A MANAGEMENT TOOL FOR HIV DRUG-DRUG INTERACTIONS

Canadian HIV and Viral Hepatitis Pharmacists Network

2019

INTRODUCTION

Advances in antiretroviral therapy have turned HIV into a chronic, manageable disease. Patients often require treatment for co-morbid conditions as well as HIV, and consequently, pharmacokinetic interactions between antiretrovirals (ARVs) and other drug classes are an increasing concern. This tool has been updated and expanded to reflect the aging demographics of people living with HIV in Canada. It is meant to serve as a quick reference to assist clinicians in the clinical management of these interactions and is intended for use by and with experienced physicians, nurses and pharmacists.

Disclaimer
The information within is not intended to replace sound professional judgment in individual situations, and should be used in conjunction with other reliable sources of information. Due to the rapidly changing nature of information about HIV treatment and therapies, users are advised to recheck the information contained herein with the original source before applying it to patient care. Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.

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ACID SUPPRESSING DRUGS:
ANTACIDS, H2-RECEPTOR ANTAGONISTS, PROTON PUMP INHIBITORS

	INSTIs	NNRTIs		PIs	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)* • RALTEGRAVIR *(Isentress)*	• RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)*	Boosted with ritonavir (Norvir) or cobicistat • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
ANTACIDS CONTAINING MAGNESIUM, ALUMINUM OR CALCIUM					
• Antacids *(Tums, Maalox, Mylanta, Gaviscon)*	↓ INSTI Raltegravir 600 mg HD tablets Raltegravir 400 mg OK with calcium	↓ rilpivirine		↓ atazanavir	
H2 RECEPTOR ANTAGONISTS					
• Famotidine *(Pepcid)*, nizatidine *(Axid)*, ranitidine *(Zantac)*		↓ rilpivirine		↓ atazanavir	
PROTON PUMP INHIBITORS (PPIs)					
• Esomeprazole *(Nexium)*, lansoprazole *(Prevacid)*, omeprazole *(Losec)*, pantoprazole *(Pantoloc)*, rabeprazole *(Pariet)*		↓ rilpivirine		↓ atazanavir with low dose PPI ↓↓ atazanavir with high dose PPI	

Mechanism of Drug Interactions, Management and Monitoring

Acid Suppressing Drugs	Mechanism of Interaction	Management
Antacids	**Integrase Inhibitors:** chelation leading to poor absorption	**Bictegravir:** Take bictegravir 2 hours before or after medications or supplements containing polyvalent cations. If given with food, may be taken at same time as calcium and iron supplements. **Dolutegravir**: Administer 2 hours before or 6 hours after medications containing polyvalent cations (Mg, Al, Fe or Ca) including antacids or laxatives, sucralfate, oral iron or calcium supplements and buffered medications. If given with food, may be taken at same time as calcium and iron supplements. **Elvitegravir:** Separate by at least 2 hours from antacids containing Al, Mg or Ca. **Raltegravir:** Do not coadminister with Mg or Al containing antacids. Calcium-containing antacids may be coadministered with raltegravir 400 mg tablets, but not 600 mg HD tablets.
	Atazanavir: increase in gastric pH leads to poor absorption	**Atazanavir:** administer 2 hours before or 1 hour after antacids.
	Rilpivirine: increase in gastric pH leads to poor absorption	**Rilpivirine:** Administer antacids at least 2 hours before or 4 hours after rilpivirine.
H_2RAs	**Atazanavir:** increase in gastric pH leads to poor absorption	**Atazanavir:** Give simultaneously with or 10 hours after H_2RA. If also on tenofovir-containing regimen increase to atazanavir 400 mg and ritonavir 100 mg in experienced patients.
	Rilpivirine: increase in gastric pH leads to poor absorption	**Rilpivirine:** Give rilpivirine 4 hours before or 12 hours after H_2RA.
Proton Pump Inhibitors	**Atazanavir, rilpivirine:** increase in gastric pH leads to poor absorption	**Atazanavir:** Coadministration with omeprazole 40 mg (or equivalent) is contraindicated. If unavoidable, increase atazanavir dose to 400 mg with 100 mg of ritonavir and do not exceed doses of omeprazole 20mg or comparable. **Rilpivirine:** contraindicated with PPIs.

Legend:		No dose adjustment required.
		Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
		Contraindicated/avoid combination.

ANALGESICS
OPIOIDS, OPIOID-SUBSTITUTION, NON-NARCOTICS

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)*	•TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
OPIOIDS							
• Codeine		Potential ↓ analgesic effect		Potential ↓ analgesic effect	Potential ↓ analgesic effect		
• Hydrocodone *(Hycodan)* • Oxycodone *(Percocet)*		↑ oxycodone ↑ hydrocodone		↓ oxycodone ↓ hydrocodone	↑ oxycodone ↑ hydrocodone		
• Fentanyl *(Duragesic)*		↑ fentanyl		↓ fentanyl	↑ fentanyl		
• Morphine • Hydromorphone *(Dilaudid)*							
• Tramadol *(Tramacet)*		↑ tramadol		↓ tramadol	↑ tramadol		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)*	•TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
PARTIAL AGONIST/ANTAGONIST							
• Buprenorphine/ naloxone *(Suboxone)*				Potential for ↓ buprenorphine	Potential for ↑ buprenorphine		
• Methadone *(Metadol, Methadose)*				Potential for ↓ methadone, withdrawal (EFV, NVP)	Potential for ↑/↓ methadone with PIs (may not be clinically significant)		
• Naloxone *(Narcan)*					PI/Ritonavir: potential ↓ naloxone PI/cobicistat		
NON-NARCOTIC ANALGESICS							
• Acetaminophen *(Tylenol)*							
• NSAIDS: ASA, celecoxib, diclofenac, ibuprofen, naproxen		*caution: ↑ risk renal toxicity with TDF-containing formulations	*caution: ↑ risk renal toxicity with TDF-containing formulations	*caution: ↑ risk renal toxicity with TDF-containing formulations		Potential renal toxicity with high dose/prolonged NSAID use	

Mechanism of Drug Interactions, Management and Monitoring

Analgesic	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Buprenorphine/naloxone	CYP3A4, UGT	PIs, cobicistat may increase buprenorphine Enzyme inducing NNRTIs (efavirenz, etravirine, nevirapine) may decrase buprenorphine	Possible increases in buprenorphine effect. Possible decreases in buprenorphine effect.	Monitor for increase in opioid side effects. Monitor for symptoms of opiate withdrawal.
Codeine	Conversion of codeine to morphine via CYP2D6 Inactivated via UGT and CYP3A4	Ritonavir, cobicistat may inhibit conversion to morphine Enzyme-inducing NNRTIs efavirenz, etravirine and nevirapine	Possible decrease in analgesic effect.	Monitor for analgesia.
Fentanyl	CYP3A4 inhibition CYP3A4 induction	Cobicistat and Protease Inhibitors Enzyme-inducing NNRTIs efavirenz, etravirine and nevirapine	Possible significant increases in fentanyl levels Possible decrease in fentanyl levels	*The Duragesic® (fentanyl) monograph states: “The concomitant use of CYP3A4 inhibitors and DURAGESIC MAT is not recommended, unless the patient is closely monitored.”
Methadone	CYP3A4 and 2D6 metabolism induction	Efavirenz and nevirapine	Possible decrease in methadone levels potentially leading to withdrawal or loss of pain control	Monitor for symptoms of opiate withdrawal or increase in pain and increase methadone dose by 10 mg increments
Morphine & hydromorphone	Mostly UGT metabolized; renal elimination	None	None	None
Hydrocodone, oxycodone, tramadol	CYP2D6 and 3A4 metabolism inhibition CYP3A4 Induction	Cobicistat and Protease Inhibitors	Possible increases in narcotic levels	Monitor for increase opioid side effects; symptoms of overdose

Analgesic	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
		Enzyme-inducing NNRTIs efavirenz, etravirine and nevirapine	Possible decrease in narcotic levels	Monitor pain symptoms and adjust narcotic doses incrementally as needed.
Naloxone	UGT2B7 Induction (ritonavir)	Ritonavir-boosted PIs	Possible decrease in naloxone levels	May need to increase dose in reversal of narcotic overdose.
NSAIDS	Combining nephrotoxic agents	Tenofovir DF-containing regimens	Consider alternate pain control Consider alternate NRTI (TAF, abacavir)	Monitor Renal function Assess OTC NSAID use

Legend:		No dose adjustment required.
		Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
		Contraindicated/avoid combination.

ANTICONVULSANTS

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
• Carbamazepine *(Tegretol)*	Potential for ↓ bictegravir ↓ dolutegravir; use 50 mg BID Raltegravir: use 400 mg BID, not 1200 mg daily	Potential for ↓ INSTI	↓ NNRTI	↓ NNRTI	Cobicistat-boosted PIs: ↓ PI, ↑ carbamazepine Ritonavir-boosted PIs: ↑ carbamazepine, potential ↓ PI	↓ TAF	
• Clobazam *(Frisium)*		Potential for ↑ clobazam		Potential for ↓ clobazam	Potential for ↑ clobazam		
• Gabapentin *(Neurontin)*, levetiracetam *(Keppra)*, pregabalin *(Lyrica)*, topiramate *(Topamax)*							

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
• Lamotrigine *(Lamictal)*				Potential for ↓ lamotrigine	Cobicistat-boosted PIs: may be used without dose adjustment Ritonavir-boosted PIs: potential for ↓ lamotrigine		
• Phenytoin *(Dilantin)*, phenobarbital	Potential for ↓ bictegravir ↓ dolutegravir; use 50 mg BID Raltegravir: use 400 mg BID, not 1200 mg daily	Potential for ↓ INSTI	Potential for ↓ NNRTI	Potential for ↓ NNRTI Nevirapine: ↓ NNRTI and/or anticonvulsant	↓ cobicistat-boosted PIs ↓ ritonavir-boosted PIs; unpredictable ↑ or ↓ anticonvulsant	Potential for ↓ TAF	
• Valproate *(Epival, Depakene)*	Potential ↓ total dolutegravir; not likely clinically significant				Cobicistat-boosted PIs: may be used without dose adjustment Ritonavir-boosted PIs: potential for ↓ valproate		

Mechanism of Drug Interactions, Management and Monitoring

Anticonvulsant	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Gabapentin, Pregabalin, Topiramate, Levetiracetam	Primarily excreted unchanged in urine	None	None	None
Carbamazepine	CYP3A4 substrate and inducer of CYP3A, 2C19, UGT. Potential for decreased antiretrovirals or increased carbamazepine.	Ritonavir and cobicistat-boosted protease inhibitors or any products containing bictegravir, dolutegravir, elvitegravir, raltegravir, doravirine rilpivirine, tenofovir alafenamide	Avoid with cobicistat-boosted PIs, NNRTIs, bictegravir and elvitegravir/cobicistat. May need to reduce carbamazepine dose with ritonavir-boosted PIs. Increase dolutegravir to 50 mg BID; use raltegravir with caution.	Antiretroviral efficacy. Carbamazepine concentrations and toxicity (somnolence, dizziness).
Phenobarbital, Phenytoin	Substrate of 2C9, 2C19 and potent inducers of CYP3A4, 2C9/19, UGT. Potential for decreased antiretrovirals or decreased anticonvulsants.	Ritonavir and cobicistat-boosted protease inhibitors or any products containing bictegravir, dolutegravir, elvitegravir, raltegravir, doravirine rilpivirine, efavirenz, tenofovir alafenamide	Avoid these anticonvulsants if others are available and efficacious. Increase dolutegravir to 50 mg BID; use raltegravir 400mg BID with caution.	Antiretroviral efficacy. Monitor for CBZ toxicity, loss of seizure control. Monitor TDM if possible with DTG and RAL or at least close surveillance of antiretroviral efficacy
Lamotrigine, Valproate	Primarily cleared via UGT Lamotrigine: mild UGT inducer Valproate: Inhibitor of UGT, CYP2C9/19	Potential for decreased anticonvulsants due to UGT induction by ritonavir-boosted PIs and efavirenz. Reductions in dolutegravir concentrations have been observed with concomitant valproic acid. Mechanism presumed to be displacement of protein binding; free dolutegravir concentrations unchanged and thus this interaction is not likely not clinically significant.	May have to increase dose of anticonvulsant if ARV regimen cannot be changed and/or if there is no other suitable anticonvulsant.	Monitor for loss of seizure control Monitor for antiretroviral efficacy.

Anticonvulsant	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Clobazam	CYP3A4 substrate. Potential for increased clobazam with boosted regimens and decreased concentrations with NNRTIs	Ritonavir and cobicistat-boosted protease inhibitors or elvitegravir, Enzyme-inducing NNRTIs (efavirenz, etravirine, nevirapine)	May increase levels of clobazam, increasing potential for toxicity May decrease levels of clobazam	Monitor for signs of toxicity and reduce dose if necessary Monitor for loss of seizure control

Legend:

No dose adjustment required.

Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.

Contraindicated/avoid combination.

ANTI-INFECTIVES:
AZOLE ANTIFUNGALS AND MACROLIDES

	INSTIs		NNRTIs			PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)*	• ETRAVIRINE *(Intelence)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
AZOLE ANTIFUNGALS						
• Fluconazole *(Diflucan)*		Potential for ↑ azole		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Efavirenz Potential for ↑ nevirapine; monitor for toxicity.	
• Itraconazole *(Sporanox)*		Potential for ↑ azole. Use maximum 200 mg itraconazole per day.		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Potential for ↓ azole	Potential for ↑ azole. Use maximum 200 mg itraconazole per day.
• Ketoconazole *(Nizoral)*		Potential for ↑ azole. Use maximum 200 mg ketoconazole per day.		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Potential for ↓ azole	Potential for ↑ azole. Use maximum 200 mg ketoconazole per day.
• Posaconazole *(Posanol)*		Potential for ↑ azole		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Efavirenz: potential for ↓ azole Potential for ↑ nevirapine; monitor for toxicity.	Potential for ↑ PI concentrations. Monitor for toxicity.

	INSTIs		NNRTIs			PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)*	• ETRAVIRINE *(Intelence)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
• Voriconazole *(Vfend)*		Potential for ↑ azole		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Efavirenz: potential for ↓ voriconazole and ↑ efavirenz. Potential for ↓ azole	Potential for ↑/↓ voriconazole concentrations.
MACROLIDES						
• Azithromycin *(Zithromax)*						
• Clarithromycin *(Biaxin)*		↑ clarithromycin. Adjust dose with renal impairment.		Etravirine: Potential for ↓ clarithromycin and ↑ 14-OH metabolite and increased risk of rash.	Potential for ↑ rilpivirine, potential QT prolonga-tion	Potential for ↓ clarithromycin and ↑ 14-OH metabolite and increased risk of rash.	↑ clarithromycin. Adjust dose with renal impairment.
• Erythromycin							

Mechanism of Drug Interactions, Management and Monitoring

Azole Agent	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Fluconazole	Inhibition of CYP3A4	Doravirine, rilpivirine, etravirine, nevirapine, elvitegravir/cobicistat	Use standard doses of both drugs.	Antiretroviral toxicity
Itraconazole, ketoconazole, posaconazole	Inhibition of CYP3A4 (antiretrovirals)	Ritonavir and cobicistat-boosted PIs, elvitegravir/cobicistat	Use maximum 200 mg ketoconazole or itraconazole daily	Azole toxicity
	Substrate of CYP3A4, induction by most NNRTIs	Efavirenz, etravirine, nevirapine	Avoid efavirenz and nevirapine if possible. Use etravirine with caution and consider increasing azole dose if necessary.	Azole efficacy
Voriconazole	Induction of CYP2C19 by some antiretrovirals; voriconazole also inhibits CYP3A4.	Ritonavir-boosted PIs, efavirenz	Ritonavir-boosted PIs: avoid coadministration. Efavirenz: increase voriconazole to 400 mg q12hours and decrease efavirenz to 300 mg daily if therapy lasts more than few days.	Voriconazole efficacy.
	Inhibition of CYP2C19	Etravirine		Etravirine toxicity
	Inhibition of CYP3A4 (antiretrovirals and voriconazole)	Cobicistat-boosted PIs and elvitegravir/cobicistat		Voriconazole toxicity
Azithromycin	Substrate of CYP3A4 (minor)	Ritonavir- and cobicistat-boosted PIs and elvitegravir/cobicistat	Use standard doses of both drugs	Monitor for QT interval prolongation in patients with other pre-existing risk factors

Azole Agent	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Clarithromycin	Inhibition of CYP3A4 (ritonavir, cobicistat) Protease inhibitors inhibit the metabolism of clarithromycin via CYP3A4 and increase concentrations of clarithromycin. This may lead to a decrease in CLA-14 OH metabolite, reducing antibacterial activity versus gram-negative organisms.	Elvitegravir/cobicistat and boosted protease inhibitors	Atazanavir: reduce clarithromycin dose by 50% to avoid QTc prolongation and consider alternate agent for non-MAC infections. Elvitegravir/cobicistat: Reduce dose of clarithromycin by 50% if CrCl is between 50-60mL/min. Do not administer clarithromycin if CrCl <50mL/min. Darunavir and lopinavir: reduce clarithromycin dose by 50% if CrCl 30-60mL/min; by 75% if CrCl <30mL/min.	Monitor patients for signs of clarithromycin toxicity including QT interval prolongation
	Induction of CYP3A4 resulting in decreased clarithromycin and increased CLA-14 OH metabolite, which has reduced activity against Mycobacterium avium complex (MAC)	Efavirenz, etravirine, nevirapine	May wish to consider switching to azithromycin, particularly if treating MAC infection or consider non-interaction NNRTI such as doravirine.	Clarithromycin efficacy and potential rash
Clarithromycin, erythromycin	Inhibition of CYP3A4 (clarithromycin, erythromycin)	Rilpivirine	Use with caution.	Monitor for QT interval prolongation in patients with other pre-existing risk factors

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

ANTI-INFECTIVES:
MEDICATIONS FOR TUBERCULOSIS

	INSTIs		NNRTIs		PIs	RTI	
	• DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• BICTEGRAVIR *(Biktarvy)* • ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
RIFAMYCINS							
• Rifabutin *(Mycobutin)*		Potential for ↓ INSTI and ↑ rifabutin (with elvitegravir/c)	Potential for ↓ doravirine. Use 100 mg BID. Potential for ↓ rilivirine. Use 50 mg daily.	Efavirenz: potential ↓ rifabutin. Use rifabutin 450-600 mg daily or 600 mg three times weekly. Etravirine, nevirapine	Potential for ↑ rifabutin. Use rifabutin 150 mg daily.	Potential for ↓ TAF	
• Rifampin *(Rofact, Rifadin)*	Potential for ↓ dolutegravir. Use 50 mg BID. Potential for ↓ raltegravir. Use 800 mg BID.	Potential for ↓ INSTI	Potential for ↓ NNRTI	Efavirenz Etravirine, nevirapine	Potential for ↓ PI	Potential for ↓ TAF	
• Rifapentine *(Priftin)*	Raltegravir, dolutegravir OK with	Potential for ↓ INSTI	Potential for ↓ NNRTI	Efavirenz ok with daily or once-weekly rifapentine	Potential for ↓ PI	Potential for ↓ TAF	

	INSTIs		NNRTIs		PIs	RTI	
	• DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• BICTEGRAVIR *(Biktarvy)* • ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
	once weekly rifapentine.			Potential for ↓ etravirine, nevirapine			

OTHER ANTIMYCOBACTERIALS

• Ethambutol, Isoniazid, Pyrazinamide							

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Drug	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Rifampin	Rifampin is a potent CYP3A4 and P-gp inducer.	Integrase inhibitors: bictegravir, dolutegravir, elvitegravir, raltegravir	Increase dolutegravir to 50 mg BID and consider alternate therapy if patient is integrase inhibitor experienced. Increase raltegravir to 800 mg BID and use with caution in patients initiating ARV therapy with high initial viral loads due to risk of development of resistance. **Do not coadminister with bictegravir or elvitegravir/cobicistat.**	Watch for virologic breakthrough and efficacy of antiretroviral
		Protease inhibitors (atazanavir, darunavir, lopinavir)	**Do not coadminister** Increasing dosage of LPV/r to 800/200 BID overcomes induction effect of rifampin but may result in intolerable adverse effects	
		NNRTI: efavirenz	Product monograph suggests increasing to 800 mg efavirenz daily while on rifampin in patients >50 kg. However current guidelines suggest that standard 600 mg dose may be used with close monitoring of efavirenz levels and/or monitoring of virologic response.	Monitor for virologic response and efavirenz drug levels with TDM if available
		NNRTIs: doravirine, rilpivirine, efavirenz, etravirine, nevirapine NRTI: TAF	**Do not coadminister** due to failures of antiretroviral therapy.	

Drug	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Rifabutin	Rifabutin is a substrate and moderate inducer of CYP3A4 and P-gp	Integrase inhibitors: bictegravir, elvitegravir/cobicistat	**Avoid combination. Consider alternate integrase inhibitor if possible.**	
	Induction of CYP3A4 (rifabutin) and inhibition of CYP3A4 (protease inhibitors)	All protease inhibitors	When administering rifabutin with a protease inhibitor reduce dose to 150 mg QD or 300 mg 3x/week	Rifabutin toxicity
	Induction of CYP3A4 (rifabutin and NNRTIs)	NNRTIs: doravirine, rilpivirine, efavirenz	Increase dose of doravirine to 100 mg BID Increase dose of rilpivirine to 50 mg QD (regular dose 25 mg) Increase rifabutin to 450-600 mg QD or 600 mg 3x/week when given with efavirenz Nevirapine or etravirine may be used without dose adjustment	Virologic response to antiretrovirals and antimycobacterial effect of rifabutin.
	Induction of P-gp	NRTI: tenofovir alafenamide	Do not coadminister. Consider using tenofovir disproxil instead if possible	
Rifapentine	Rifapentine is a potent CYP3A4 and P-gp inducer	Integrase inhibitors: bictegravir, elvitegravir	Do not coadminister. Consider using raltegravir or possibly dolutegravir.	
	Induction of CYP3A4	All protease inhibitors	Do not coadminister.	
	Induction of CYP3A4	NNRTIs: doravirine, etravirine, nevirapine, rilpivirine	Do not coadminister. Consider using efavirenz if possible.	
	Induction of P-gp	NRTI: tenofovir alafenamide	Do not coadminister. Consider using tenofovir disproxil instead if possible	

HEPATITIS C AGENTS

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)*	•TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
DIRECT ACTING ANTIVIRALS (DAAs)							
• Glecaprevir + pibrentasvir *(Maviret)*				Potential for ↓ glecaprevir, pibrentasvir	Potential for ↑ glecaprevir, pibrentasvir		
• Ledipasvir + sofosbuvir *(Harvoni)*						Potential for ↑ tenofovir	
• Velpatasvir + sofosbuvir *(Epclusa)*				Potential for ↓ velpatasvir		Potential for ↑ tenofovir	
• Velpatasvir + voxilaprevir + sofosbuvir *(Vosevi)*				Potential for ↓ velpatasvir, voxilaprevir	darunavir Atazanavir, lopinavir: potential for ↑ voxilaprevir	Potential for ↑ tenofovir	
• Elbasvir + grazoprevir *(Zepatier)*		Potential for ↑ elbasvir, grazoprevir		Potential for ↓ elbasvir, grazoprevir	Potential for ↑ elbasvir, grazoprevir		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)*	•TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
Ribavirin							

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Hepatitis C Agent	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Glecaprevir/ Pibrentasvir (Maviret®)	Glecaprevir and pibrentasvir inhibit P-gp, BCRP, OATP1B1/3 and are substrates of P-gp and/or BCRP.	Boosted protease inhibitors. Efavirenz can reduce DAA concentrations.	Select INSTI or non-inducing NNRTI (e.g., doravirine, rilpivirine).	
Ledipasvir/ Sofosbuvir (Harvoni®)	Ledipasvir is a mild inhibitor of PgP, BCRP, OATP1B1 and OATP1B2.	Tenofovir DF containing products (including single tablet regimens with darunavir, elvitegravir, rilpivirine and doravirine). Increased tenofovir levels can potentially lead to renal toxicity.	If pre-existing renal compromise, consider switching to non-tenofovir backbone or regimen. Otherwise, monitor renal function closely.	Monitor renal function when used with tenofovir: eGFR, serum creatinine and phosphate; urine creatinine and phosphate if assessing tubular damage.
Velpatasvir/Sofosbuvir (Epclusa®)	Velpatasvir is a substrate of CYP3A4, 2C8, 2B6, OATP1B1/3, Pgp, BCRP and inhibits Pgp, BCRP, OATP1B1/3	Efavirenz can reduce DAA concentrations.	Select non-inducing NNRTI (e.g., doravirine, rilpivirine) or another drug class.	
		Tenofovir DF containing products (including single tablet regimens with darunavir, elvitegravir, rilpivirine and doravirine). Increased tenofovir levels can potentially lead to renal toxicity.	If pre-existing renal compromise, consider switching to non-tenofovir backbone or regimen. Otherwise, monitor renal function closely.	Monitor renal function when used with tenofovir: eGFR, serum creatinine and phosphate; urine creatinine and phosphate if assessing tubular damage.

