

## Peri-operative Surgery and Anaesthetic interactions with anti-retroviral agents

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

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

**Non-nucleoside reverse transcriptase inhibitors (NNRTI):-** efavirenz, etravirine, nevirapine, and rilpivirine.

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

**Cobicistat (contained in Evotaz, Genvoya®, Rezolsta® and Stribild®):** - pharmacokinetic enhancer of anti-retrovirals but no anti HIV activity.

**Please note there are no interactions documented with the anaesthetic agents with nucleoside reverse transcriptase inhibitors (NRTIs):-** abacavir, emtricitabine, lamivudine, tenofovir disoproxil fumarate, tenofovir alafenamide fumarate, and zidovudine. Also **integrase inhibitors (INI):-** dolutegravir (Triumeq®) and raltegravir.

## Contra-indicated interactions with anti-retroviral agents

	ANTI-RETROVIRAL	RECOMMENDATION
Alfentanil/ fentanyl	Saquinavir	Co-administration is contra-indicated: <b>AVOID.</b> (Contra-indicated with saquinavir: - potential life-threatening cardiac arrhythmias.)
Amiodarone	PIs, rilpivirine and elvitegravir/cobicistat and cobicistat.	Co-administration is contra-indicated: <b>AVOID.</b> (Contra-indicated: - potential life-threatening cardiac arrhythmias. Prolonged QTc interval has been seen with higher doses of rilpivirine. )
Lidocaine (systemic)	Darunavir and saquinavir	Co-administration is contra-indicated: <b>AVOID.</b> (Contra-indicated: - potential for life threatening cardiac arrhythmia.)
Midazolam (oral)	PIs, efavirenz, elvitegravir/cobicistat 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.
Midazolam (parenteral)	Efavirenz	Co-administration is contra-indicated: <b>AVOID.</b> (Contra-indicated: increased midazolam concentrations, the potential for serious and/or life-threatening events. Alternative: sublingual lorazepam.
Triamcinolone	PIs and elvitegravir/cobicistat 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
Alfentanil/ fentanyl	<p>Contra-indicated with saquinavir see above</p> <p>Atazanavir, darunavir, kaletra, elvitegravir/cobicistat and cobicistat will <b>increase</b> alfentanil/fentanyl levels.</p> <p>Efavirenz, etravirine and nevirapine will <b>decrease</b> alfentanil/fentanyl level</p>	<p>Consider reducing dose of alfentanil, and titrating up. There is a risk of prolonged or delayed respiratory depression.</p> <p>Monitor analgesic effect and titrate to pain response.</p>
Amiodarone	<p>Contra-indicated with PIs, rilpivirine, elvitegravir/cobicistat and cobicistat see above</p> <p>Efavirenz, etravirine and nevirapine</p>	<p>Co-administration may decrease amiodarone concentrations. Dose adjustment may be needed due to possible decrease in clinical effect.</p>
Atenolol	<p>PIs may potentially <b>increase</b> atenolol levels.</p>	<p>Potential impact of PIs with other drugs that prolong the PR interval has not been evaluated. Co-administration should be undertaken with caution and clinical monitoring is recommended.</p>
Atracurium	None	No dose changes necessary

### B

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

### D

	ANTI-RETROVIRAL	RECOMMENDATION
Desflurane	None	No dose changes necessary
Diamorphine	<p>PIs, elvitegravir/cobicistat and cobicistat may <b>decrease</b> diamorphine levels.</p> <p>Efavirenz may <b>increase</b> diamorphine levels.</p>	<p>Monitor analgesic effect and signs of opiate toxicity or withdrawal titrate to pain response. Due to potential increased levels of metabolite monitor signs of opiate toxicity.</p> <p>Consider reducing dose of diamorphine and monitor for signs of opiate toxicity.</p>
Diazepam	<p>Efavirenz and nevirapine will <b>decrease</b> diazepam levels.</p> <p>PIs and etravirine will <b>increase</b> diazepam levels.</p>	<p>Monitor clinical effect and withdrawal symptoms. An increase in diazepam dose maybe needed.</p> <p>Monitor closely; start with a lower than normal dose and titrate according to response.</p> <p>Use lorazepam, temazepam or oxazepam if excessive drowsiness.</p>

## E

	ANTI-RETROVIRAL	RECOMMENDATION
Etomidate	None	No dose changes necessary

## F

	ANTI-RETROVIRAL	RECOMMENDATION
Fentanyl	See Alfentanil	

## G

	ANTI-RETROVIRAL	RECOMMENDATION
Glycopyrronium	Possible reduced/delayed absorption of PIs.	No dose change necessary for short term use. Discuss with HIV team if co-administration is greater than 7 days.

## I

	ANTI-RETROVIRAL	RECOMMENDATION
Isoflurane	None	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.

## L

	ANTI-RETROVIRAL	RECOMMENDATION
Labetolol	PIs may potentially <b>increase</b> labetolol levels.	Potential impact of PIs with other drugs that prolong the PR interval has not been evaluated. Co-administration should be undertaken with caution and clinical monitoring is recommended.
Levobupivacaine	PIs may <b>increase</b> levobupivacaine levels.	Consider a dose reduction and monitoring.
Lidocaine (systemic and local)	Contra-indicated with darunavir and saquinavir see above  Atazanavir, kaletra, elvitegravir/cobicistat and cobicistat, will <b>increase</b> lidocaine levels.  Efavirenz, etravirine and nevirapine may <b>decrease</b> lidocaine levels	Consider a dose reduction and monitoring.  Dose adjustment may be needed due to possible decrease in clinical effect.

## M

	ANTI-RETROVIRAL	RECOMMENDATION
Midazolam (oral and parental)	Oral route contra-indicated with PIs, efavirenz, elvitegravir/cobicistat and cobicistat. see above  Etravirine and nevirapine and will <b>decrease</b> midazolam levels.	Titrate up dose and monitor clinical effect and withdrawal symptoms.

Mivacurium	None	No dose changes necessary
Morphine	PIs, elvitegravir/cobicistat and cobicistat may decrease morphine levels.  Efavirenz and etravirine could <b>increase</b> morphine levels	Monitor analgesic effect and signs of opiate toxicity or withdrawal titrate to pain response. Due to potential increased levels of metabolite monitor signs of opiate toxicity.  Consider reducing dose of morphine and monitor for signs of opiate toxicity.

## N

	ANTI-RETROVIRAL	RECOMMENDATION
Neostigmine	None	No dose changes necessary

## O

	ANTI-RETROVIRAL	RECOMMENDATION
Ondansetron	PIs, elvitegravir/cobicistat and cobicistat.	Consider alternative (metoclopramide) as can induce QT interval prolongation

## P

	ANTI-RETROVIRAL	RECOMMENDATION
Pancuronium	None	No dose changes necessary
Pethidine	PIs, elvitegravir/cobicistat and cobicistat will <b>increase</b> pethidine levels.  Efavirenz, etravirine and nevirapine will <b>increase</b> pethidine levels.	Consider alternative to pethidine due to risk of respiratory depression and toxicity. N.B Long term use of pethidine and atazanavir/ritonavir and darunavir/ritonavir is not recommended due to the increased concentration of normepethidine which may increase the risk of seizures.  Consider alternative to pethidine as increased risk of seizures due to increased levels of neurotoxic metabolite.
Propofol	PIs, efavirenz and nevirapine will <b>decrease</b> propofol levels.	Monitor clinical effect and dose adjust if needed.
Propranolol	PIs may potentially <b>increase</b> propranolol levels.  Elvitegravir/cobicistat and cobicistat may potentially <b>increase</b> propranolol levels.	Potential impact of PIs with other drugs that prolong the PR interval has not been evaluated. Co-administration should be undertaken with caution and clinical monitoring is recommended.  Clinical monitoring is recommended and a dose decrease of propranolol may be necessary

## R

	ANTI-RETROVIRAL	RECOMMENDATION
Remifentanyl	None	No dose changes necessary
Rocuronium	PIs and efavirenz may <b>increase</b> rocuronium levels	Monitor clinical effect and reduce rocuronium dosage if needed.

## **S**

	<b>ANTI-RETROVIRAL</b>	<b>RECOMMENDATION</b>
Sevoflurane	PIs and rilpivirine may also prolong QT interval.	Monitor ECG and any other concomitant medications which may prolong QT interval.
Sugammadex	None	No dose changes necessary
Suxamethonium	None	No dose changes necessary

## **I**

	<b>ANTI-RETROVIRAL</b>	<b>RECOMMENDATION</b>
Thiopentone	None	No dose changes necessary
Triamcinolone	Contra-indicated with PIs and elvitegravir/cobicistat 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**

	<b>ANTI-RETROVIRAL</b>	<b>RECOMMENDATION</b>
Vecuronium	None	No dose changes necessary