

## Guideline for the Management of Drug Interactions between HIV Antiretroviral Therapy and Anaesthetic Agents used during Surgery and Peri-Operatively

These tables contain information on interactions between commonly used anaesthetic agents and the following anti-retrovirals:

**Protease inhibitors (PIs):** - atazanavir (Evotaz®), darunavir (Rezolsta®, Symtuza®), lopinavir/ritonavir (Kaletra®), and ritonavir.

**Non-nucleoside reverse transcriptase inhibitors (NNRTI):** - doravirine (Pifeltro®, Delstrigo®), efavirenz, etravirine, nevirapine, and rilpivirine (Eviplera®, Odefsey®, Juluca®)

**Integrase inhibitors (INI):** - bictegravir (Biktarvy®), dolutegravir (Triumeq®, Dovato®, Juluca®) and raltegravir

**Boosted integrase inhibitor:** - elvitegravir/cobicistat (contained in Genvoya® and Stribild®)

**Cobicistat (contained in Evotaz®, Genvoya®, Rezolsta®, Symtuza®, and Stribild®):** - pharmacokinetic

enhancer of anti-retrovirals but no anti HIV activity.

There is low interaction potential between **NRTIs** and other medication including anaesthetic agents: - abacavir, emtricitabine, lamivudine, tenofovir disoproxil fumarate, tenofovir alafenamide fumarate, and zidovudine.

**This is not a comprehensive list. For advice on drugs not included in this guideline, please contact the HIV pharmacist (ext 63078) or <https://www.hiv-druginteractions.org>**

### Contra-indicated interactions with anti-retroviral agents

	ANTI-RETROVIRAL	RECOMMENDATION
Amiodarone	PIs and cobicistat.	Co-administration is contra-indicated: <b>AVOID</b> . (Contra-indicated: - potential life-threatening cardiac arrhythmias.)
Dexamethasone > single doses	PIs, NNRTIs, bictegravir and cobicistat	Continuous co-administration is contra-indicated: <b>AVOID</b> (Contra-indicated: - may reduce ARVs levels due to induction effect. Avoid long term use and consider alternatives.)
Ergometrine	PIs, efavirenz, etravirine and cobicistat.	Co-administration is contra-indicated: <b>AVOID</b> . (Contra-indicated: - potential for serious and/or life-threatening events such as acute ergot toxicity characterized by peripheral vasospasm and ischemia of the extremities and other tissues.)
Midazolam (oral)	PIs, efavirenz and cobicistat.	Co-administration is contra-indicated: <b>AVOID</b> . (Contra-indicated: - increased midazolam concentrations, causing potentially serious or life-threatening side effects such as increased sedation or respiratory depression.)  Alternative: sublingual lorazepam.
Proton Pump Inhibitors	Atazanavir and rilpivirine.	Co-administration is contra-indicated: <b>AVOID</b> . (Contra-indicated: - reduces ARVs levels due to changes in gastric pH. Consider using an alternative.)
Triamcinolone (all routes)	PIs and cobicistat.	Co-administration is contra-indicated: <b>AVOID</b> . (Contra-indicated: - Cushing's syndrome reported after single dose use.)

**Other Interactions: -**

**A**

	ANTI-RETROVIRAL	RECOMMENDATION
Adrenaline	None reported.	No dose changes necessary.
Alfentanil/ fentanyl	PIs and cobicistat will <b>increase</b> alfentanil/fentanyl levels.	Consider reducing dose of alfentanil/fentanyl and titrating up. There is a risk of prolonged or delayed respiratory depression.
	Efavirenz, etravirine and nevirapine will <b>decrease</b> alfentanil/fentanyl level.	Monitor analgesic effect and titrate to pain response.
Amiodarone	Contra-indicated with PIs and cobicistat see above.	
	Etravirine and nevirapine may decrease amiodarone concentrations.	Dose adjustment may be needed due to possible decrease in clinical effect.
	Efavirenz unpredictable effect	Caution and monitor therapeutic effect
	QT caution with rilpivirine.	Monitor
Atenolol	Bictegravir, dolutegravir, elvitegravir and cobicistat may increase atenolol levels.	Start with low dose and adjust according to response.
	Caution with PIs with other drugs that prolong the PR interval	Monitor
Atracurium	None reported.	No dose changes necessary.

**B**

	ANTI-RETROVIRAL	RECOMMENDATION
Bupivacaine	PIs and cobicistat may <b>increase</b> bupivacaine levels.	Consider a dose reduction and monitoring.
	Efavirenz, etravirine and nevirapine <b>decrease</b> bupivacaine levels.	Titrate to response.
Beta-blockers	See atenolol, labetalol and propranolol.	

**C**

	ANTI-RETROVIRAL	RECOMMENDATION
Carboprost	None reported.	No dose changes necessary.
Cisatracurium	None reported.	No dose changes necessary.
Clonidine	None reported.	No dose changes necessary.
Cyclizine	None reported.	No dose changes necessary.

## D

	ANTI-RETROVIRAL	RECOMMENDATION
Desflurane	None reported.	No dose changes necessary.
Dexamethasone	Single doses only. Continuous co-administration contra- indicated with PIs, NNRTIs, bicitegravir and cobicistat see above.	Alternative: prednisolone (reduce dose by a third with PIs cobicistat)
Diamorphine	PIs, cobicistat and efavirenz may potentiate opioid toxicity	Titrate to analgesic effect and monitor for signs of opiate toxicity.
Diazepam	PIs, cobicistat, efavirenz, etravirine and nevirapine will increase diazepam or active metabolite levels.	Monitor and titrate according to response. Use lorazepam, temazepam or oxazepam if excessive drowsiness.
Diclofenac	Efavirenz and etravirine may increase levels  Additive renal toxicity with tenofovir	Use lowest dose for shortest period (especially in CV patients)  Monitor
Dobutamine	None reported.	No dose changes necessary.
Droperidol	PIs and cobicistat increase droperidol levels – toxicity and QT caution.  Rilpivirine QT caution	Consider dose reduction and monitor (ECG), or use an alternative agent  Monitor or use alternative agent.

## E

	ANTI-RETROVIRAL	RECOMMENDATION
Ephedrine	Dolutegravir, bicitegravir and lamivudine potentially increase ephedrine levels	Monitor clinical effect and adjust ephedrine dose accordingly
Eptifibatide	None reported.	No dose changes necessary
Ergometrine	Contraindicated with PIs, efavirenz, etravirine and cobicistat see above.  Nevirapine may decrease ergometrine levels.	Dose adjustment may be needed
Etomidate	None reported.	No dose changes necessary.

## F

	ANTI-RETROVIRAL	RECOMMENDATION
Famotidine	Atazanavir and rilpivirine.	Famotidine dosed 20-40mg <b>ONCE DAILY</b> administered 4 to 12 hours after atazanavir/rilpivirine
Fentanyl	See Alfentanil.	No dose changes necessary.

## G

	ANTI-RETROVIRAL	RECOMMENDATION
Gabapentin	None reported.	
Glycopyrronium	None reported.	No dose changes necessary.
Granisetron	PIs and cobicistat increase levels. Rilpivirine – QT caution.  Efavirenz, etravirine, nevirapine may decrease levels	Consider alternative (QT prolongation).  Monitor response.

## H

	ANTI-RETROVIRAL	RECOMMENDATION
H <sub>2</sub> Antagonists	See Famotidine	
Hyoscine hydrobromide	None reported.	No dose changes necessary.

## I

	ANTI-RETROVIRAL	RECOMMENDATION
Iohexol	None reported.	No dose changes necessary.
Isoflurane	None reported.	No dose changes necessary.

## K

	ANTI-RETROVIRAL	RECOMMENDATION
Ketamine	PIs, elvitegravir/cobicistat and cobicistat will <b>increase</b> ketamine levels.	A dose adjustment may be needed, titrate according to response.
	Efavirenz, etravirine and nevirapine may <b>decrease</b> ketamine levels.	Monitor clinical effect and adjust dosage if needed.
Ketorolac	Additive renal toxicity with tenofovir	Monitor

## L

	ANTI-RETROVIRAL	RECOMMENDATION
Labetolol	Atazanavir may <b>increase</b> labetolol levels.	Co-administration should be undertaken with caution and clinical monitoring is recommended.
	Ritonavir, efavirenz, etravirine and nevirapine may decrease labetolol,	Monitor efficacy and titrate
	PR caution with PIs	Potential impact of PIs with other drugs that prolong the PR interval has not been evaluated.
Lansoprazole	Contra-indicated with atazanavir and rilpivirine see above.	
Levetiracetam	None reported.	No dose changes necessary
Levobupivacaine	PIs and cobicistat may <b>increase</b> levobupivacaine levels.	Consider a dose reduction and monitoring.
	Efavirenz, etravirine, nevirapine may decrease levels.	Titrate to response.
Lidocaine (systemic and local)	PIs and cobicistat will <b>increase</b> lidocaine levels.	Consider a dose reduction and monitoring.
	Efavirenz, etravirine and nevirapine may <b>decrease</b> lidocaine levels.	Monitor efficacy and titrate.

## M

	ANTI-RETROVIRAL	RECOMMENDATION
Magnesium sulphate	No interaction with IV formulation Chelation with INI if oral	Separate times
Metaraminol	None reported.	No dose changes necessary.
Midazolam (oral and parental)	<b>Oral route</b> contra-indicated with PIs, efavirenz and cobicistat. See above. <b>Parental route:</b> PIs efavirenz and cobicistat will <b>increase</b> midazolam levels approximately 4 fold. Etravirine and nevirapine potentially <b>decrease</b> midazolam levels.	Risk of respiratory depression and prolonged sedation. Use low dose with careful monitoring Titrate up dose and monitor clinical effect and withdrawal symptoms.
Mivacurium	None reported.	No dose changes necessary.
Morphine	PIs, cobicistat, efavirenz and etravirine may potentiate opioid effects in the CNS.	Titrate to analgesic effect and monitor for signs of opiate toxicity.

## N

	ANTI-RETROVIRAL	RECOMMENDATION
Naloxone	PIs can decrease naloxone concentrations	Monitor and increase dose of naloxone in case of incomplete opioid intoxication reversal
Neostigmine	None reported.	No dose changes necessary.
Noradrenaline	None reported.	No dose changes necessary.

## O

	ANTI-RETROVIRAL	RECOMMENDATION
Omeprazole	Contra-indicated with atazanavir and rilpivirine see above.	
Ondansetron	PIs and cobicistat may increase levels. QT caution with rilpivirine.	Consider alternative, risk of QT prolongation Monitor
Oxycodone	PIs and and cobicistat may <b>increase</b> oxycodone levels. Efavirenz, etravirine and nevirapine may <b>decrease</b> oxycodone level.	Consider a dose reduction of oxycodone to avoid opioid-related adverse effects. Monitor analgesic effect and titrate to pain response.
Oxytocin	QT caution with PIs and rilpivirine	No dose changes necessary. Monitor.

## P

	ANTI-RETROVIRAL	RECOMMENDATION
Pancuronium	None reported.	No dose changes necessary.
Paracetamol	None reported.	No dose changes necessary.
Pethidine	PIs, cobicistat, efavirenz, etravirine and nevirapine: unpredictable pethidine levels, increased levels neurotoxic metabolite.	Consider alternative.
Pregabalin	None reported.	No dose changes necessary.
Prilocaine	None reported.	No dose changes necessary.
Prochlorperazine	QT caution with PIs, cobicistat, rilpivirine	Monitor
Propofol	Ritonavir, efavirenz and nevirapine may decrease propofol levels.  QT caution with PIs and rilpivirine	Titrate to response.  Monitor.
Propranolol	PIs and cobicistat may increase propranolol levels.  PR interval caution with PIs	Dose cautiously, monitor for toxicity.  Monitor.

## R

	ANTI-RETROVIRAL	RECOMMENDATION
Remifentanyl	None reported.	No dose changes necessary.
Rocuronium	PIs, cobicistat and efavirenz may increase rocuronium levels.	Monitor clinical effect and reduce rocuronium dosage if needed.
Ropivacaine	PIs and cobicistat may increase levels.	Titrate with caution and monitor.

## S

	ANTI-RETROVIRAL	RECOMMENDATION
Sevoflurane	QT caution with PIs, cobicistat and rilpivirine.	Monitor ECG and any other concomitant medications which may prolong QT interval.
Sugammadex	None reported.	No dose changes necessary.
Suxamethonium	None reported.	No dose changes necessary.

## T

	ANTI-RETROVIRAL	RECOMMENDATION
Thiopentone	None reported.	No dose changes necessary.
Tirofiban	None reported.	No dose changes necessary.
Triamcinolone	Contra-indicated with PIs and cobicistat. See above.  Efavirenz, etravirine and nevirapine may decrease triamcinolone levels.	Monitor for possible diminished effect of steroid, and the dosage should be adjusted accordingly.

## V

	ANTI-RETROVIRAL	RECOMMENDATION
Vecuronium	None reported.	No dose changes necessary.