



Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Table 19c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated July 14, 2016; last reviewed July 14, 2016) (page 1 of 3)

Concomitant Drug Class/Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
Non-ARV Antivirals			
Adefovir	TDF	No data	Do not coadminister. Serum concentrations of TDF and/or other renally eliminated drugs may be increased.
Ganciclovir Valganciclovir	TDF	No data	Serum concentrations of these drugs and/or TDF may be increased. Monitor for dose-related toxicities.
	ZDV	No significant effect	Potential increase in hematologic toxicities
Ledipasvir/ Sofosbuvir	TAF	No significant effect	No dose adjustment
	TDF	<ul style="list-style-type: none"> Ledipasvir ↑ TDF AUC 40% to 98% when TDF given with RPV and EFV Further ↑ TDF possible if TDF given with PIs 	<p>No dose adjustment necessary. Monitor for TDF toxicity.</p> <p>The safety of increased TDF exposure when ledipasvir/sofosbuvir is coadministered with TDF and a PI/r, ATV/c, or DRV/c has not been established. Consider alternative HCV or ARV drugs to avoid increased TDF toxicities. If coadministration is necessary, monitor for TDF-associated adverse reactions.</p> <p>Coadministration of ledipasvir/sofosbuvir with EVG/c/TDF/FTC is not recommended.</p>
Ribavirin	ddl	↑ intracellular ddl	Contraindicated. Do not coadminister. Fatal hepatic failure and other ddl-related toxicities have been reported with coadministration.
	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 dosage adjustment
	TDF	<ul style="list-style-type: none"> TDF AUC ↑ 12% and C_{min} ↑ 19% DTG ↔ 	No dosage adjustment
RAL	TDF	RAL AUC ↑ 49%	No dosage adjustment
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	3TC, ddl, TDF, TAF, ZDV	No significant effect	No dosage adjustment
Methadone	ABC	Methadone clearance ↑ 22%	No dosage adjustment
	d4T	d4T AUC ↓ 23%	No dosage adjustment
	ZDV	ZDV AUC ↑ 29% to 43%	Monitor for ZDV-related adverse effects.
NNRTIs			
RPV	ddl	RPV, ddl ↔ when RPV taken 2 hours after ddl	Administer RPV with food 4 hours before or 2 hours after ddl.

Table 19c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated July 14, 2016; last reviewed July 14, 2016) (page 2 of 3)

Concomitant Drug Class/Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
NRTIs			
ddl	d4T	No significant PK interaction	Do not coadminister. Additive toxicities of peripheral neuropathy, lactic acidosis, and pancreatitis seen with this combination.
	TDF	ddl-EC AUC and C _{max} ↑ 48% to 60%	Avoid coadministration.
Other			
Allopurinol	ddl	ddl AUC ↑ 113% <u>In patients with renal impairment:</u> • ddl AUC ↑ 312%	Contraindicated. Potential for increased ddl-associated toxicities.
Atovaquone	ZDV	ZDV AUC ↑ 31%	Monitor for ZDV-related adverse effects.
Anticonvulsants Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin	TAF	↓ TAF possible	Consider alternative anticonvulsant.
Antimycobacterial Rifabutin, Rifampin, Rifapentine	TAF	↓ TAF possible	Coadministration is not recommended.
Herbal Products St. John's wort	TAF	↓ TAF possible	Coadministration is not recommended.
PIs			
ATV +/- RTV or COBI	ddl	<u>With ddl-EC plus ATV (with food):</u> • ddl AUC ↓ 34% • ATV no change	Administer ATV with food 2 hours before or 1 hour after ddl.
	TAF	<u>TAF 10 mg with ATV/r:</u> TAF AUC ↑ 91%	No dosage adjustment (use TAF 25mg).
	TDF	<u>With ATV (unboosted):</u> • ATV AUC ↓ 25% and C _{min} ↓ 23% to 40% (higher C _{min} with RTV than without RTV) • TDF AUC ↑ 24% to 37%	Avoid concomitant use without RTV or COBI. <u>Dose:</u> • 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 ART-experienced patients, use ATV 400 mg daily plus (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicity.
	ZDV	<u>With ATV (unboosted):</u> • ZDV C _{min} ↓ 30% and 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
DRV/c	TAF	TAF 25 mg with DRV/c: TAF AUC ↔	No dosage adjustment
	TDF	Increased TDF possible	Monitor for TDF-associated toxicity.
DRV/r	TAF	TAF 10 mg with DRV/r: TAF AUC ↔	No dosage adjustment
	TDF	TDF AUC ↑ 22% and C _{min} ↑ 37%	Clinical significance unknown. Monitor for TDF toxicity.
LPV/r	TAF	TAF 10 mg with DRV/r: • TAF AUC ↑ 47%	No dosage adjustment
	TDF	• LPV/r AUC ↓ 15% • TDF AUC ↑ 34%	Clinical significance unknown. Monitor for TDF toxicity.
TPV/r	ABC	ABC AUC ↓ 35% to 44%	Appropriate doses for this combination have not been established.
	ddl	ddl-EC AUC ↔ and C _{min} ↓ 34% TPV/r ↔	Separate doses by at least 2 hours.
	TAF	↓ TAF expected	Coadministration is not recommended.
	TDF	• TDF AUC ↔ • TPV/r AUC ↓ 9% to 18% and C _{min} ↓ 12% to 21%	No dosage adjustment necessary.
	ZDV	• ZDV AUC ↓ 35% • TPV/r AUC ↓ 31% to 43%	Appropriate doses for this combination have not been established.

Key to Symbols: ↑ = increase, ↓ = decrease, ↔ = no change

Key to Abbreviations: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; d4T = stavudine; ddl = didanosine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; EVG/c/TDF/FTC = elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; **TAF = tenofovir alafenamide**; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine