Recreational Drugs and HIV Antiretrovirals

A Guide to Interactions for Clinicians

2009

Recreational Drugs and HIV Antiretrovirals – A Guide to Interactions for Clinicians

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Disclaimer: Neither the AIDS Education and Training Centers nor HRSA condone or recommend the use of illicit drugs in any context. The data in this guide are intended for use by clinicians and other health care providers to provide advice that may reduce harm to patients who use these substances in conjunction with antiretroviral agents.

The data in this guide are a compilation of information obtained from published and anecdotal studies through November 2009.

*** PLEASE REFER TO PAGE 10 OF THIS GUIDE FOR IMPORTANT HARM REDUCTION THAT SHOULD BE SHARED WITH PATIENTS.**

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GENERAL

ALCOHOL

Confusion, disorientation, incoordination, loss of balance and judgement, respiratory depression, stupor, coma

PHARMACOKINETICS

Metabolized by alcohol dehydrogenase and aldehyde dehydrogenase; alcohol may induce CYP2E1 and CYP3A

KNOWN DRUG INTERACTIONS

NNRTI's

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

NRTI's

- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
- * Combivir (AZT/3TC)
- didanosine (ddI, Videx)
- * emtricitabine (FTC, Emtriva)
- Epzicom (3TC/ABC)
- lamivudine (3TC, Epivir)
- stavudine (d4T, Zerit)
- tenofovir (TDF,Viread)
- * Trizivir (AZT/3TC/ABC)
- * Truvada (FTC/TDF)
- zidovudine (AZT, ZDV, Retrovir)

Protease Inhibitors

- amprenavir (Agenerase)
- fosamprenavir (Lexiva)
- atazanavir (Reyataz)
- darunavir (Prezista)
- indinavir (Crixivan)
- lopinavir/ritonavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor

- Maraviroc (Selzentry)

Integrase Inhibitor

- Raltegravir (Isentress)

No known interactions specific to this combination

Increases abacavir AUC ~40% (decreased abacavir metabolism by alcohol dehydrogenase)

Increased risk of pancreatitis

*SEE INDIVIDUAL COMPONENTS

No known interactions specific to this combination. Caution with amprenavir and fosamprenavir oral solution as increased risk of propylene glycol toxicity possible.

No known interactions specific to this combination

No known interactions specific to this combination

AMPHETAMINES (Crystal)

Paranoia, anxiety, depression, hallucinations, tachycardia, hypertension, stroke, myocardial infarction, hyperthermia, rhabdomyolysis, diarrhea, erectile dysfunction, teeth grinding

Metabolized by hydroxylation and deamination via CYP2D6 pathway; CYP2D6 inhibitors may increase amphetamine levels (try to avoid)

KNOWN DRUG INTERACTIONS

NNRTI's

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

NRTI's

- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
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- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor

- Maraviroc (Selzentry)

Integrase Inhibitor

- Raltegravir (Isentress)

No known interactions specific to this combination

*SEE INDIVIDUAL COMPONENTS

Use of full dose ritonavir or low dose ritonavir for boosting other protease inhibitors has the potential to increase amphetamine levels in the blood.

No known interactions specific to this combination. Refer to comments for this drug class in general

Increases amphetamine blood levels 2-3 times

No known interactions specific to this combination

No known interactions specific to this combination

AMYL NITRITE (amyl nitrate, poppers)

Reduces glutathioine levels; inhaling the fumes acts as a vasodilator (hypotension, tachycardia, headaches), skin flushing

GENERAL

PHARMACOKINETICS

KNOWN DRUG INTERACTIONS

NNRTI's
- delivirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

NRTI's
- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
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- didanosine (ddI, Videx)
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- darunavir (Prezista)
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- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor
- Maraviroc (Selzentry)

Integrase Inhibitor
- Raltegravir (Isentress)

No known interactions specific to this combination

*SEE INDIVIDUAL COMPONENTS

No known interactions

No known interactions specific to this combination

No known interactions specific to this combination

BENZODIAZEPINES

CNS depression, drowsiness, memory loss, impaired coordination

Most agents extensively metabolized in the liver by the CYP3A4 system; lorazepam, oxazepam, and temazepam metabolized by conjugation via glucuronidation.

KNOWN DRUG INTERACTIONS

NNRTI's
- delivirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

NRTI's
- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
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- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor
- Maraviroc (Selzentry)

Integrase Inhibitor
- Raltegravir (Isentress)

Likely inhibits benzodiazepine metabolism through CYP3A4 inhibition and increases risk of adverse effects; concomitant use should be avoided

No known interactions specific to this combination

Diazepam drug levels may be increased by etravirine; a decrease in diazepam dosage may be needed

*SEE INDIVIDUAL COMPONENTS

Likely to interfere with metabolism and increase AUC of benzodiazepines; use of PIs with benzodiazepines should be avoided due to increased risk of sedation and respiratory depression; midazolam and triazolam specifically contraindicated with all PIs. DHHS guidelines recommend that parenteral midazolam can be used with caution as a single dose if given in a monitored situation for procedural sedation.

No known interactions specific to this combination. Refer to comments for this drug class in general

Decreases therapeutic effect of lorazepam, oxazepam, and temazepam (monitor for withdrawal)

No known interactions specific to this combination

No known interactions specific to this combination

COCAINE (coke, blow)

GENERAL

Increases rate of HIV viral replication in vitro, hypertension, cardiac dysrhythmias, myocardial infarction, seizures, depression, anxiety

PHARMACOKINETICS

Mainly metabolized by nonspecific tissue and plasma esterases; some cocaine metabolism (~10%) via CYP3A4

KNOWN DRUG INTERACTIONS

NNRTI's

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

No known interactions specific to this combination

NRTI's

- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
- * Combivir (AZT/3TC)
- didanosine (ddI, Videx)
- emtricitabine (FTC, Emtriva)
- * Epzicom (3TC/ABC)
- lamivudine (3TC, Epivir)
- stavudine (d4T, Zerit)
- tenofovir (TDF,Viread)
- * Trizivir (AZT/3TC/ABC)
- * Truvada (FTC/TDF)

*SEE INDIVIDUAL COMPONENTS

- zidovudine (AZT, ZDV, Retrovir)

No known interactions

Protease Inhibitors

- amprenavir (Agenerase)
- fosamprenavir (Lexiva)
- atazanivir (Reyataz)
- darunavir (Prezista)
- indinavir (Crixivan)
- lopinavir/ritonavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor

- Maraviroc (Selzentry)

No known interactions specific to this combination

Integrase Inhibitor

- Raltegravir (Isentress)

No known interactions specific to this combination

ECSTASY (X, MDMA)

Tachycardia, hypertension, hyperthermia, dehydration, dry mouth, tense jaw, teeth grinding, depression

CYP2D6 demethylation important in metabolism; 2D6 inhibitors are likely to increase ecstasy levels

KNOWN DRUG INTERACTIONS

NNRTI's

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

No known interactions specific to this combination

NRTI's

- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
- * Combivir (AZT/3TC)
- didanosine (ddI, Videx)
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- * Trizivir (AZT/3TC/ABC)
- * Truvada (FTC/TDF)

*SEE INDIVIDUAL COMPONENTS

Increase levels of ecstasy

- zidovudine (AZT, ZDV, Retrovir)

No known interactions specific to this combination. Refer to comments for this drug class in general

Protease Inhibitors

- amprenavir (Agenerase)
- fosamprenavir (Lexiva)
- atazanivir (Reyataz)
- darunavir (Prezista)
- indinavir (Crixivan)
- lopinavir/ritonavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

Increases risk of kidney stones due to dehydration

Potential to increase ecstasy levels

Increases ecstasy levels 5-10 times (AVOID)

CCR5 Inhibitor

- Maraviroc (Selzentry)

No known interactions specific to this combination

Integrase Inhibitor

- Raltegravir (Isentress)

No known interactions specific to this combination

Erectile Dysfunction Agents

(sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra))

GENERAL

Hypotension, tachycardia, arrhythmias (cardiac arrest and death), headache, flushing, rhinitis, dyspepsia, nausea, and visual effects (e.g. light sensitivity, changes in color vision), priapism

PHARMACOKINETICS

Metabolized in the liver via CYP3A4

KNOWN DRUG INTERACTIONS

NNRTI's

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

NRTI's

- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
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- indinavir (Crixivan)
- lopinavir/ritonavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor

- Maraviroc (Selzentry)

Integrase Inhibitor

- Raltegravir (Isentress)

Potential to significantly increase sildenafil, tadalafil, and vardenafil concentrations. Use sildenafil at reduced doses of 25 mg every 48 hours, tadalafil at reduced doses of 10 mg every 72 hours, vardenafil at reduced doses of no more than 2.5 mg every 72 hours and monitor closely for adverse effects.

No known interactions specific to this combination.

Etravirine has been shown to decrease sildenafil concentrations, though may be used together without sildenafil dosage adjustment. Sildenafil dosage may need to be adjusted based upon clinical effect. Similar interactions are also predicted with tadalafil and vardenafil.

*SEE INDIVIDUAL COMPONENTS

Potential to significantly increase sildenafil, tadalafil, and vardenafil concentrations. Use sildenafil at reduced doses of 25 mg every 48 hours, tadalafil at reduced doses of 10 mg every 72 hours, vardenafil at reduced doses of no more than 2.5 mg every 72 hours and monitor closely for adverse effects.

No known interactions specific to this combination. Refer to comments for this drug class in general

Increases sildenafil AUC ~340% and vardenafil AUC 16-fold. May increase tadalafil concentrations. Refer to comments for this drug class in general. Monitor closely for adverse effects.

Increases sildenafil AUC 1000%, tadalafil AUC 124%, and vardenafil AUC 49-fold and half-life 5-6 fold. Refer to comments for this drug class in general. Monitor closely for adverse effects.

Increases sildenafil AUC ~210%. May increase tadalafil and vardenafil concentrations. Refer to comments for this drug class in general. Monitor closely for adverse effects.

No known interactions specific to this combination

No known interactions specific to this combination

GHB

(gamma-hydroxy-butyrate, grievous bodily harm, liquid X)

GENERAL Seizures, bradycardia, severe respiratory depression, hypotension, vomiting coma, death

PHARMACOKINETICS Utilizes CYP2D6 pathway for metabolism

KNOWN DRUG INTERACTIONS

NNRTI's

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

No known interactions specific to this combination

NRTI's

- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
- * Combivir (AZT/3TC)
- didanosine (ddI, Videx)
- emtricitabine (FTC, Emtriva)
- * Epzicom (3TC/ABC)
- lamivudine (3TC, Epivir)
- stavudine (d4T, Zerit)
- tenofovir (TDF,Viread)
- * Trizivir (AZT/3TC/ABC)
- * Truvada (FTC/TDF)

*SEE INDIVIDUAL COMPONENTS

- zidovudine (AZT, ZDV, Retrovir)

PIs potentially increase drug levels of GHB

Protease Inhibitors

- amprenavir (Agenerase)
- fosamprenavir (Lexiva)
- atazanivir (Reyataz)
- darunavir (Prezista)
- indinavir (Crixivan)
- lopinavir/ritonavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

No known interactions specific to this combination. Refer to comments for this drug class in general

CCR5 Inhibitor

- Maraviroc (Selzentry)

No known interactions specific to this combination

Integrase Inhibitor

- Raltegravir (Isentress)

No known interactions specific to this combination

HEROIN (smack, brown junk, China White)

Dreamlike state of warmth and well-being with small doses; CNS depression, drowsiness, respiratory depression, constricted pupils, nausea/vomiting with excessive doses

Utilizes CYP3A4 pathway for metabolism

KNOWN DRUG INTERACTIONS

NNRTI's

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

No known interactions specific to this combination

NRTI's

- abacavir (ABC,Ziagen)
- * Atripla (EFV/TDF/FTC)
- * Combivir (AZT/3TC)
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- stavudine (d4T, Zerit)
- tenofovir (TDF,Viread)
- * Trizivir (AZT/3TC/ABC)
- * Truvada (FTC/TDF)

*SEE INDIVIDUAL COMPONENTS

- zidovudine (AZT, ZDV, Retrovir)

Possible decrease in heroin levels

Protease Inhibitors

- amprenavir (Agenerase)
- fosamprenavir (Lexiva)
- atazanivir (Reyataz)
- darunavir (Prezista)
- indinavir (Crixivan)
- lopinavir/ritonavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

No known interactions specific to this combination. Refer to comments for this drug class in general

Reduces heroin levels by 50%

CCR5 Inhibitor

- Maraviroc (Selzentry)

No known interactions specific to this combination

Integrase Inhibitor

- Raltegravir (Isentress)

No known interactions specific to this combination

KETAMINE (K, Special K)

GENERAL Paranoia, anxiety, mania, hallucinations, "K-hole" (semi-catatonic stupor). Elevated levels may cause tachycardia, hypertension, respiratory depression

PHARMACOKINETICS Undergoes N-demethylation and hydroxylation (possibly mediated by CYP3A4); possible weak inhibitor of CPY2D1 and CYP3A4

KNOWN DRUG INTERACTIONS

NNRTI's
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- nevirapine (Viramune)
- etravirine (Intelence)

NRTI's
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- tipranavir (Aptivus)

CCR5 Inhibitor
- Maraviroc (Selzentry)

Integrase Inhibitor
- Raltegravir (Isentress)

No known interactions specific to this combination

*SEE INDIVIDUAL COMPONENTS

Likely increase the effect of ketamine (more sedation, increased heart rate and blood pressure). Effects last longer

No known interactions specific to this combination. Refer to comments for this drug class in general

Combination may increase risk of drug induced hepatitis

No known interactions specific to this combination

No known interactions specific to this combination

LSD (acid)

Paranoia, visual and auditory hallucinations

KNOWN DRUG INTERACTIONS

NNRTI's
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- tipranavir (Aptivus)

CCR5 Inhibitor
- Maraviroc (Selzentry)

Integrase Inhibitor
- Raltegravir (Isentress)

No known interactions specific to this combination

*SEE INDIVIDUAL COMPONENTS

No known interactions

No known interactions specific to this combination

No known interactions specific to this combination

GENERAL

MARIJUANA (Tetrahydrocannabinol;THC)
Tachycardia, loss of inhibitions, dry mouth, visual hallucinations

METHADONE
Generalized CNS depression

PHARMACOKINETICS

Metabolized in the liver to active metabolite (11-hydroxy THC) via CYP3A4, 2C9, and 2C6; inhibitors/inducers of CYP3A4 may interfere with THC metabolism

Primarily utilizes CYP3A4 pathway for metabolism; inhibitor of CYP2D6 and CYP3A4

KNOWN DRUG INTERACTIONS

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- delavirdine (Rescriptor)
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- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor
- Maraviroc (Selzentry)

Integrase Inhibitor
- Raltegravir (Isentress)

No known interactions specific to this combination

*SEE INDIVIDUAL COMPONENTS

Potential to increase THC levels

No known interactions specific to this combination. Refer to comments for this drug class in general

In one study, concentrations of atazanavir were reduced up to 60% in patients using marijuana. Study did not differentiate whether atazanavir was boosted with ritonavir or not.

