleep medications; antipsychotics; nonopioid pain medications; opioid analgesics and tramadol; hormonal contraceptives; erectile and sexual dysfunction agents; alpha-adrenergic antagonists for benign prostatic hyperplasia; tobacco and smoking cessation products; alcohol, disulfiram, and acamprosate; methadone, buprenorphine, naloxone, and naltrexone; immunosuppressants; COVID-19 therapeutics; gender-affirming hormones; ADHD medications and lithium.

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. *Ann Pharmacother* 2016;50(11):942-52. [PMID: 27465879] https://pubmed.ncbi.nlm.nih.gov/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):1029-40. [PMID: 24958564] https://pubmed.ncbi.nlm.nih.gov/24958564