

# Recreational drug use

## How to manage drug interactions with HIV/Hepatitis C meds

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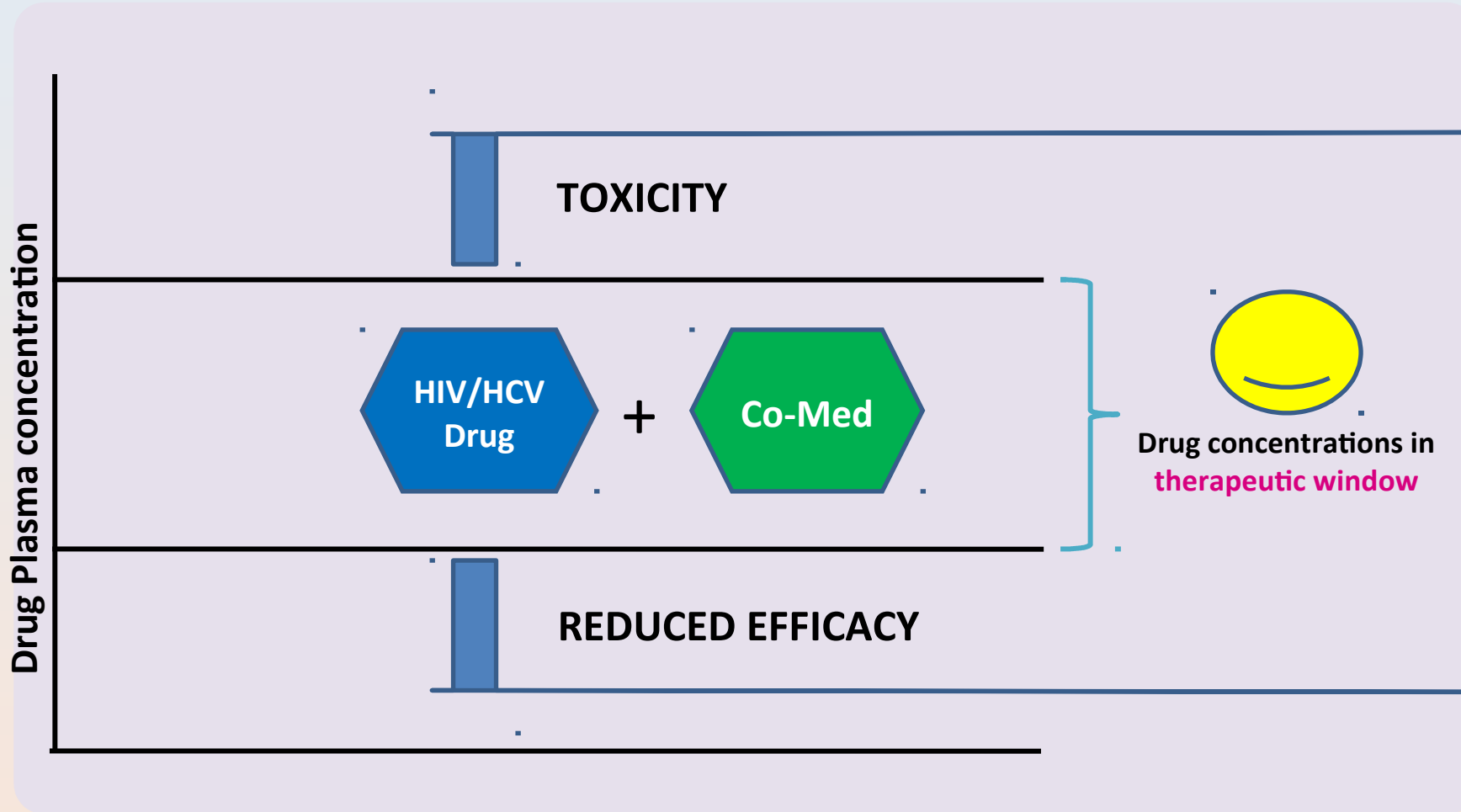
University of Liverpool

# Overview

- What are the risks/implications of drug-drug interactions (DDIs) with HIV/HCV meds and recreational drugs?
- How can we manage these risks?
  - Available resources
  - Full disclosure of current drug use
  - Consider “safer” prescribing options where possible

What are the possible implications of any drug interaction.....

**Therapeutic Window** – There is an upper and lower drug level associated with desired effect vs adverse (side) effects for all drugs (although not always known)



# What are the possible implications of interactions with recreational drugs.....

- Data from formal interaction studies lacking
- Case reports

## **Fatal interaction between ritonavir and MDMA**

*J A Henry, I R Hill*

THE LANCET • Vol 352 • November 28, 1998

## **Life-Threatening Interactions Between HIV-1 Protease Inhibitors and the Illicit Drugs MDMA and $\gamma$ -Hydroxybutyrate**

Robert D. Harrington, MD; Jane A. Woodward, PharmD; Thomas M. Hooton, MD; et al

*Arch Intern Med* 1999; 159:2221

### **Letter**

## **Possible fatal interaction between protease inhibitors and methamphetamine**

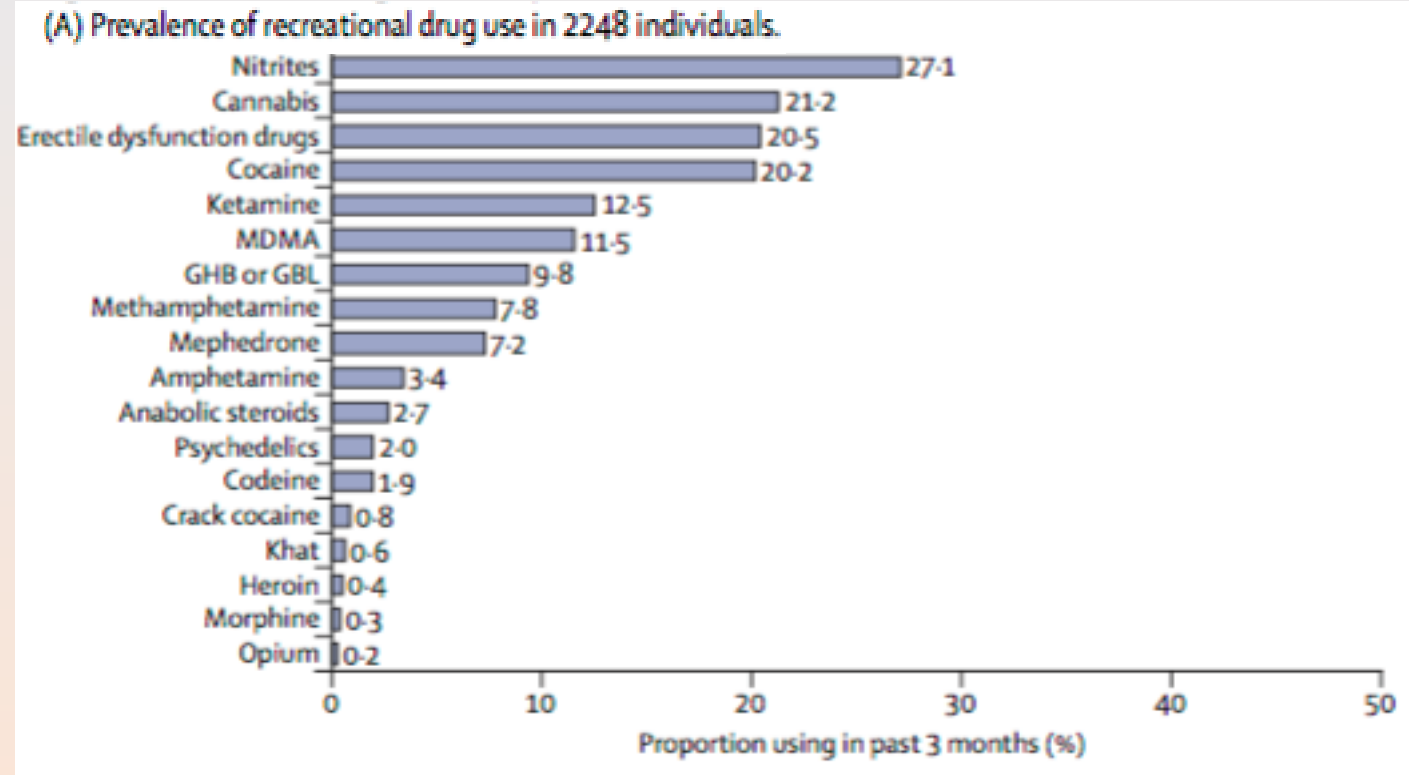
*Gillian Hales<sup>1\*</sup>, Norm Roth<sup>2</sup> and Don Smith<sup>1</sup>*

*Antiviral therapy* 2000; 5:19

## Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: results from the cross-sectional ASTRA study

Marina Daskalopoulou, Alison Rodger, Andrew N Phillips, Lorraine Sherr, Andrew Speakman, Simon Collins, Jonathan Elford, Margaret A Johnson, Richard Gilson, Martin Fisher, Ed Wilkins, Jane Anderson, Jeffrey McDonnell, Simon Edwards, Nicky Perry, Rebecca O'Connell, Monica Lascar, Martin Jones, Anne M Johnson, Graham Hart, Alec Miners, Anna-Maria Geretti, William J Burman, Fiona C Lampe

- Polydrug use prevalent in HIV-diagnosed MSM and strongly associated with condomless sex
- ~50% reported use of recreational drugs in the previous 3 months
- Almost half of those using drugs took 3+ drugs and one fifth took 5+ drugs



# DDI potential between ARVs and recreational drugs

**Higher** potential for DDI with **ritonavir** or **cobicistat** containing regimens

**Low** potential with raltegravir, dolutegravir, bictegravir, rilpivirine, maraviroc and NRTIs

Illicit drug	Metabolism, theoretical DDI with RTV/Cobi	Signs of toxicity	Recommendations
<b>Methamphetamine</b> <b>MDMA (ecstasy)</b>	CYP2D6: RTV/cobi as boosters limited CYP2D6 inhibition BUT small changes in PK could be relevant due to <b>non linear PK</b> . Cave: large variability in actual amount of drug and presence of other substances	Hypertension, seizure, hyperthermia, arrhythmia, tachycardia, teeth grinding	<ul style="list-style-type: none"><li>• <u>Avoid combination if possible</u></li><li>• If unavoidable, start with <b>1/4-1/2</b> of the usual amount and watch for signs of toxicity</li></ul>
<b>Mephedrone</b>	CYP2D6: RTV/cobi as boosters limited CYP2D6 inhibition	Tachycardia, agitation, tachycardia	<ul style="list-style-type: none"><li>• <u>Use lower dose</u>, inform users of signs of toxicity</li></ul>
<b>GHB</b>	GHB dehydrogenase, CYP? : Risk DDI unknown. Caution due to GHB <b>narrow therapeutic index</b> .	Seizure, bradycardia, respiratory depression	<ul style="list-style-type: none"><li>• <u>Use with caution</u>, use lower dose, inform users of signs of toxicity</li></ul>
<b>Cocaine</b>	CYP3A4 (minor): low-moderate risk of DDI	Tremor, paranoia, seizure, headache, hyperthermia	<ul style="list-style-type: none"><li>• Clinical relevance unknown, inform users of signs of toxicity</li></ul>
<b>Ketamine</b>	CYP3A4: <b>high potential for DDI</b>	Respiratory depression, hallucinations	<ul style="list-style-type: none"><li>• <u>Avoid combination if possible</u></li><li>• If unavoidable, start with <b>1/3-1/2</b> of the usual amount</li></ul>
<b>Benzodiazepines</b>	CYP3A4: <b>high potential for DDI</b>	Drowsiness, disorientation	<ul style="list-style-type: none"><li>• <u>Avoid midazolam, triazolam</u></li><li>• Caution with other BZD, use lower dose</li></ul>
<b>Sildenafil, tadalafil, vardenafil</b>	CYP3A4: <b>high potential for DDI</b>	Chest pain, nausea, irregular heart beat	<ul style="list-style-type: none"><li>• Lower dose: sildenafil <b>25mg/48h</b>, tadalafil: <b>10mg/72h</b>, vardenafil: <b>2.5 mg/72h</b></li></ul>
<b>Nitrites (poppers)</b>	Non CYP mediated: no DDI	Dizziness, hypotension	