Hepatitis C Agent	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Velpatasvir/Voxilaprevir/ Sofosbuvir (Vosevi®)	Voxilaprevir is a substrate of Pgp, BCPR, OAT1B1/3 as well as CYP3A4. Voxilaprevir inhibits Pgp, BCRP, OATP1B1/3 and OATP2B1.	Atazanavir, lopinavir: potential for increase in voxilaprevir.	Consider using darunavir or an alternate non-interacting antiretroviral class	
		Efavirenz can reduce DAA concentrations.	Select non-inducing NNRTI (e.g., doravirine, rilpivirine) or another drug class.	
		Tenofovir DF containing products (including single tablet regimens with darunavir, elvitegravir, rilpivirine and doravirine). Increased tenofovir levels can potentially lead to renal toxicity.	If pre-existing renal compromise, consider switching to non-tenofovir backbone or regimen. Otherwise, monitor renal function closely.	Monitor renal function when used with tenofovir: eGFR, serum creatinine and phosphate; urine creatinine and phosphate if assessing tubular damage.
Elbasvir/Grazoprevir (Zepatier®)	Elbasvir/grazoprevir are substrates of CYP3A4, Pgp and OATP	Ritonavir- or cobicistat-boosted regimens may increase elbasvir/grazoprevir. Efavirenz may decrease elbasvir/grazoprevir.	Select unboosted integrase inhibitor, doravirine or rilpivirine.	

CARDIOVASCULAR DRUGS:
ANTIHYPERTENSIVES AND DIGOXIN

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
ACEI					
• Benazepril, enalapril, lisinopril, perindopril, ramipril, etc.					
ARBs					
• Eprosartan, olmesartan, telmisartan, valsartan					
• Losartan, candesartan, irbesartan		Potential for ↑/↓ ARB		Potential for ↑/↓ ARB	Potential for ↑/↓ ARB
BETA-BLOCKERS					
• Atenolol, nadolol					

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
• Acebutolol, bisoprolol, carvedilol, metoprolol, propranolol		Potential for ↑ beta-blocker		Potential for ↓ beta-blocker	Potential for ↑ beta-blocker
CALCIUM CHANNEL BLOCKERS					
• Amlodipine, diltiazem, felodipine, nifedipine, verapamil		Potential for ↑ CCB. Consider 50% dose ↓ or start with lowest dose possible		Potential for ↓ CCB	Potential for ↑ CCB. Consider 50% dose ↓ or start with lowest dose possible
DIURETICS					
• Amiloride, hydrochloro-thiazide, furosemide, spironolactone, triamterene					
• Indapamide		Potential for ↑ indapamide		Potential for ↓ indapamide	Potential for ↑ indapamide
DIGOXIN		Potential for ↑ digoxin		Potential for ↑ digoxin (etravirine)	Potential for ↑ digoxin

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
ACEI	Renally cleared.	No significant interactions predicted.	Use standard drug doses.	
ARBs	Conversion via 2C9 to active metabolite (losartan), Substrate of 2C9 (candesartan, irbesartan)	Elvitegravir (induction), efavirenz, etravirine (inhibition)	Adjust losartan, candesartan, irbesartan dose according to response/toxicity. Other ARBs may be used without dose adjustment.	ARB efficacy and toxicity
Beta-blockers	Mixed CYP substrates (propranolol, acebutolol, bisoprolol, labetalol, metoprolol, pindolol)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir (inhibition); efavirenz, etravirine, nevirapine (induction).	Adjust beta-blocker dose according to response/toxicity. Other beta-blockers (atenolol, nadolol) may be used without dose adjustment.	Beta-blocker toxicity: heart rate, blood pressure, shortness of breath
Calcium channel blockers	Inhibition of CYP3A4	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Consider 50% dose reduction in CCB	CCB toxicity: heart rate, blood pressure, shortness of breath, dizziness.
	Induction of CYP3A4	Efavirenz, etravirine, nevirapine	Adjust CCB dose according to efficacy/toxicity.	CCB efficacy.
Diuretics	Mixed CYP substrates (indapamide)	Ritonavir and cobicistat-boosted protease inhibitors, elvitegravir, efavirenz, etravirine and nevirapine.	Adjust indapamide dose according to response/toxicity. Other diuretics may be used without dose adjustment.	Indapamide toxicity: dizziness, headache, hyperglycemia, hypokalemia
Digoxin	Inhibition of P-glycoprotein	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir, etravirine	Adjust digoxin dose according to response/toxicity	Digoxin concentrations, toxicity (arrhythmias, ventricular tachycardia, bradycardia, AV block, anorexia, nausea, blurred/yellow vision, headache)

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

CARDIOVASCULAR DRUGS:
ANTIPLATELETS AND ANTICOAGULANTS

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Dovato, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)*	•TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
ANTICOAGULANTS							
• Apixaban *(Eliquis)*		Potential for ↑ apixaban and toxicity		Potential for ↓ apixaban	Potential for ↑ apixaban and toxicity		
• Dabigatran *(Pradaxa)*		Potential for ↑ dabigatran and toxicity			PI/ritonavir: Potential for ↑ dabigatran PI/cobicistat: Potential for ↑ dabigatran and toxicity		
• Edoxaban *(Lixiana)*		Potential for ↑ edoxaban and toxicity			Potential for ↑ edoxiban and toxicity		
• Rivaroxaban *(Xarelto)*		Potential for ↑ rivaroxaban and toxicity		Potential for ↓ rivaroxaban	Potential for ↑ rivaroxaban and toxicity		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Dovato, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	•TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)*	•TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
• Warfarin *(Coumadin)*		Potential for ↓ warfarin		Potential for ↓ warfarin (nevirapine) or ↑ warfarin (efavirenz, etravirine)	Potential for ↓ warfarin (ritonavir) or ↑ warfarin (cobicistat)		
ANTIPLATELETS							
• ASA						Potential for renal toxicity with high dose or prolonged ASA use	
• Clopidogrel *(Plavix)*		Potential for ↓ active metabolite of clopidogrel		Potential for ↓ active metabolite of clopidogrel (efavirenz, etravirine)	Potential for ↓ active metabolite of clopidogrel		
• Prasugrel *(Effient)*							
• Ticagrelor *(Brilinta)*		Potential for ↑ ticagrelor and toxicity		Potential for ↓ ticagrelor and toxicity	Potential for ↑ ticagrelor and toxicity		