No known interactions specific to this combination

No known interactions specific to this combination

KNOWN DRUG INTERACTIONS

NNRTI's
- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)
- etravirine (Intelence)

NRTI's
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- * Atripla (EFV/TDF/FTC)
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- darunavir (Prezista)
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- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)
- tipranavir (Aptivus)

CCR5 Inhibitor
- Maraviroc (Selzentry)

Integrase Inhibitor
- Raltegravir (Isentress)

No known interactions specific to this combination

Decreases methadone AUC significantly (~60%); titrate methadone dose to effect

Decreases methadone AUC significantly (~40-50%); titrate methadone dose to effect

Etravirine and methadone may be used together without dosage adjustments; monitor as needed

Increases methadone clearance ~22% (an increase in methadone dose may be required in some patients)

Decreases didanosine AUC ~41-60% (consider didanosine tablet form dose increase or switch to enteric-coated formulation which may not be affected to the same degree)

Decreases stavudine AUC~23%

Increases zidovudine AUC ~40% (increases AUC ~29% during chronic treatment)

Interaction highly variable and patients should be evaluated on an individual basis

Decreases methadone levels ~13-30%; monitor for withdrawal and consider methadone dose increase if needed

Decreases methadone AUC ~16-36% (may require methadone dose increase)

Decreases methadone AUC ~26-53% (may require methadone dose increase)

Decreases methadone AUC ~47% (may require methadone dose increase)

Decreases methadone AUC ~37% (may require methadone dose increase)

Decrease methadone AUC by ~50% (may require methadone dosage increase)

No known interactions specific to this combination

PATIENT INFORMATION TO REDUCE HARM

ALCOHOL

If you take ddI, do not drink alcohol. Try to avoid alcohol or use modestly.

AMYL NITRITE (amyl nitrate, poppers)

Do not use with sildenafil (Viagra), vardenafil (Levitra) or tadalafil (Cialis). Heart problems, glaucoma, or anemia make poppers more dangerous.

COCAINE (coke, blow)

Don't get so high you forget to stick to your antiretroviral regimen. Avoid cocaine if you have heart or liver problems, or high blood pressure

Erectile Dysfunction Agents

Do not mix with amyl or butyl nitrates (poppers). Combination can cause sudden drop in blood pressure leading to fainting or heart attack.

GHB

Start with half-teaspoon, wait half-hour before taking more. Do not mix with alcohol, tranquilizers, pain-killers, or allergy medications. Do not use if you are alone. The dose you used last week can kill you this week.

KETAMINE (K, Special K)

Start with 1/3 or 1/2 of usual dose. Wait a half-hour before doing more. Always use with a friend, never alone.

AMPHETAMINES (Crystal)

Avoid use if you have heart or liver problems, or high blood pressure. Recent reports of transmitted HIV resistance in patients using methamphetamine and practicing unsafe sex.

BENZODIAZEPINES

Any changes to your methadone regimen or HIV medications should be reported to both providers to ensure potential interactions are identified.

ECSTASY (X, MDMA)

Start with 1/4 or 1/2 tablet. Drink plenty of water.

HEROIN (smack, brown junk, China, White)

Start with normal dose and increase only if you experience less of a hit and less buzz. Safe injecting. Do not mix with other recreational drugs.

METHADONE

Any changes to your methadone regimen or HIV medications should be reported to both providers to ensure potential interactions are identified.

RESOURCES

The National AETC Program also includes the following services:

National HIV/AIDS Clinicians Consultation Center: 1-800-933-3413
Offering treating clinicians current HIV clinical and drug information and individualized, expert case consultation.

Post-Exposure Prophylaxis 24 hour hotline: 1-888-HIV-4911
Providing consulation for occupational exposures.

Perinatal Hotline: 1-888-448-8765
Providing consulation for perinatal exposure and treatment.

AETC HIV/AIDS National Resource Center: http://www.aidsetc.org/
Providing resources (including curricula and lecture slide sets) on HIV disease treatment, education and data.

FOR FURTHER INFORMATION, PLEASE VISIT ONE OF THE FOLLOWING WEBSITES:

NY/NJ AIDS Education and Training Center
www.nynjaetc.org

U.S. DHHS AIDS Info
aidsinfo.nih.gov

NYSDOH AIDS Institute Clinical Resources
www.hivguidelines.org

Substance Abuse and Mental Health Services Administration
www.samhsa.gov

Addiction Technology Transfer Center
www.nattc.org

Harm Reduction Coalition
www.harmreduction.org