

# Illicit Drug Interactions

Drug	Action	Comment
<b>Alcohol</b>		
<u>PIs</u> atazanavir darunavir/rtv fosamprenavir indinavir  lopinavir/rtv nelfinavir  saquinavir/rtv tipranavir/rtv ritonavir boosted	Interaction not likely Interaction not likely Interaction not likely Interaction not likely  Interaction not likely Interaction not likely  Interaction not likely Interaction not likely Interaction not likely	- - - Indinavir concentrations were not different between acute and chronic (>70drinks/month) drinkers in an investigation of 3 HIV+ patients - Nelfinavir exposure was comparable when given to heavy drinkers alone or with alcohol and was 17% higher in the heavy drinkers (41912 ng.h/L, n=12) than in the light drinkers (35846 ng/h/ml, n=15) in an investigation - - -
<u>NRTIs</u> Didanosine	Avoid combination if possible.	Possible ↑ risk of pancreatitis when used in combination. Monitor for signs and symptoms of pancreatitis.
<u>NNRTIs</u> efavirenz etravirine nevirapine	Interaction not likely Interaction not likely Interaction not likely	- - -
<u>Integrase</u> raltegravir	No data	-
<u>CCR5</u> maraviroc	No data	-
<b>Amphetamines</b>		
<u>PIs</u> ritonavir boosted	May ↑ plasma levels of amphetamines	Avoid combination if possible or reduce normal amphetamine dose when appropriate
<u>NNRTIs</u> efavirenz nevirapine	Interaction unlikely Interaction unlikely	- -
<u>Integrase</u> raltegravir	No data	-
<u>CCR5</u> maraviroc	No data	-

Drug	Action	Comment
<b>Benzodiazepines</b>		
<u>PIs</u> atazanavir, darunavir, fosamprenavir, lopinavir, nelfinavir, saquinavir, tipranavir indinavir	May ↑ plasma levels of benzodiazepines	Monitor for signs/symptoms of toxicities (oversedation) with alprazolam, diazepam, zolpidem, IV midazolam. AVOID oral midazolam (3-4 fold increase in plasma levels) or triazolam. Interaction unlikely with lorazepam.
ritonavir boosted	Initially ↑ plasma levels of benzodiazepines, then levels ↓ over time	Monitor for signs/symptoms of toxicities (oversedation) with zolpidem, or IV midazolam. AVOID alprazolam, diazepam, oral midazolam (3-4 fold increase in plasma levels) or triazolam. Interaction unlikely with lorazepam.
<u>NNRTIs</u> efavirenz	May alter plasma levels of benzodiazepines	Monitor for signs/symptoms of toxicities (oversedation) with alprazolam, diazepam, zolpidem. AVOID oral/IV midazolam and triazolam (potentially life threatening oversedation and respiratory depression). Interaction can increase lorazepam levels, but not clinically significant. Efavirenz clearance can be increased via 3A4 autoinduction.
etravirine	May alter plasma levels of benzodiazepines	Monitor for signs/symptoms of toxicities (oversedation) and/or withdrawal with alprazolam, diazepam, zolpidem, midazolam, and triazolam. Interaction unlikely with lorazepam. Etravirine induces 3A4 elimination of amiodarone.
nevirapine	May alter plasma levels of benzodiazepines	Monitor for signs/symptoms of toxicities (oversedation) and/or withdrawal with alprazolam, diazepam, zolpidem, midazolam, and triazolam. Interaction unlikely with lorazepam. Nevirapine clearance can be increased via 3A4 autoinduction.
<u>Integrase</u> raltegravir	Interaction not likely	-
<u>CCR5</u> maraviroc	Interaction not likely	-
<b>Cocaine</b>		
<u>PIs</u> All	May ↑ plasma levels of norcocaine	Use cautiously. Possible cocaine overdose (rhabdomyolysis, arrhythmias, hyperthermia, agitation, cardiovascular collapse) or increased hepatotoxicity. Risk may be higher if patient is cholinesterase deficient.
<u>NRTIs</u> All	Interaction not likely	-
<u>NNRTIs</u> All	May alter plasma levels of norcocaine	Use cautiously. Possible cocaine overdose (rhabdomyolysis, arrhythmias, hyperthermia, agitation, cardiovascular collapse) or increased hepatotoxicity. Risk may be higher if patient is cholinesterase deficient.

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<b><u>Integrase</u></b> raltegravir	Interaction not likely	-
<b><u>CCR5</u></b> maraviroc	Interaction not likely	-
<b>Flunitrazepam (Rohypnol)</b>		
<b><u>PIs</u></b> All	May ↑ plasma levels of flunitrazepam	Flunitrazepam metabolized via 3A4 and 2C19. Use cautiously. Monitor for signs and symptoms of toxicity (hypotension, confusion, visual disturbances, urinary retention, aggressive behavior).
<b><u>NRTIs</u></b> All	Interaction not likely	-
<b><u>NNRTIs</u></b> efavirenz, etravirine, nevirapine	May alter plasma levels of flunitrazepam	Flunitrazepam metabolized via 3A4 and 2C19. Use cautiously. Monitor for signs and symptoms of toxicity (hypotension, confusion, visual disturbances, urinary retention, aggressive behavior).
<b><u>Integrase</u></b> raltegravir	Interaction not likely	-
<b><u>CCR5</u></b> maraviroc	Interaction not likely	-
<b>Gamma-hydroxybutyrate (GHB)</b>		
<b><u>PIs</u></b> atazanavir, darunavir/rtv, fosamprenavir, indinavir, lopinavir/rtv, nelfinavir, tipranavir/rtv, ritonavir boosted saquinavir/rtv	Potential interaction	Potential interaction with all PI's, only case report of interaction for Saq/rtv
	Potential interaction, may require increased monitoring	Co-administration may increase GHB concentrations (case report of near fatal reaction from small dose of GHB ~10mg/kg while on saq/rtv)
<b><u>NNRTIs</u></b> efavirenz, etravirine, nevirapine	Interaction not likely	-
<b><u>Integrase</u></b> raltegravir	No data	-
<b><u>CCR5</u></b> maraviroc	No data	-

Drug	Action	Comment
<b>Heroin</b>		
<u>PIs</u> ritonavir	Interaction not likely	Ritonavir induces UGT 1A1. Morphine (by-product of heroin metabolized by esterases) is metabolized by UGTs 1A3 and 2B7. Possible opiate withdrawal due to increased glucuronidation of morphine.
Other PIs	Interaction not likely	-
<u>NRTIs</u> All	Interaction not likely	-
<u>NNRTIs</u> All	Interaction not likely	-
<u>Integrase</u> raltegravir	No data	-
<u>CCR5</u> maraviroc	No data	-
<b>Ketamine</b>		
<u>PIs</u> All	May ↑ plasma levels of 3A4 substrates	Animal models suggest ketamine to be a 3A4 inhibitor. Watch for signs and symptoms of ARV toxicity.
<u>NRTIs</u> All	Interaction not likely	-
<u>NNRTIs</u> All	May ↑ plasma levels of 3A4 substrates	Animal models suggest ketamine to be a 3A4 inhibitor. Watch for signs and symptoms of ARV toxicity.
<u>Integrase</u> raltegravir	Interaction not likely	-
<u>CCR5</u> maraviroc	May ↑ plasma levels of maraviroc	Animal models suggest ketamine to be a 3A4 inhibitor. Watch for signs and symptoms of ARV toxicity.
<b>Lysergic acid diethylamide (LSD)</b>		
<u>PIs</u> P450 inhibitors	May ↑ plasma levels of LSD	Use cautiously. Monitor for signs and symptoms of toxicity (hallucinations, agitation, psychosis, flashbacks). Invitro studies showed human liver hepatocytes to be involved in the metabolism of LSD.
<u>NRTIs</u> All	Interaction not likely	-
<u>NNRTIs</u> P450 inducers/inhibitors	May alter plasma levels of LSD	Use cautiously. Monitor for signs and symptoms of toxicity (hallucinations, agitation, psychosis, flashbacks). Invitro studies showed human liver hepatocytes to be involved in the metabolism of LSD.
<u>Integrase</u> raltegravir	Interaction not likely	-
<u>CCR5</u> maraviroc	Interaction not likely	-

Drug	Action	Comment
<b>MDMA (ecstasy)</b>		
<b>PIs</b> ritonavir	May ↑ plasma concentrations of MDMA	MDMA is metabolized mainly by 2D6. Case report of ritonavir causing a 10-fold increase in MDMA level. Avoid combination if possible or use reduced dose of MDMA and monitor for signs and symptoms of toxicity (hyponatremia, hyperthermia, arrhythmias, tremor, seizures, tachycardia, rhabdomyolysis).
<b>NRTIs</b> All	Interaction not likely	-
<b>NNRTIs</b> All		Possible interaction, monitor for signs and symptoms of toxicity (hyponatremia, hyperthermia, arrhythmias, tremor, seizures, tachycardia, rhabdomyolysis).
<b>Integrase</b> raltegravir	Interaction not likely	-
<b>CCR5</b> maraviroc	Interaction not likely	-
<b>Phencyclidine (PCP)</b>		
<b>PIs</b> 3A4 inhibitors	May ↑ plasma concentrations of PCP	Use cautiously. Monitor for signs and symptoms of toxicity (seizures, hypertension, rhabdomyolysis, hyperthermia)
<b>NRTIs</b> All	Interaction not likely	-
<b>NNRTIs</b> 3A4 inducers/inhibitors	May alter plasma concentrations of PCP	Use cautiously. Monitor for signs and symptoms of toxicity (seizures, hypertension, rhabdomyolysis, hyperthermia)
<b>Integrase</b> raltegravir	Interaction not likely	-
<b>CCR5</b> maraviroc	Interaction not likely	-
<b>Tetrahydrocannabinol (THC, Marijuana)</b>		
<b>PIs</b> 3A4 Inhibitors  indinavir, nelfinavir	May ↑ plasma levels of THC THC may ↓ plasma levels of ARVs	Monitor for signs and symptoms of toxicity (hallucinations, delusions, anxiety, orthostatic hypotension, and tachycardia). May not be clinically significant when THC is used in moderate amounts. Interaction may not be clinically relevant.
<b>NRTIs</b> All	Interaction not likely	-
<b>NNRTIs</b> 3A4 Inducers	May ↓ plasma levels of THC	Potential for ↓ duration of THC effect.
<b>Integrase</b> raltegravir	Interaction not likely	-
<b>CCR5</b> maraviroc	Interaction not likely	-