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Antiplatelets	Inhibition of CYP3A4, P-gp (ticagrelor)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Contraindicated. Prasugrel may be used.	Ticagrelor toxicity: dyspnea, headache, epistaxis, chest pain, bleeding events
	Induction of CYP3A4, P-gp (ticagrelor)	Efavirenz, etravirine, nevirapine	Avoid coadministration. Prasugrel may be used.	Ticagrelor efficacy
	Inhibition of 2C19 (clopidogrel)	Etravirine, efavirenz	Use with caution. May wish to consider alternatives to clopidogrel, such as prasugrel.	Antiplatelet activity
	Inhibition of 3A4 (activation of prodrug of clopidogrel)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir.	Use with caution. May wish to consider alternatives to clopidogrel, such as prasugrel.	Antiplatelet activity
	Combining nephrotoxic agents (ASA)	Tenofovir disoproxil (TDF) containing regimens	Avoid high-dose or prolonged ASA use if possible. Consider alternate HIV agent, such as abacavir or tenofovir alafenamide TAF.	Monitor renal function. Assess OTC NSAID use.
Direct acting oral anticoagulants (DOACs)	Inhibition of CYP3A4, P-gp (rivaroxaban, apixaban)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir.	Apixaban and rivaroxaban are contraindicated.	Anticoagulant toxicity.
	Induction of CYP3A4, P-gp (rivaroxaban, apixaban)	Enzyme-inducing NNRTIs (efavirenz, etravirine, nevirapine)	Avoid use. Consider alternative anticoagulant such as warfarin.	Anticoagulant efficacy.
	Inhibition of P-gp (dabigatran,edoxaban)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Dabigatran and edoxaban monograph advises caution with P-gp inhibitors. Preliminary pharmacokinetic data suggest that a clinically significant interaction may occur more so with cobicistat due to intestinal PgP inhibition.	Anticoagulant toxicity
Warfarin	Induction of CYP2C9	Ritonavir boosted regimens, nevirapine, elvitegravir/cobicistat	Increase warfarin dose as needed to maintain therapeutic INR.	Anticoagulant efficacy
	Inhibition of CYP2C9	Efavirenz, etravirine	Decrease warfarin dose as needed to maintain therapeutic INR.	Warfarin toxicity: bleeding, dizziness, headache,shortness of breath, hypotension

Legend:

No dose adjustment required.

Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.

Contraindicated/avoid combination.

CARDIOVASCULAR DRUGS:
STATINS AND LIPID LOWERING AGENTS

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca, Dovato)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
STATINS					
• Atorvastatin *(Lipitor)*		Potential for ↑ statin		Potential for ↓ statin	Potential for ↑ statin. Use lowest statin dose possible (maximum 20 mg atorvastatin daily).
• Rosuvastatin *(Crestor)*		Potential for ↑ statin			Potential for ↑ statin. Use lowest statin dose possible (maximum 10 mg rosuvastatin daily).
• Pitavastatin *(Livalo)*					
• Pravastatin *(Pravachol)*		Potential for ↑ statin			Potential for ↑ statin
• Lovastatin *(Mevacor)*, simvastatin *(Zocor)*		Potential for ↑ statin and toxicity		Potential for ↓ statin	Potential for ↑ statin and toxicity

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
FIBRATES					
• Fenofibrate, bezafibrate, gemfibrozil					
CHOLESTEROL ABSORPTION INHIBITOR					
• Ezetimibe *(Ezetrol)*					
GASTROINTESTINAL LIPASE INHIBITOR					
• Orlistat *(Xenical)*	Potential for ↓ ARV absorption				
BILE ACID SEQUESTRANTS					
• Cholestyramine *(Olestyr)*, colestipol *(Colestid)*	Potential for ↓ ARV absorption				

Mechanism of Drug Interactions, Management and Monitoring

	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Hmg-Coa Reductase Inhibitors (Statins)				
Lovastatin, simvastatin	Inhibition of CYP3A4	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Contraindicated. Use alternate statin.	Statin toxicity: myalgia, rhabdomyolysis
Atorvastatin, rosuvastatin, pravastatin	Inhibition of CYP3A4, OATP1B1, BCRP	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Use lowest statin dose possible and titrate to effect	Statin toxicity: myalgia, rhabdomyolysis
Pitavastatin	Primarily cleared via UGT, OATP1B1	None	Most ARVs may be used	Statin toxicity: myalgia, rhabdomyolysis
Orlistat	Reduced absorption of ARVs by decreasing dietary fat absorption	All antiretrovirals, particularly lipophilic agents	Take ARVs at least 2 hours before/after orlistat	Antiretroviral efficacy
Bile acid sequestrants	Reduced absorption of ARVs	All antiretrovirals	Take ARVs either 1 hour before or 4-6 hours after bile acid sequestrants	Antiretroviral efficacy

Legend:		No dose adjustment required.
		Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
		Contraindicated/avoid combination.

CORTICOSTEROIDS:
INHALED, INTRANASAL, INJECTABLE, ORAL

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
INTRANASAL OR ORAL INHALATION					
• Beclomethasone *(Qvar, Beconase)*					
• Budesonide *(Pulmicort, Symbicort, Rhinocort)* • Ciclesonide *(Alvesco)* • Mometasone *(Asmanex, Zenhale, Nasonex)*		Potential ↑ systemic corticosteroid and risk of Cushing's syndrome and adrenal failure.			Potential ↑ systemic corticosteroid and risk of Cushing's syndrome and adrenal failure.
• Fluticasone *(Flovent, Advair, Flonase, Avamys)*		Potential ↑ systemic corticosteroid and risk of Cushing's syndrome and adrenal failure. Avoid combination.			Potential ↑ systemic corticosteroid and risk of Cushing's syndrome and adrenal failure. Avoid combination.

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
INJECTABLE					
• Triamcinolone		Potential ↑ systemic corticosteroid and risk of Cushing's syndrome and adrenal failure.			Potential ↑ systemic corticosteroid and risk of Cushing's syndrome and adrenal failure.
ORAL					
• Dexamethasone	Potential for ↓ bictegravir with chronic dexamethasone; intermittent dexamethasone is OK Dolutegravir, raltegravir	Potential for ↑ dexamethasone and ↓ INSTI with chronic dexamethasone; intermittent dexamethasone is OK	Potential for ↓ NNRTI with chronic dexamethasone; intermittent dexamethasone is OK More than single dose of dexamethasone is contraindicated with rilpivirine	Potential for ↓ dexamethasone and ↓ NNRTI with chronic dexamethasone; intermittent dexamethasone is OK	Potential for ↑ dexamethasone and ↓ PI with chronic dexamethasone; intermittent dexamethasone is OK

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Dexamethasone (oral)	Dexamethasone is a substrate of CYP3A4.	Ritonavir- or cobicistat boosted regimens may increase dexamethasone.	Use with caution or switch to non-interacting antiretroviral if chronic administration is required.	Monitor for symptoms of Cushing's syndrome (moon face, buffalo hump, obesity, striations, acne, hirsutism, hypertension, osteoporosis, glucose intolerance, increased risk of infections) Plasma cortisol and ACTH could be done if adrenal suppression is suspected.
		NNRTIs efavirenz, etravirine, nevirapine may decrease dexamethasone.		Monitor for dexamethasone efficacy
	With chronic administration, dexamethasone induces CYP3A4	PIs, NNRTIs, elvitegravir, possibly bictegravir	Pulse dosing of dexamethasone is OK. Daily/chronic dexamethasone may decrease antiretroviral drugs and should be avoided if possible. Rilpivirine is contraindicated with more than a single dose of dexamethasone.	Antiretroviral efficacy.
Budesonide Fluticasone Mometasone (inhaled, intranasal)	Inhibition of CYP3A4	Protease inhibitors (PI) with ritonavir or cobicistat, elvitegravir/ cobicistat (Stribild, Genvoya)	Prefer beclomethasone which does not interact because it is not metabolised by CYP3A4.	Monitor for symptoms of Cushing's syndrome (moon face, buffalo hump, obesity, striations, acne, hirsutism, hypertension, osteoporosis, glucose intolerance, increased risk of infections). Plasma cortisol and ACTH could be done if adrenal suppression is suspected
Ciclesonide (inhaled)	Inhibition CYP3A4 of the active metabolite of the ciclesonide.	Protease inhibitors (PI) with ritonavir or cobicistat, elvitegravir/	Use with caution.	Monitor for symptoms of Cushing's syndrome (moon face, buffalo hump, obesity, striations, acne, hirsutism,

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
	Potential but does not seem to be clinically significant.	cobicistat (Stribild, Genvoya)		hypertension, osteoporosis, glucose intolerance, increased risk of infections). Plasma cortisol and ACTH could be done if adrenal suppression is suspected.
Triamcinolone Injection	Inhibition of CYP3A4	Protease inhibitors (PI) with ritonavir or cobicistat, elvitegravir/ cobicistat	Cushing's syndrome and adrenal suppression have been reported after even single injections of triamcinolone. There is insufficient information to indicate whether other injectable steroids present a lower risk. Consider use of an alternate anti-inflammatory agent or modify to a non-interacting antiretroviral regimen if possible.	Monitor for symptoms of Cushing's syndrome (moon face, buffalo hump, obesity, striations, acne, hirsutism, hypertension, osteoporosis, glucose intolerance, increased risk of infections) Plasma cortisol and ACTH could be done if adrenal suppression is suspected

CHEMOTHERAPY REGIMENS:
FOR NON-HODGKIN'S LYMPHOMA, HODGKIN'S LYMPHOMA, ANAL CARCINOMA, & PROSTATE CANCER

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
FOR NON-HODGKIN'S LYMPHOMA							
• **CHOP, CHOP-R** (doxorubicin, vincristine, cyclophosphamide, prednisone ± rituximab)		↑ cyclophosphamide, doxorubicin, vincristine, prednisone and risk of toxicity		potential ↓ doxorubicin, vincristine, prednisone ; potential ↑ toxicity of cyclophosphamide	↑ cyclophosphamide, doxorubicin, vincristine, prednisone and risk of toxicity		
HODGKIN'S LYMPHOMA							
• **ABVD** (doxorubicin, vinblastine, bleomycin, dacarbazine)		↑ doxorubicin & vinblastine and risk of toxicity		potential ↓ doxorubicin & vinblastine	↑ doxorubicin & vinblastine and risk of toxicity		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
ANAL CARCINOMA							
• 5-FU, mitomycin							Potential additive nephrotoxicity with TDF & mitomycin
• **FOLFOX** (oxaliplatin, leucovorin, 5-FU)							
PROSTATE CANCER							
• Abiraterone *(Zytiga)* • Denosumab *(Prolia)* • Lenalidomide *(Revlimid)*		Potential for ↑ abiraterone but likely not clinically significant			Potential for ↑ abiraterone but likely not clinically significant		
• Aplutamide *(Erleada)* • Enzalutamide *(Xtandi)*	↓ INSTI	↓ INSTI	↓ NNRTI	↓ NNRTI	↓ PI	↓ TAF	

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Cyclophosphamide	Transformation to inactive and possibly toxic metabolites CYP 3A4 Inhibition of CYP3A4 may increase drug availability for hydroxylation route thereby leading to increased efficacy and toxicity of cyclophosphamide. Cyp2B6 and CYP2C19 induction by ritonavir may possibly increased the active metabolite.	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring of side effects
	Induction of CYP 3A4 may increase toxic metabolite	Efavirenz, etravirine, nevirapine	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring of side effects (neurotoxicity)
Doxorubicin	Enzyme inhibitors may decrease reduction to free radicals via inhibition of cytochrome P450 which may decrease both antineoplastic and cytotoxic properties; however, they may also increase intracellular accumulation of doxorubicin via inhibition of PgP, which may enhance cytotoxic effects and/or systemic toxicity.	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring efficacy and side effects

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Doxorubicin	Enzyme inducers may increase reduction to free radicals via induction of cytochrome P450 which may increase both antineoplastic and cytotoxic properties	Efavirenz, etravirine, nevirapine	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring efficacy and side effects
Enzalutamide, apalutamide	Strong inducers of CYP3A4, 2C19, UGT, Pgp, BCRP, OATP1B1.	May decrease concentrations of INSTIs, PIs, NNRTI, and TAF.	If possible, consider non-inducing antiandrogen agent. May consider using increased antiretroviral doses with therapeutic drug monitoring	Antiretroviral efficacy (viral load, CD4, antiretroviral concentrations if available)
Prednisone	Possible increased level with CYP3A4 inhibitors	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Not well studied. Dose modification could be suggested	Close monitoring of corticosteroids side effects
Prednisone	Possible decreased level with CYP3A4 inducers	Efavirenz, etravirine, nevirapine	Not well studied. Dose modification could be suggested	None. Steroid efficacy?
Vinblastine, vincristine	Possible increased level with CYP3A4 inhibitors	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring of side effects (peripheral and autonomic neuropathy, myelosuppression)
Vinblastine, vincristine	Possible decreased level with CYP3A4 inducers	Efavirenz, etravirine, nevirapine	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring of efficacy

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

DIABETES MEDICATIONS
ANTIHYPERGLYCEMICS

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
α GLUCOSIDASE INHIBITORS					
• Acarbose *(Prandase, Glucobay)*					
BIGUANIDES					
• Metformin *(Glucophage, Glumetza, Avandamet, Janumet)*	Bictegravir, raltegravir Dolutegravir: ↑ metformin				
DPP-4 INHIBITORS					
• Alogliptin *(Nesina)* • Sitagliptin *(Januvia)*, sitagliptin/ metformin *(Janumet)*	Bictegravir, raltegravir Dolutegravir: ↑ metformin				

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
• Linagliptin *(Trajenta)* • saxagliptin *(Onglyza)*, saxagliptin/ metformin *(Kombiglyze)*	Bictegravir, raltegravir Dolutegravir: ↑ metformin			Potential ↓ DPP-4 inhibitor	
HUMAN GLUCAGON-LIKE PEPTIDE (GLP-1 AGONISTS)					
• Dulaglutide *(Trulicity)* • Exenatide *(Byetta)* • Liraglutide *(Victoza)* • Lixisenatide *(Adlyxine)* • Semaglutide *(Ozempic)*			doravirine Potential for additive PR prolongation (rilpivirine)		Potential for additive PR prolongation
MEGLITINIDES					
• Repaglinide *(Gluconorm)* • Nateglinide *(Starlix)*		Potential ↑ repaglinide, potential ↑/↓ nateglinide		Potential ↓ repaglinide; potential ↑ nateglinide with etravirine and efavirenz	Potential ↑ repaglinide, potential ↑/↓ nateglinide

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
SGLT2 INHIBITORS					
• Canagliflozin *(Invokana)*				Potential ↓ canagliflozin with efavirenz	Potential ↓ canagliflozin with ritonavir-boosted PIs Cobicistat-boosted PIs: no expected interaction
• Dapagliflozin *(Forxiga)* • Empagliflozin *(Jardiance)*					
SULFONYLUREAS					
• Gliclazide *(Diamicron)* • Glimepiride *(Amaryl)* • Glyburide *(Diabeta)*		Potential ↓ sulfonyurea		Potential ↑ sulfonylurea with etravirine and efavirenz	Potential ↓ sulfonylurea with ritonavir-boosted PIs Cobicistat-boosted PIs: no expected interaction
THIAZOLIDINEDIONES (TZDs)					
• Pioglitazone *(Actos)*				Potential for ↓ pioglitazone	Potential ↑ pioglitazone

<table>
<tr><th></th><th colspan="2">INSTIs</th><th colspan="2">NNRTIs</th><th>PIs</th></tr>
<tr><td></td><td>• BICTEGRAVIR (Biktarvy)
• DOLUTEGRAVIR (Tivicay, Triumeq, Juluca)
• RALTEGRAVIR (Isentress)</td><td>• ELVITEGRAVIR/ COBICISTAT (Stribild, Genvoya)</td><td>• DORAVIRINE (Pifeltro, Delstrigo)
• RILPIVIRINE (Edurant, Complera, Odefsey, Juluca)</td><td>• EFAVIRENZ (Sustiva, Atripla)
• ETRAVIRINE (Intelence)
• NEVIRAPINE (Viramune)</td><td>Boosted with ritonavir (Norvir) or cobicistat
• ATAZANAVIR (Reyataz, Evotaz)
• DARUNAVIR (Prezista, Prezcobix, Symtuza)
• LOPINAVIR (Kaletra)</td></tr>
<tr><td>• Rosiglitazone (Avandia), rosiglitazone/ metformin (Avadamet)</td><td>Bictegravir, raltegravir
Dolutegravir: ↑ metformin</td><td></td><td></td><td></td><td>Potential ↑ rosiglitazone with unboosted atazanavir</td></tr>
</table>

Legend:

No dose adjustment required.

Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.

Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Metformin	Metformin: excreted 100% as unchanged drug by glomerular filtration plus active tubular secretion via OCT2 and MATE-1-2K	Dolutegravir	If a patient is already receiving dolutegravir, start with low metformin dose and gradually increase. If a patient is starting/stopping dolutegravir while on metformin, a metformin dose adjustment may be necessary. Select an alternative antidiabetic agent or antiretroviral if high-dose metformin is not tolerated.	Metformin side effects (primarily gastrointestinal)
DPP-4 Inhibitors	Linagliptin: inhibition of CYP3A4 and P-gp Saxagliptin: inhibition of CYP3A4	Boosted protease inhibitors and elvitegravir/cobicistat	May not be clinically significant, since linagliptin and saxagliptin have a large safety window. No dose adjustment necessary.	No monitoring suggested
	Linagliptin, saxagliptin: induction of CYP3A4/P-gp	Efavirenz, etravirine, nevirapine	Adjust linagliptin and saxagliptine doses if needed	Close monitoring of efficacy
GLP-1 Agonists	Potential for additive PR prolongation.	Protease inhibitors, rilpivirine	Use with caution, particularly in patients with underlying conduction or cardiac rhythm disturbances.	Monitor for symptoms of syncope, lightheadedness, consider ECG monitoring.
Meglitinides	Repaglinide: inhibition OATP1B1 and CYP3A4	Boosted protease inhibitors and elvitegravir/cobicistat	Adjust dose if needed	Close monitoring of side effects
	Nateglinide: induction CYP2C9	Elvitegravir	Adjust dose as needed	Antihyperglycemic efficacy
	Nateglinide: inhibition CYP2C9	Efavirenz, etravirine	Adjust dose as needed	Close monitoring of side effect. May potentiate the hypoglycemic action
SGLT2 Inhibitors	Canagliflozin: induction UGT	Ritonavir protease inhibitors boosted and efavirenz	Adjust dose as needed	Antihyperglycemic efficacy
Sulfonylureas	Gliclazide, glimepiride and glyburide: 2C9 induction	Ritonavir PIs boosted elvitegravir	Adjust dose as needed	Antihyperglycemic efficacy

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
	Gliclazide, glimepiride and glyburide: 2C9 inhibition	Efavirenz and etravirine	Adjust dose as needed	Sulfonylureas side effects
Thiazolidinediones	Pioglitazone: 3A4 inhibition	Boosted protease inhibitors and elvitegravir/cobicistat	Adjust dose as needed	Close monitoring of side effects
	Pioglitazone: 3A4 induction	Efavirenz, nevirapine and etravirine	Adjust dose as needed	Antihyperglycemic efficacy
	Rosiglitazone: 2C8 inhibition	Unboosted atazanavir	Adjust dose as needed	Close monitoring of side effects

GENITOURINARY DRUGS:

PDE5 INHIBITORS FOR ERECTILE DYSFUNCTION (ED) or PULMONARY ARTERIAL HYPERTENSION (PAH)

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
TREATMENT OF ERECTILE DYSFUNCTION (ED)					
• Sildenafil *(Viagra)*		Potential for ↑ sildenafil. Decrease sildenafil dose to 25 mg every 48 hours.		Potential for ↓ sildenafil	Potential for ↑ sildenafil. Decrease sildenafil dose to 25 mg every 48 hours.
• Tadalafil *(Cialis)*		Potential for ↑ tadalafil. Decrease tadalafil dose to 10 mg every 72 hours, maximum 3 times per week.		Potential for ↓ tadalafil	Potential for ↑ tadalafil. Decrease tadalafil dose to 10 mg every 72 hours, maximum 3 times per week.
• Vardenafil *(Levitra)*		Potential for ↑ vardenafil and toxicity		Potential for ↓ vardenafil	Potential for ↑ vardenafil and toxicity
TREATMENT OF PULMONARY ARTERIAL HYPERTENSION (PAH)					
• Sildenafil *(Revatio)*		Potential for ↑ sildenafil and toxicity		Potential for ↓ sildenafil	Potential for ↑ sildenafil and toxicity
• Tadalafil *(Adcirca)*		Potential for ↑ tadalafil. Start at 20 mg daily and titrate to 40 mg daily based on tolerability.		Potential for ↓ tadalafil	Potential for ↑ tadalafil. Start at 20 mg daily and titrate to 40 mg daily based on tolerability.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
PDE5 inhibitors (sildenafil, tadalafil, vardenafil)	Inhibition of CYP3A4	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	PAH: • Sildenafil is contraindicated • Tadalafil: start at 20 mg daily and titrate to 40 mg daily based on tolerability ED: • Vardenafil is contraindicated. • Sildenafil: use 25 mg every 48 hours. • Tadalafil: 10 mg every 72 hours, maximum 3 times per week.	PDE5 toxicity: headache, flushing, dyspepsia, nasal congestion, flushing, diarrhea, dizziness.
	Induction of CYP3A4	Efavirenz, etravirine, nevirapine	Adjust dose according to efficacy/toxicity	PDE5 efficacy

Legend:		No dose adjustment required.
		Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
		Contraindicated/avoid combination.

GENITOURINARY DRUGS:
TREATMENT FOR BENIGN PROSTATIC HYPERPLASIA (BPH) or LOWER URINARY TRACT SYMPTOMS (LUTS)

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
5 ALPHA REDUCTASE INHIBITORS					
• Dutasteride *(Avodart)*		Potential for ↑ dutasteride		Potential for ↓ dutasteride	Potential for ↑ dutasteride
• Finasteride *(Proscar)*					
ALPHA 1 ADRENERGIC RECEPTOR BLOCKERS (NON-SELECTIVE)					
• Doxazosin *(Cardura)*		Potential for ↑ doxazosin		Potential for ↓ doxazosin	Potential for ↑ doxazosin
• Terazosin *(Hytrin)*		Potential for ↑ terazosin		Potential for ↓ terazosin	Potential for ↑ terazosin
ALPHA 1 ADRENERGIC RECEPTOR BLOCKERS (SELECTIVE)					
• Alfuzosin *(Xatral)*		Potential for ↑ alfuzosin and toxicity		Potential for ↓ alfuzosin	Potential for ↑ alfuzosin and toxicity

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
• Silodosin *(Rapaflo)*		Potential for ↑ silodosin. Use 4 mg dose and monitor for toxicity.		Potential for ↓ silodosin	Potential for ↑ silodosin. Use 4 mg dose and monitor for toxicity.
• Tamsulosin *(Flomax CR)*		Potential for ↑ tamsulosin. Use 0.4 mg dose and monitor for toxicity.		Potential for ↓tamsulosin	Potential for ↑ tamsulosin. Use 0.4 mg dose and monitor for toxicity.
PDE5 INHIBITORS					
• Tadalafil *(Cialis)*		Potential for ↑ tadalafil but dose adjustment not required (*for 5 mg daily dose only)		Potential for ↓ tadalafil	Potential for ↑ tadalafil but dose adjustment not required (*for 5 mg daily dose only)

*NB: for tadalafil, this table refers to the daily dose of 5 mg for benign prostatic hyperplasia. Please refer to **"Genitourinary Drugs: PDE5 Inhibitors for Erectile Dysfunction (ED) or Pulmonary Arterial Hypertension (PAH)"** table for recommendations on higher or intermittent dosing of tadalafil with antiretrovirals.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
5 alpha reductase inhibitors	Inhibition of CYP3A4 (dutasteride)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Finasteride may be used	Dutasteride toxicity: erectile dysfunction, decreased libido
	Induction of CYP3A4 (dutasteride)	Efavirenz, etravirine, nevirapine	Finasteride may be used	Dutasteride efficacy
Alpha 1 adrenergic blockers (non-selective)	Inhibition of CYP3A4 (doxazosin, terazosin)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Adjust dose according to efficacy/toxicity	Toxicity: hypotension, dizziness, headache, asthenia, nasal congestion
	Induction of CYP3A4 (doxazosin, terazosin)	Efavirenz, etravirine, nevirapine		Doxazosin & terazosin efficacy
Alpha 1 adrenergic blockers (selective)	Inhibition of CYP3A4 (alfuzosin>silodosin, tamsulosin)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Alfuzosin: consider low-dose silodosin or tamsulosin with monitoring or change antiretroviral regimen.	Toxicity: hypotension, dizziness, headache, diarrhea, nasal congestion
	Induction of CYP3A4 (all)	Efavirenz, etravirine, nevirapine		Alfuzosin, silodosin, tamsulosin efficacy
PDE5 Inhibitor Tadalafil 5 mg daily dose ONLY*	Inhibition of CYP3A4 (tadalafil)	May be used with all ARVs	Daily tadalafil 5 mg may be used without dose adjustment. May ↓ to 2.5 mg daily based on tolerability.	Monitor for toxicity: headache, dyspepsia, flushing, back pain, nasal congestion.

