# Resource: ART Drug-Drug Interactions

*April 2023*

| **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<br>[Jafari, et al. 2014] | • Adefovir and tenofovir have similar mechanisms of action and elimination as well as overlapping adverse effect profiles.<br>• 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<br>[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.<br>• **TAF:** Using TAF in these instances may be preferable because TAF is less nephrotoxic. |
| Sofosbuvir/velpatasvir/ voxilaprevir [brand name Vosevi]<br>[Garrison, et al. 2017] | • TDF and TAF are substrates for BCRP and P-gP.<br>• Voxilaprevir is a BCRP inhibitor.<br>• Velpatasvir inhibits BCRP and P-gP. | • **TDF:** Avoid concomitant use if possible to avoid TDF-associated adverse effects.<br>• **TAF:** Using TAF in these instances may be preferable. |
| Potent CYP3A4 or P-gP inducers (phenytoin, carbamazepine, St. John's wort, etc.)<br>[Gibson, et al. 2016] | • CYP3A4 is a minor metabolic pathway for TAF, and as such, potent inducers of this enzyme may modestly reduce concentrations.<br>• 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.<br>• **Rifampin, rifapentine:** CYP3A induction may reduce TAF concentrations.<br>• **Rifampin, rifabutin, rifapentine**: No clinically significant interactions with TDF are expected. | • **TAF:**<br>– **Rifampin:** Do not coadminister with TAF; consider TDF as alternative.<br>– **Rifabutin, rifapentine:** Do not coadminister with TAF unless benefit outweighs risk; monitor closely for virologic response.<br>• **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). |

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| **Class or Drug** | **Mechanism of Action** | **Clinical Comments** |
| Mpox treatments | **Cidofovir** is eliminated via glomerular filtration and active renal secretion by OAT1 and OAT3. | • **Cidofovir:** Avoid coadministration with nephrotoxic agents. Consider us of TAF in place of TDF and monitor for renal-related adverse effects.<br>• **Brincidofovir, tecovirimat, VIGIV:** Drug interactions are unlikely. |
| **Abbreviations:** BCRP, breast cancer resistance protein; CYP, cytochrome P450; OAT, organic anion transporter; P-gP, P-glycoprotein; VIGIV, vaccinia immune globulin intravenous.<br>**No significant interactions/no dose adjustments necessary:** Common oral antibiotics (Table 19); drugs used as antihypertensive medicines (Table 20); anticoagulants (Table 21); antiplatelet drugs (Table 22); statins (Table 23); antidiabetic drugs (Table 24); acid-reducing agents (Table 25); polyvalent cations (Table 26); asthma and allergy medications (Table 27); long-acting beta agonists (Table 28); inhaled and injected corticosteroids (Table 29); antidepressants (Table 30); benzodiazepines (Table 31); sleep medications (Table 32); antipsychotics (Table 33); nonopioid pain medications (Table 35); opioid analgesics and tramadol (Table 36); hormonal contraceptives (Table 37); erectile and sexual dysfunction drugs (Table 38); alpha-adrenergic antagonists for benign prostatic hyperplasia (Table 39); tobacco and smoking cessation products (Table 40); alcohol, disulfiram, and acamprosate (Table 41); methadone, buprenorphine, naloxone, and naltrexone (Table 42); immunosuppressants (Table 43); COVID-19 therapeutics (Table 45); gender-affirming hormones (Table 47). | | |

## 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):942-52. [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