Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)
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Recommendations for managing a particular drug interaction may differ depending on whether a new 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.

Note: Interactions associated with ddI and d4T are **not** included in this table. Please refer to FDA product labels for information regarding interactions between ddI or d4T and other concomitant drugs.

Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
Cytomegalovirus and Hepatitis B Antivirals			
Adefovir	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.
	ZDV	No significant effect	Potential increase in hematologic toxicities.
Hepatitis C Antiviral Agents			
Glecaprevir/Pibrentasvir	TAF, TDF	No significant effect	No dose adjustment necessary.
Ledipasvir/Sofosbuvir, Sofosbuvir/Velpatasvir, Sofosbuvir/Velpatasvir/ Voxilaprevir	TAF	No significant effect	No dose adjustment.
	TDF	Ledipasvir ↑ TFV AUC 40% to 98% when TDF is given with RPV and EFV Further ↑ TFV possible if TDF is given with PIs	No dose adjustment necessary. The safety of increased TFV exposure when ledipasvir/sofosbuvir is coadministered with TDF plus a PI/r or PI/c has not been established. Consider alternative HCV or ARV drugs to avoid increased TFV toxicities. Consider using TAF in patients at risk of TDF-associated adverse events. If TDF is used in these patients, monitor for TDF toxicity. **Coadministration of ledipasvir/sofosbuvir with EVG/c/TDF/FTC is not recommended.**
Ribavirin	TDF	With Sofosbuvir 400 mg: • ↔ TFV AUC	No dose adjustment necessary.
	ZDV	Ribavirin inhibits phosphorylation of ZDV.	Avoid coadministration if possible, or closely monitor HIV virologic response and possible hematologic toxicities.
INSTIs			
DTG	TAF	↔ TAF AUC	No dose adjustment necessary.
	TDF	↔ TDF AUC ↔ DTG AUC	No dose adjustment necessary.
RAL	TDF	RAL AUC ↑ 49%	No dose adjustment necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	3TC, TDF, TAF, ZDV	No significant effect	No dose adjustment necessary.

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Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
Narcotics/Treatment for Opioid Dependence, continued			
Methadone	ABC	Methadone clearance ↑ 22%	No dose adjustment necessary.
	ZDV	ZDV AUC ↑ 29% to 43%	Monitor for ZDV-related adverse effects.
Other			
Atovaquone	ZDV	ZDV AUC ↑ 31%	Monitor for ZDV-related adverse effects.
Anticonvulsants Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	TAF	With Carbamazepine: • TAF AUC ↓ 55% ↓ TAF possible with other anticonvulsants	**Coadministration is not recommended.**
Antimycobacterial Rrifampin	TAF	TAF AUC ↓ 55% TFV-DP (intracellular active moiety) AUC ↓ 36% TAF plus Rifampin Compared with TDF Alone: • TFV-DP (intracellular active moiety) AUC ↑ 4.2-fold With Twice-Daily TAF 25 mg Compared with Once-Daily TAF without Rifampin: • TAF AUC ↓ 14% • TFV-DP (intracellular active moiety) AUC ↓ 24%	**Coadministration is not recommended.**
	TDF	↔ AUC TFV	No dose adjustment necessary.
Rifabutin, Rifapentine	TAF	↓ TAF possible	**Coadministration is not recommended.**
St. John's Wort	TAF	↓ TAF possible	**Coadministration is not recommended.**
PIs (HIV)			
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 (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%	**Avoid concomitant use without RTV or COBI.** Dose: • ATV 300 mg daily plus (RTV 100 mg or COBI 150 mg) daily when coadministered with TDF 300 mg daily • If using TDF and H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg daily plus (RTV 100 mg or COBI 150 mg) daily Monitor for TDF-associated toxicity.
	ZDV	With ATV (Unboosted): • ZDV C_{min} ↓ 30% and ↔ ZDV AUC	Clinical significance unknown.

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Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
PIs (HIV), continued			
DRV/c	TAF	TAF 25 mg with DRV/c: • ↔ TAF	No dose adjustment necessary.
	TDF	↑ TDF possible	Monitor for TDF-associated toxicity.
DRV/r	TAF	TAF 10 mg with DRV/r: • ↔ TAF	No dose adjustment necessary.
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance unknown. Monitor for TDF-associated toxicity.
LPV/r	TAF	TAF 10 mg with DRV/r: • TAF AUC ↑ 47%	No dose adjustment necessary.
	TDF	↔ LPV/r AUC TFV AUC ↑ 32%	Clinical significance unknown. Monitor for TDF-associated toxicity.
TPV/r	ABC	ABC AUC ↓ 35% to 44%	Appropriate doses for this combination have not been established.
	TAF	↓ TAF expected	**Coadministration is not recommended.**
	TDF	↔ TDF AUC TPV AUC ↓ 9% to 18% and C_{min} ↓ 12% to 21%	No dose adjustment necessary.
	ZDV	ZDV AUC ↓ 31% to 42% ↔ TPV AUC	Appropriate doses for this combination have not been established.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key to Acronyms: 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; d4T = stavudine; ddI = didanosine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FDA = Food and Drug Administration; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitors; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine