

Table 22c. Drug Interactions Among Antiretrovirals and Other Drugs: NRTIs (Updated October 10, 2006)

Drug Interactions Requiring Dose Modifications or Cautious Use				
Drugs Affected	Didanosine (ddI)	Stavudine (d4T)	Tenofovir (TDF)	Zidovudine (ZDV)
Atazanavir (ATV)	Levels: Simultaneous EC ddi + ATV (with food): ↓ AUC of ddi 34%. ATV no change. Administer separately; ATV should be taken with food and ddi-EC on an empty stomach.	No data.	ATV 400mg + TDF 300mg - Levels: ATV AUC ↓ 25% and Cmin ↓ 40%. TDF AUC ↑ 24%. Avoid concomitant use without RTV. ATV + RTV 300/100mg QD + TDF 300mg QD - Levels: ATV AUC ↓ 25% and Cmin ↓ 23%; ATV Cmin higher with RTV than without. TDF AUC ↑ 30%; monitor for toxicities. Dose: ATV + RTV 300/100mg QD coadministered with TDF 300mg QD.	ZDV: No change in AUC but 30% ↓ in Cmin. Significance unknown.
Cidofovir, Ganciclovir, Valganciclovir	Buffered ddi + ganciclovir (GCV): ddi AUC ↑ 50%–111%; GCV AUC ↓ 21% when ddi administered 2 hours prior to oral GCV; no change in IV GCV concentrations. Appropriate doses for the combination of ddi and GCV have not been established.	No data.	Serum concentration of these drugs and/or tenofovir may be increased. Monitor for dose-related toxicities.	Ganciclovir + ZDV: No significant changes in levels for either drug. Potential increase in hematologic toxicities.
Darunavir (DRV)	No data.	No data.	Levels: Tenofovir AUC ↑ 22%, Cmax ↑ 24% and Cmin ↑ 37%. Clinical significance unknown; monitor for tenofovir toxicity.	No data.
Didanosine	•	Peripheral neuropathy, lactic acidosis, and pancreatitis seen with this combination; should be avoided unless potential benefit far outweighs potential risks.	Levels: ddi EC AUC ↑ by 48%–60%, Cmax ↑ by 48%–64% For patients >60 kg, 250mg/day of ddi EC is recommended; for patients <60 kg, 200mg EC ddi is recommended; the ddi doses apply to patients with creatinine clearance >60 mL/min. Monitor for ddi-associated toxicities.	No significant interactions.
Indinavir (IDV)	EC ddi can be taken together with IDV.	No significant PK interaction.	Levels: IDV Cmax ↑ 14%. Dose: Standard.	No significant PK interaction.
Lopinavir/ritonavir (LPV/r)	No data.	No data.	LPV/r 400/100mg AUC ↓ 15%; TDF AUC ↑ 34%; clinical significance of interaction is unknown; monitor for tenofovir toxicities.	No data.
Methadone	Levels: EC ddi unchanged. Dose: No change EC ddi.	Levels: d4T ↓ 27%; methadone unchanged. Dose: No dose adjustment.	No change in methadone or TDF levels.	ZDV AUC ↑ 43%. Monitor for ZDV-related adverse effects.
Ribavirin	Coadministration not recommended. Ribavirin increases the intracellular levels of the active metabolite of ddi and may cause serious toxicities.	No data.	Level: Ribavirin unchanged; no data on TDF level.	Ribavirin inhibits phosphorylation of ZDV; this combination should be avoided if possible, or closely monitor virologic response.
Tipranavir/ ritonavir	Levels: EC ddi ↓ 10%. ^a TPV Cmin ↓ 34% with EC ddi. ^a Dose: EC ddi and TPV/r should be separated by at least 2 hours.	No significant PK interaction.	TPV AUC and Cmin ↓ 9%–18% and 12%–21%, respectively ^a ; clinical significance is unknown.	Levels: ZDV AUC and Cmax ↓ 31%–42% and 46%–51%, respectively. ^a Appropriate doses for the combination of ZDV and TPV/r have not been established.

^a Study conducted with TPV/r dose(s) other than FDA-approved dose of 500/200mg BID.