Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

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This table provides information on the known or predicted interactions between nucleoside reverse transcriptase inhibitors (NRTIs) and non-antiretroviral drugs.

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Interactions associated with zidovudine are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between these NRTIs and other drugs.

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials			
Rifabutin	TAF	↓ TAF possible	Do not coadminister unless benefits outweigh risks. If coadministered, monitor for virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed.
Rifampin	TAF	TAF With Rifampin Compared With TDF Alone • TFV-DP AUC ↑ 4.2-fold TAF With Rifampin Compared With TAF Alone • TAF AUC ↓ 55% • TFV-DP AUC ↓ 36% TAF 25 mg Twice Daily With Rifampin Compared With TAF Once Daily Alone • TAF AUC ↓ 14% • TFV-DP AUC ↓ 24%	Do not coadminister unless benefits outweigh risks. Intracellular TFV-DP levels are higher when TAF is coadministered with rifampin than when TDF is administered alone, but clinical outcomes have not been studied. If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed.

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Rifapentine	TAF	↓ TAF possible	Do not coadminister unless benefits outweigh risks. If coadministered, monitor for virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed.
Antivirals—Orthopoxviruses (Smallpox, Mpox)			
Brincidofovir	All NRTIs	↔ brincidofovir expected	No dose adjustment needed.
Cidofovir	ABC, 3TC, FTC, TAF	↔ cidofovir expected	No dose adjustment needed.
	TDF	↑ TDF and cidofovir possible	Potential for renal toxicity when TDF is given with a nephrotoxic agent, such as cidofovir. If concomitant use is necessary, closely monitor renal function.
Tecovirimat	All NRTIs	↔ tecovirimat expected	No dose adjustment needed.
Cytomegalovirus and Hepatitis B Antivirals			
Adefovir	TAF, TDF	No data	Do not coadminister. Serum concentrations of TDF and/or other renally eliminated drugs may increase.
Ganciclovir, Valganciclovir	TAF, TDF	No data	Serum concentrations of ganciclovir and/or TFV may increase. Monitor for dose-related toxicities.
Hormonal Therapies			
17-β-estradiol	FTC	FTC AUC ↓ 14% to 24%	No dose adjustment needed.
	TDF	TFV AUC ↓ 12% to 27%	No dose adjustment needed.
Other hormones used for contraception, gender affirming therapy, or menopausal replacement therapy	All NRTIs	No change expected.	No dose adjustment needed.
Hepatitis C Antiviral Agents			
Glecaprevir/Pibrentasvir	TAF	↔ TFV AUC	No dose adjustment needed.
	TDF	TFV AUC ↑ 29%	No dose adjustment needed.
Ledipasvir/Sofosbuvir	TAF	TFV AUC ↑ 27%	No dose adjustment needed.

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	TDF	Ledipasvir ↑ TFV AUC 35% to 98% when TDF is given with various PIs and NNRTIs. Ledipasvir ↑ TFV C_{min} 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs. Further ↑ TFV AUC and C_{max} possible when TDF, ledipasvir/sofosbuvir, and PIs are coadministered.	Do not coadminister with EVG/c, TDF, or FTC. If TDF is used, monitor for TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events. Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established.
Ribavirin	TDF	Ribavirin With Sofosbuvir 400 mg • ↔ TFV AUC	No dose adjustment needed.
Sofosbuvir/Velpatasvir	TAF	↔ TFV expected	No dose adjustment needed.
	TDF	TFV C_{max} ↑ 44% to 46% and AUC ↑ 40% when coadministered with various ARV combinations.	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Sofosbuvir/Velpatasvir/ Voxilaprevir	TAF	↔ TAF expected	No dose adjustment needed.
	TDF	TFV C_{max} ↑ 48% and AUC ↑ 39% when coadministered with various ARV combinations.	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	3TC, TDF	↔ 3TC, TDF, and buprenorphine	No dose adjustment needed.
	TAF	↔ TAF expected	No dose adjustment needed.
Methadone	ABC	Methadone clearance ↑ 22%	No dose adjustment needed.

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Other Drugs			
Anticonvulsants Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	TAF	With Carbamazepine • TAF AUC ↓ 55% • ↓ TAF possible with other anticonvulsants	Do not coadminister.
Riociguat	ABC	Riociguat AUC ↑ 200%	If coadministered, initiate riociguat at 0.5 mg three times daily and monitor for riociguat-related adverse effects (e.g., hypotension).
St. John's Wort	TAF	↓ TAF possible	Do not coadminister.
Antiretroviral Drugs			
Capsid Inhibitor			
LEN (IM and PO)	ABC, FTC, 3TC	↔ ABC, FTC, 3TC, LEN expected	No dose adjustment needed.
	TAF	TAF AUC ↑ 32% ↔ LEN	No dose adjustment needed.
	TDF	TDF AUC ↑ 47% ↔ LEN	No dose adjustment needed.
INSTIs			
DTG	TAF	↔ TAF AUC	No dose adjustment needed.
	TDF	↔ TDF AUC ↔ DTG AUC	No dose adjustment needed.
RAL	TDF	RAL AUC ↑ 49%	No dose adjustment needed.
PIs			
ATV (Unboosted), ATV/c, ATV/r	TAF	TAF 10 mg With ATV/r • TAF AUC ↑ 91% TAF 10 mg With ATV/c • TAF AUC ↑ 75%	No dose adjustment needed (use TAF 25 mg).
	TDF	With ATV (Unboosted) • ATV AUC ↓ 25% and C_{min} ↓ 23% to 40% (higher C_{min} with RTV than without RTV) • TFV AUC ↑ 24% to 37%	Do not coadminister unboosted ATV with TDF. Use ATV 300 mg plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily. If using TDF and an H2 receptor antagonist in an ART-experienced

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			patient, use ATV 400 mg plus (RTV 100 mg or COBI 150 mg) daily Monitor for TDF-associated toxicities.
DRV/c	TAF	TAF 25 mg With DRV/c • ↔ TAF	No dose adjustment needed.
	TDF	TFV ↑ possible	Monitor for TDF-associated toxicities.
DRV/r	TAF	TAF 10 mg With DRV/r • ↔ TAF AUC	No dose adjustment needed.
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance is unknown. If coadministered, monitor for TDF-associated toxicities.
LPV/r	TAF	TAF 10 mg With LPV/r • TAF AUC ↑ 47%	No dose adjustment needed.
	TDF	↔ LPV/r AUC TFV AUC ↑ 32%	Clinical significance is unknown. If coadministered, monitor for TDF-associated toxicities.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate