

Interaction Potential of Chemsex Drugs

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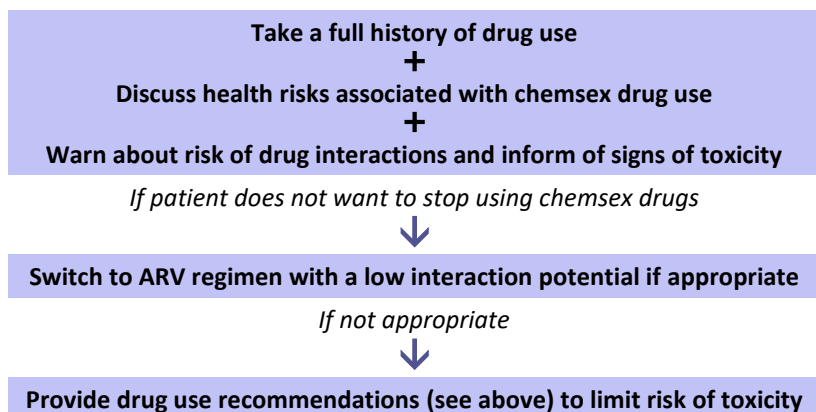
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Drug	Metabolism	Interaction Potential		Signs of Toxicity	Recommendations with cobicistat, ritonavir or lenacapavir containing regimens
		Cobicistat (Cobi) Ritonavir (RTV) Lenacapavir (LEN)	BIC, CAB, DOR, DTG, FTR, MVC, RAL, RPV, NRTIs		
Benzodiazepines: Midazolam, Triazolam	CYP3A4	High (Cobi, RTV) Moderate (LEN)	Low	- Drowsiness - Disorientation	Contraindicated with cobicistat and ritonavir.
Benzodiazepines: Others	CYP3A4	High (Cobi, RTV) Moderate (LEN)	Low	- Drowsiness - Disorientation	Caution– use lower dose of benzodiazepine.
Cocaine	CYP3A4 (minor)	Low-moderate	Low (Note, caution with FTR and RPV due to known risk of QT prolongation with cocaine)	- Tremors - Paranoia - Seizures - Headache - Hyperthermia	- Clinical relevance unknown. - Inform users of signs of toxicity.
Ecstasy (MDMA)	CYP2D6	Limited CYP2D6 inhibition but small PK changes could be significant due to non-linear PK (Cobi, RTV) Low (LEN)	Low	- Hypertension - Seizures - Hyperthermia - Arrhythmia - Tachycardia - Teeth grinding	- Avoid if possible. - If unavoidable with cobicistat or ritonavir, start with ~25-50% of the usual amount of ecstasy. - Inform users of signs of toxicity.
GHB	GHB dehydrogenase CYP?	Unknown - caution due to GHB narrow therapeutic index (RTV, LEN) Low (Cobi)	Low	- Seizures - Bradycardia - Respiratory depression	- Use with caution. - Use lower dose. - Inform users of signs of toxicity.
Ketamine	CYP3A4	High (Cobi, RTV) Moderate (LEN)	Low	- Respiratory depression - Hallucinations	- Avoid if possible. - If unavoidable with cobicistat or ritonavir, start with ~33-50% of the usual amount of ketamine.
Mephedrone	CYP2D6	Limited CYP2D6 inhibition (Cobi, RTV) Low (LEN)	Low	- Tachycardia - Agitation	- Use lower dose with cobicistat and ritonavir. - Inform users of signs of toxicity.
Methamphetamine	CYP2D6	Limited CYP2D6 inhibition but small PK changes could be significant due to non-linear PK (Cobi, RTV) Low (LEN)	Low	- Hypertension - Seizures - Hyperthermia - Arrhythmia - Tachycardia - Teeth grinding	- Avoid if possible. - If unavoidable with cobicistat or ritonavir, start with ~25-50% of the usual amount of methamphetamine. - Inform users of signs of toxicity.
Methylone	CYP2D6 CYP2C19 CYP2B6 CYP1A2	Limited CYP2D6 inhibition (Cobi, RTV) Low (LEN)	Low	- Anxiety - Psychosis - Hallucinations	- Use lower dose with cobicistat and ritonavir. - Inform users of signs of toxicity.
Monkey dust	CYP2D6 CYP2C19 CYP1A2	Limited CYP2D6 inhibition (Cobi, RTV) Low (LEN)	Low	- Paranoia - Hallucination - Violent behaviour	- Use lower dose with cobicistat and ritonavir. - Inform users of signs of toxicity.
Poppers (nitrites)	Non-CYP mediated	Low	Low	- Dizziness - Hypotension	Inform users of signs of toxicity.
Sildenafil Tadalafil Vardenafil	CYP3A4	High (Cobi, RTV) Moderate (LEN)	Low	- Chest pain - Nausea - Arrhythmia	Use lower dose: Sildenafil – 25 mg in 48 h Tadalafil – 10 mg in 72 h Vardenafil – 2.5 mg in 72 h (5 mg in 24 h with lenacapavir)

Note: interactions and their effects are difficult to predict due to variability in the amount of recreational drug and the possible presence of other substances. Residual lenacapavir concentrations may affect exposure of sensitive CYP3A4 substrates initiated within 9 months after stopping subcutaneous lenacapavir.

Flow Chart for Clinical Practice



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Abbreviations BIC bictegravir CAB cabotegravir DOR doravirine DTG dolutegravir FTR fostemsavir MVC maraviroc RAL raltegravir RPV rilpivirine
NRTIs Nucleoside/tide Reverse Transcriptase Inhibitors (abacavir, emtricitabine, lamivudine, tenofovir alafenamide, tenofovir-DP, zidovudine)

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