Recreational Drugs and HIV Antiretrovirals

A Guide to Interactions for Clinicians

Summer 2005
Recreational Drugs and HIV Antiretrovirals –
A Guide to Interactions for Clinicians

Prepared by: Christine Kubin, PharmD and Antonio Urbina, MD

This clinical support tool is sponsored by the New York/New Jersey AIDS Education Training Center (NY/NJ AETC). The NY/NJ AETC is funded by the Health Resources and Services Administration (HRSA) and is part of the National AIDS Education Training Center Program, a network of federally funded regional and national centers that conduct targeted multidisciplinary HIV/AIDS education and training programs for health care providers.

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 as of June 2005.
### Known Drug Interactions

#### Alcohol
- Metabolized by alcohol dehydrogenase and aldehyde dehydrogenase; alcohol may induce CYP2E1 and CYP3A.

#### Amphetamines (Crystal)
- Metabolized by hydroxylation and deamination via CYP2D6 pathway; CYP2D6 inhibitors may increase amphetamine levels (try to avoid).

#### Known Drug Interactions

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**See Individual Components**

### Patient Information to Reduce the Harm

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

**Avoid use if you have heart or liver problems, or high blood pressure.**
### 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 with glucuronic acid.

### AMYL NITRITE (amyl nitrate, poppers)

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

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.

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

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

No known interactions specific to this combination.

### PATIENT INFORMATION TO REDUCE THE HARM

- Do not use with sildenafil (Viagra), vardenafil (Levitra) or tadalafil (Cialis). Heart problems, glaucoma, or anemia make poppers more dangerous.
- Avoid with alcohol, opiates and other sedatives.

### KNOWN DRUG INTERACTIONS

#### GENERAL

**PHARMACOKINETICS**

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**KNOWN DRUG INTERACTIONS**

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

* 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.

* 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

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**COCAIN** (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

**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

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

#### NRTI’s
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**Patient Information to Reduce the Harm**

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

Start with 1/4 or 1/2 tablet. Drink plenty of water.
**Erectile Dysfunction Agents**

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

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

**GENERAL**

**PHARMACOKINETICS**

Metabolized in the liver via CYP3A4

**KNOWN DRUG INTERACTIONS**

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**PATIENT INFORMATION TO REDUCE THE HARM**

Do not mix with amyl or butyl nitrates (poppers).

Combination can cause sudden drop in blood pressure leading to fainting or heart attack.

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.

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

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

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

* SEE INDIVIDUAL COMPONENTS
**GHB**

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

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

Utilizes CYP2D6 pathway for metabolism

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**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

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**KNOWN DRUG INTERACTIONS**

- *No known interactions specific to this combination*
- *Possible decrease in heroin levels*
- *Reduces heroin levels by 50%*
- *No known interactions specific to this combination. Refer to comments for this drug class in general*

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**GENERAL**

**PHARMACOKINETICS**

**PATIENT INFORMATION TO REDUCE THE HARM**

- 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.

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**PATIENT INFORMATION TO REDUCE THE HARM**

- 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.
**KETAMINE (K, Special K)**

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.

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**KNOWN DRUG INTERACTIONS**

- Likely increase the effect of ketamine (more sedation, increased heart rate and blood pressure). Effects last longer.
- Combination may increase risk of drug induced hepatitis.
- No known interactions specific to this combination.

**LSD (acid)**

Paranoia, visual and auditory hallucinations.

**PROTEASE INHIBITORS**

- saquinavir (Fortovase) (Invirase)
### MARIJUANA (Tetrahydrocannabinol; THC)

**Tachycardia, loss of inhibitions, dry mouth, visual hallucinations**

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

### METHADONE

**Generalized CNS depression**

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

### PHARMACOKINETICS

**GENERAL**

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**Potential to increase THC levels**

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### KNOWN DRUG INTERACTIONS

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**SEE INDIVIDUAL COMPONENTS**

### PATIENT INFORMATION TO REDUCE THE HARM

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**No known interactions specific to this combination.**

**Potential to increase THC levels**

**SEE INDIVIDUAL COMPONENTS**
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 consultation for occupational exposures.

**Perinatal Hotline: 1-888-448-8765**

**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:
- [www.hivatis.org/druginteractions.html](http://www.hivatis.org/druginteractions.html)
- [http://aidsinto.nih.gov](http://aidsinto.nih.gov)
- [www.hivguidelines.org](http://www.hivguidelines.org)
To obtain information about drug treatment and harm reduction contact:
- [www.samhasa.gov](http://www.samhasa.gov)
  or [www.nattc.org](http://www.nattc.org) (for treatment information)
- [www.harmreduction.org](http://www.harmreduction.org) (for harm reduction information)
- [www.nynjaetc.org](http://www.nynjaetc.org)