Reproduced, with kind permission, from Dr Catia Marzolini, University Hospital of Basel.

Refs: Urbina A et al. Recreational drugs and HIV, a guide for clinicians 2014, Antoniou T et al. Ann Pharmacother 2002, Bracchi M et al. AIDS 2015

# DDI potential between HCV DAAs and recreational drugs

	SOF	SOF/LDV	SOF/VEL	OBV/PTV/r + DSV	GZR/EBR	DCV	S/V/V	GLP/PIB
Methadone	◆	◆	◆	◆	◆	◆	◆	◆
Buprenorphine	◆	▲	▲	■	◆	◆	▲	◆
Naloxone	◆	◆	◆	◆	◆	◆	◆	◆
Amphetamine	◆	◆	◆	■	◆	◆	◆	◆
Cannabis	◆	◆	◆	■	◆	◆	◆	◆
Cocaine	◆	◆	◆	■	◆	◆	◆	◆
Diamorphine (heroin)	◆	◆	◆	■	◆	◆	◆	◆
Diazepam	◆	◆	◆	■	◆	◆	◆	◆
Gamma-hydroxybutyrate (GHB)	◆	◆	◆	■	■	◆	◆	■
Ketamine	◆	◆	◆	■	◆	◆	◆	◆
MDMA (ecstasy)	◆	◆	◆	■	◆	◆	◆	◆
Mephedrone	◆	◆	◆	■	◆	◆	◆	◆
Methamphetamine	◆	◆	◆	■	◆	◆	◆	◆
Phencyclidine (PCP)	◆	◆	◆	■	◆	◆	◆	◆
Temazepam	◆	◆	◆	◆	◆	◆	◆	◆

◆	No clinically significant interaction expected
▲	Potential interaction predicted to be of weak intensity

■	Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring
●	These drugs should not be co-administered

Notes:

○Some drugs may require dose modifications dependent on hepatic function. Please refer to the product label for individual drugs for dosing advice.  
○The symbol (green, amber, red) used to rank the clinical significance of the drug interaction is based on [www.hep-druginteractions.org](http://www.hep-druginteractions.org) (University of Liverpool). For additional drug-drug interactions and for a more extensive range of drugs, detailed pharmacokinetic interaction data and dosage adjustments, refer to the above-mentioned website.



[www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)

HIV iChart app users - please update to the newest version to ensure up-to-date information

## Interaction Checker

Access our free, comprehensive and user-friendly drug interaction charts

### Educational Videos

A series of mini-lectures on topics including pharmacology, HIV and drug-drug interactions

### Prescribing Resources

Interaction tables, treatment selectors, clinical prescribing resources, and pharmacokinetic fact sheets

### Twitter

 @hivinteractions

Follow us on Twitter for interaction news and for the latest additions and changes to the website

### Mobile Apps



### Hepatitis Website



### Cancer Website



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### Cancer Website





Having trouble viewing the interactions? [Click here for the Interaction Checker Lite.](#)

## HIV Drugs

efa



A-Z



Class



Trade



Ritonavir



Cobicistat (with ATV or DRV)



Elvitegravir/Cobi/FTC/TAF



Efavirenz



Efavirenz



## Co-medications

Search co-medications...



A-Z



Class



Trade

HYPERTENSION / HEART FAILURE AGENTS



ILLCIT/RECREATIONAL



Alcohol



Amphetamine



Cannabis



Cocaine



Ecstasy (MDMA)



GHB (Gamma-hydroxybutyrate)



Heroin



LSD (Lysergic acid)



## Drug Interactions



Check HIV/ HIV drug interactions

Switch to table view

Reset Checker

## Potential Interaction

Cobicistat (with ATV or DRV)

Amphetamine

More Info



## Potential Interaction

Cobicistat (with ATV or DRV)

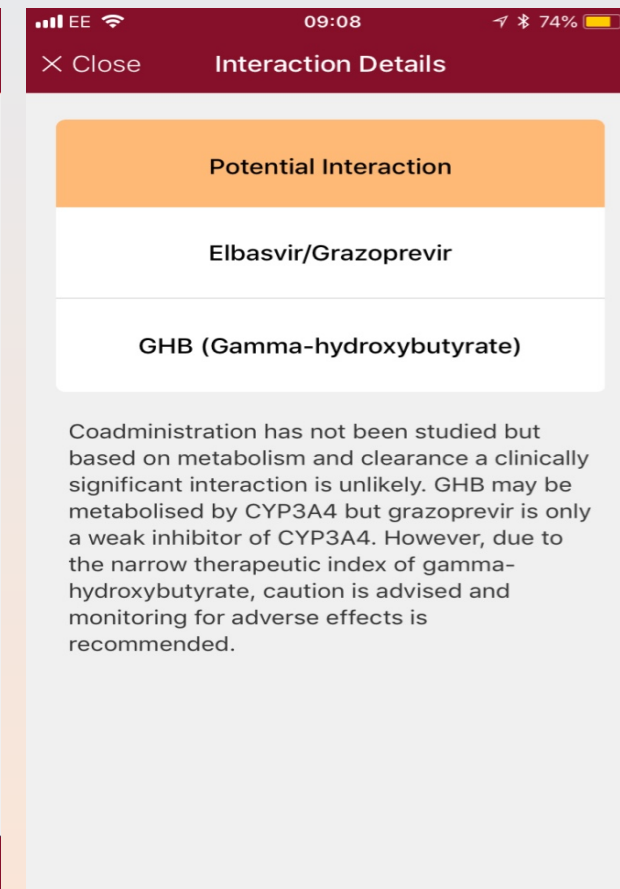
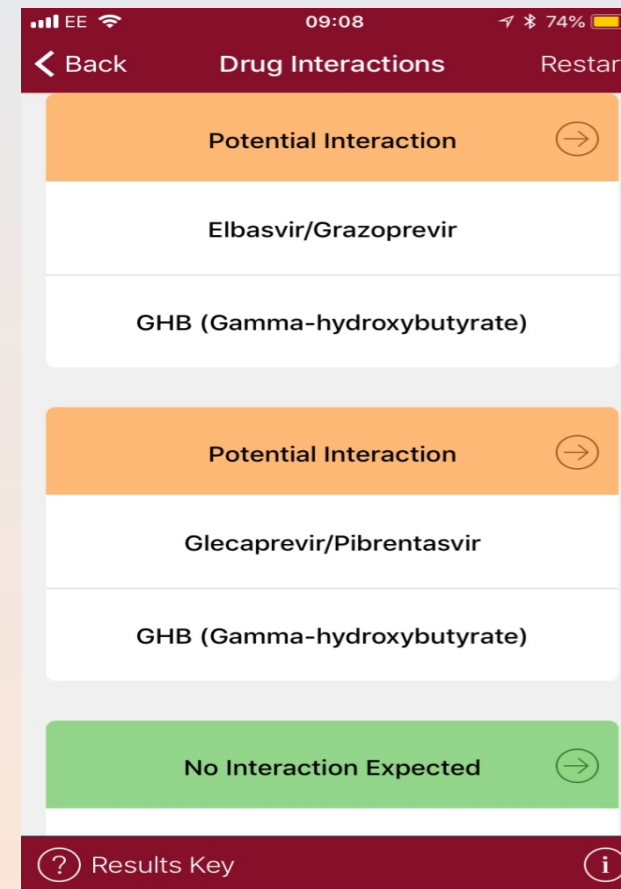
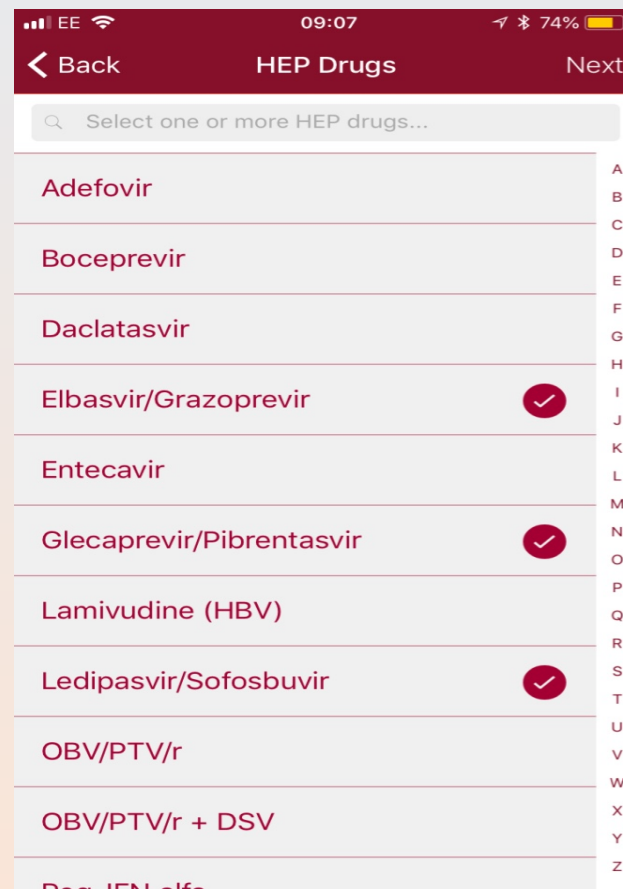
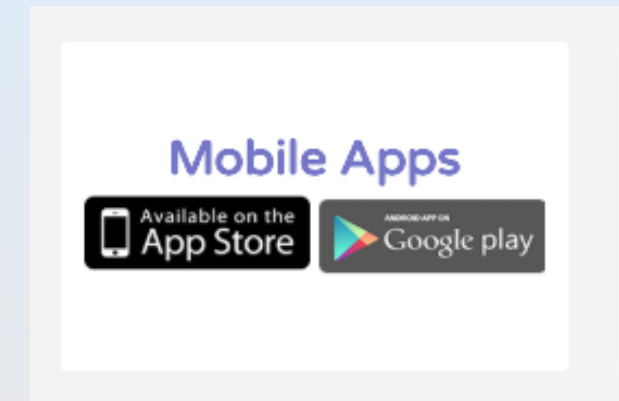
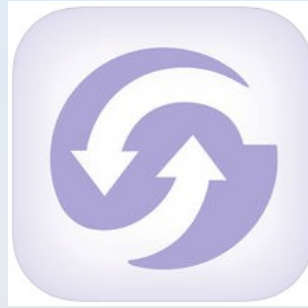
Cocaine

More Info



## Potential Interaction

# HIV and HCV iChart





## Prescribing Resources

We have produced a series of printable materials in PDF format to aid prescribing.

**Interaction Charts** provide an overview of interactions between HIV drugs and the comedications listed in the interaction checker.

**Treatment Selectors** show interactions between key antiretrovirals and drugs used to treat a range of common comorbidities or specific patient populations.

**Fact Sheets** contain information on the pharmacokinetics, metabolism and disposition of HIV drugs and have been collated from product labels and published literature on licensed doses (unless otherwise stated). Please click on the headings below to see the full range of resources within each section.

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Overview of Interactions



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Treatment Selectors (by therapeutic indication)



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Treatment Selectors (by patient characteristics)





# Antiretrovirals and Recreational Drugs

Charts revised November 2017. Full information available at [www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)

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		ATV/r	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	RAL	ABC	FTC	3TC	TDF	ZDV	E/C/F/TAF	E/C/F/TDF
Stimulants	Cocaine	↑ <sup>ab</sup>	↑ <sup>a</sup>	↑ <sup>ab</sup>	↑ <sup>c</sup>	↑ <sup>c</sup>	↑ <sup>c</sup>	↔ <sup>b</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>a</sup>	↑ <sup>a</sup>
	Ecstasy (MDMA)	↑ <sup>d</sup>	↑ <sup>d</sup>	↑ <sup>d</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>d</sup>	↑ <sup>d</sup>
	Mephedrone	↑ <sup>e</sup>	↑ <sup>e</sup>	↑ <sup>e</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>e</sup>	↑ <sup>e</sup>
	Methamphetamine	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
	Poppers (Amyl nitrate)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Depressants	Alcohol	↔	↔	↔ <sup>f</sup>	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	Alprazolam	↑ <sup>g</sup>	↑ <sup>g</sup>	↑ <sup>g</sup>	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
	Codeine	↑ <sup>i</sup>	↑ <sup>i</sup>	↑ <sup>i</sup>	↓ <sup>i</sup>	↓ <sup>i</sup>	↓ <sup>i</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>i</sup>	↑ <sup>i</sup>
	Diazepam	↑	↑	↑	↓	↑	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
	GHB (gamma hydroxybutyrate)	↑ <sup>j</sup>	↑ <sup>j</sup>	↑ <sup>j</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>j</sup>	↑ <sup>j</sup>
	Heroin (Diamorphine)	↓ <sup>k</sup>	↓ <sup>k</sup>	↓ <sup>k</sup>	↑	↔ <sup>k</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ <sup>k</sup>	↔ <sup>k</sup>
	Hydrocodone	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
	Hydromorphone	↓	↓	↓	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Ketamine	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
	Methadone	↓ <sup>b</sup>	↓16%	↓53% <sup>b</sup>	↓52%	↑6%	↓~50%	↓16%	↔	↔	↔	↓	↔	↔	↔	↑	↑7%	↑7%
	Midazolam (oral)	↑ <sup>m</sup>	↑ <sup>m</sup>	↑ <sup>m</sup>	↓ <sup>h</sup>	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>m</sup>	↑ <sup>m</sup>
	Morphine	↓ <sup>n</sup>	↓ <sup>n</sup>	↓ <sup>n</sup>	↑	↔ <sup>n</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔ <sup>n</sup>	↔ <sup>n</sup>
	Oxycodone	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
	Pethidine (Meperidine)	↓ <sup>i</sup>	↓ <sup>i</sup>	↓ <sup>i</sup>	↓ <sup>i</sup>	↓ <sup>i</sup>	↓ <sup>i</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
	Temazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Triazolam	↑ <sup>m</sup>	↑ <sup>m</sup>	↑ <sup>m</sup>	↓ <sup>h</sup>	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>m</sup>	↑ <sup>m</sup>
Hallucinogens	Cannabis	↑ <sup>o</sup> ↓	↑ <sup>o</sup>	↑ <sup>o</sup>	↑ <sup>p</sup>	↑ <sup>p</sup>	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>o</sup>	↑ <sup>o</sup>
	LSD (Lysergic acid diethylamide)	↑ <sup>q</sup>	↑ <sup>q</sup>	↑ <sup>q</sup>	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>q</sup>	↑ <sup>q</sup>
	Phencyclidine (PCP, angel dust)	↑ <sup>r</sup>	↑ <sup>r</sup>	↑ <sup>r</sup>	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑ <sup>r</sup>	↑ <sup>r</sup>

No clinically significant interaction expected.

Potential interaction predicted to be of weak intensity.

Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring.

These drugs should not be co-administered.

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[Overview of Interactions](#)

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[Treatment Selectors](#)

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[HCV DAA PK Fact Sheets](#)

## DAAs and Recreational Drugs

Charts produced April 2018.

Full information available at [www.hep-druginteractions.org](http://www.hep-druginteractions.org)

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		DCV	EBR/GZR	GLP/PIB	LED/SOF	OBV/PTV/r	OBV/PTV/r +DSV	SMV	SOF	SOF/VEL	SOF/VEL/VOX
Stimulants	Buprenorphine	↔	↔	↔	↑	↑ 51%	↑ 107%	↔	↔	↑	↑
	Naloxone	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Amphetamine	↔	↔	↔	↔	↑ <sup>a</sup>	↑ <sup>a</sup>	↔	↔	↔	↔
	Cocaine	↔	↔	↔	↔	↑ <sup>b</sup>	↑ <sup>b</sup>	↔	↔	↔	↔
	Ecstasy (MDMA)	↔	↔	↔	↔	↔ <sup>c</sup>	↔ <sup>c</sup>	↔	↔	↔	↔
	Mephedrone	↔	↔	↔	↔	↔ <sup>d</sup>	↔ <sup>d</sup>	↔	↔	↔	↔
	Methamphetamine	↔	↔	↔	↔	↔ <sup>a</sup>	↔ <sup>a</sup>	↔	↔	↔	↔
Sedatives	Alprazolam	↔	↔	↔	↔	↑	↑ 34%	↑	↔	↔	↔
	Codeine	↔	↔	↔	↔	↑ <sup>e</sup>	↑ <sup>e</sup>	↑	↔	↔	↔
	Clonazepam	↔	↔	↔	↔	↓	↓ 22%	↓	↔	↔	↔
	GHB (Gamma-hydroxybutyrate)	↔	↔ <sup>f</sup>	↔ <sup>f</sup>	↔	↑	↑	↑	↔	↔	↔
	Hydrocodone	↔	↔	↑	↔	↑	↑	↑ ↓ <sup>g</sup>	↔	↔	↔
	Hydromorphone	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔
	Ketamine	↔	↔	↔	↔	↑ <sup>h</sup>	↑ <sup>h</sup>	↑ <sup>h</sup>	↔	↔	↔
Anesthetics	Midazolam (oral)	↔	↑ <sup>i</sup>	↔	↔ <sup>j</sup>	↑	↑	45%	↔	↔	↔
	Oxycodone	↔	↑	↑	↔	↑	↑	↑	↔	↔	↔
	Temazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Hallucinogens	Triazolam	↔	↔	↔	↔	↑	↑	↑	↔	↔	↔
	Cannabis	↔	↔	↔	↔	↑ <sup>k</sup>	↑ <sup>k</sup>	↔	↔	↔	↔
	LSD (Lysergic acid diethylamide)	↔	↔	↔	↔	↑ <sup>l</sup>	↑ <sup>l</sup>	↔	↔	↔	↔
	Phencyclidine (PCP, angel dust)	↔	↔	↔	↔	↑ <sup>m</sup>	↑ <sup>m</sup>	↑ <sup>m</sup>	↔	↔	↔



No clinically significant interaction expected.



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Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring.



These drugs should not be co-administered.

# Recommendations

- ❑ Disclose the use of recreational drugs to your healthcare provider
- ❑ Your healthcare provider will inform you about the risk of drug interactions and signs of toxicity
  - A switch to an alternative HIV/HCV regimen may be considered if necessary/possible
  - Or
  - Provide recreational drug use recommendations to limit the risk of toxicity
- ❑ Practical considerations (in case of non-disclosure to your healthcare provider)
  - Take less of the recreational drug particularly if concerns re. drug interactions
  - Be aware of signs of overdose
  - Have a friend with you



# Summary

- Full disclosure of current drug use and education on the risk of DDI are essential to limit the risk of harm related to the use of illicit drugs
- HIV/HCV regimens with a lower potential for DDI should be favoured when possible in patients disclosing recreational drugs
- Online/app resources available to help guide optimal regimens