*Please refer to **"Genitourinary Drugs: PDE5 Inhibitors for Erectile Dysfunction (ED) or Pulmonary Arterial Hypertension (PAH)"** table for recommendations on higher or intermittent dosing of tadalafil with antiretrovirals

Legend:

No dose adjustment required.

Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.

Contraindicated/avoid combination.

HORMONAL AGENTS:
GENDER AFFIRMING THERAPY

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
FEMINIZING THERAPY					
Estrogens • 17-beta estradiol (oral, *Estrace)* • Transdermal estradiol *(Estraderm, Estradot)*		Potential for ↑ estradiol		Potential for ↓ estradiol	Cobicistat-boosted PIs: potential for ↑ estradiol Ritonavir-boosted PIs: potential for ↑/↓ estradiol
Antiandrogens • Spironolactone, finasteride					
• cyproterone		Potential for ↑ cyproterone		Potential for ↓ cyproterone	Potential for ↑ cyproterone
Progestins • Micronized progesterone *(Prometrium)* • Medroxy-progesterone *(Provera)*		Potential for ↑ progestin		Potential for ↓ progestin	Potential for ↑ progestin

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
MASCULINIZING THERAPY					
• Testosterone cypionate, testosterone enanthate (IM) • Testosterone patch, gel		Potential for ↑ testosterone		Potential for ↓ testosterone	Potential for ↑ testosterone

Legend:	
	No dose adjustment required.
	Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
	Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Estradiol	Substrate of CYP3A4, 1A2, UGT and OAPT1B1	Cobicistat boosted regimens may increase estradiol Ritonavir-boosted PIs may increase or decrease estradiol NNRTIs efavirenz, etravirine, nevirapine may decrease estradiol	If possible switch to non-interacting antiretroviral such as doravirine, rilpivirine, or an unboosted INSTI Otherwise, monitor for estradiol efficacy/toxicity and adjust dose of estradiol if necessary	Monitor estradiol concentrations and signs of excess estrogen Monitor estradiol concentrations and signs of estrogen deficiency
Cyproterone Progestins Testosterone	Substrates of CYP3A4	Ritonavir- or cobicistat boosted regimens may increase hormone levels NNRTIs efavirenz, etravirine, nevirapine may decrease hormone levels	If possible switch to non-interacting antiretroviral such as doravirine, rilpivirine, or an unboosted INSTI Otherwise, monitor for hormone efficacy/toxicity and adjust dose if necessary	Monitor for signs and symptoms of excess hormones Monitor for signs and symptoms of hormone deficiency

HORMONAL AGENTS:
CONTRACEPTIVES AND HORMONE REPLACEMENT THERAPY

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
CONTRACEPTIVES					
• Combined oral contraceptives • Transdermal contraceptives • Plan B • Nuva-Ring		Potential for ↓ ethinyl estradiol and ↑ progestin (combined oral, transdermal, vaginal ring)		Potential for ↓ ethinyl estradiol and ↓ progestin (combined oral, transdermal, vaginal ring)	Atazanavir/ritonavir: Use OC with <u>minimum</u> 30 mcg ethinyl estradiol Darunavir, lopinavir/r: potential for ↓ ethinyl estradiol and ↑/↓ norethindrone
• DMPA *(Depo-Provera)*					
HORMONE REPLACEMENT THERAPY					
• Estrogens, 17-beta estradiol, conjugated estrogens		Potential for ↑ estradiol		Potential for ↓ estradiol	Cobicistat-boosted PIs: potential for ↑ estradiol Ritonavir-boosted PIs: potential for ↓ estradiol
• Progestins, medroxy-progesterone		Potential for ↑ progestin		Potential for ↓ progestin	Potential for ↑ progestin, especially with cobicistat

Mechanism of Drug Interactions, Management and Monitoring

Contraceptive/HRT	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Combined Oral Contraceptives, Plan B, Nuva-ring	Induction/inhibition of CYP3A4, induction of UGT	Ritonavir-boosted protease inhibitors, elvitegravir/cobicistat, efavirenz	Use alternate non-hormonal methods of contraception Plan B and efavirenz: may need to increase progesterone dose.	Monitor for loss of contraceptive efficacy
Hormone Replacement Therapy	Inhibition of CYP3A4.	Cobicistat-boosted protease inhibitors and elvitegravir/cobicistat	Risks of potentially elevated hormone levels may carry thromboembolic risk in long term. Consider in post menopausal females when benefits outweigh the risk.	Monitor for progesterone-related side effects and estrogen risk
	Induction of CYP3A4, 1A2, UGT	Efavirenz, etravirine, nevirapine, ritonavir boosted PI's	May lower levels of estradiol and medroxyprogesterone	Dose adjustment not studied, determine risk vs benefits when using in post menopausal females

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

OSTEOPOROSIS DRUGS

BISPHOSPHONATES, SERM, MONOCLONAL ANTIBODY, ANABOLIC AGENT, CALCITONIN

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
BISPHOSPHONATES					
• Alendronate *(Fosamax)* • Etidronate *(Didrocal)* • Risedronate *(Actonel)* • Zoledronic Acid *(Aclasta)*					
SERM (selective estrogen receptor modulator)					
• Raloxifene *(Evista)*					
MONOCLONAL ANTIBODIES AGAINST RANKL (RECEPTOR ACTIVATOR OF NUCLEAR FACTOR KAPPA-B LIGAND)					
• Denosumab *(Prolia)*					

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
ANABOLIC AGENT					
• Teriparatide *(Forteo)*					
CALCITONIN					
• Calcitonin					

Legend:		No dose adjustment required.
		Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
		Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Bisphosphonates, calcitonin, denosumab	Not metabolized by the liver.	None	May be used with all antiretrovirals	
Raloxifene, teriparatide	No reported CYP metabolism	None	May be used with all antiretrovirals	

PSYCHOTROPIC DRUGS:

SEDATIVES/HYPNOTICS, ANTIDEPRESSANTS, AND ANTIPSYCHOTICS

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
SEDATIVES/HYPNOTICS							
• Lorazepam, oxazepam, temazepam							
• Alprazolam, bromazepam, buspirone, clonazepam, estazolam, flurazepam, diazepam, nitrazepam, zolpidem, zopiclone		Potential for ↑ benzodiazepine		Potential for ↓ benzodiazepine	Potential for ↑ benzodiazepine		
• Midazolam, triazolam		Potential for ↑ benzodiazepine		Potential for ↓ benzodiazepine	Potential for ↑ benzodiazepine		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
ANTIDEPRESSANTS							
• Most TCAs, duloxetine							
• Bupropion				Etravirine may be used without dose adjustment Potential for ↓ bupropion (efavirenz, nevirapine)	Cobicistat-boosted PIs: may be used without dose adjustment Ritonavir-boosted PIs: potential for ↓ bupropion		
• St. John's wort	raltegravir ↑ dolutegravir 50 mg BID bictegravir	Potential for ↓ elvitegravir and TAF	Potential for ↓ NNRTIs *including Juluca	Potential for ↓ NNRTIs	Potential for ↓ PIs	Potential for ↓ TAF	
• Most SSRIs (citalopram, escitalopram,		Potential for ↑ antidepressant		Potential for ↓ antidepressant	Potential for ↑ antidepressant		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
fluoxetine, sertraline), venlafaxine, desvenlafaxine, trazodone, reboxetine, mirtazapine							
ANTIPSYCHOTICS							
• Aripiprazole, lurasidone, modafinil, quetiapine, pimozide, paliperidone, risperidone, ziprasidone		Potential for ↑ antipsychotic Lurasidone & pimozide are contraindicated		Potential for ↓ antipsychotic	Potential for ↑ antipsychotic Lurasidone & pimozide are contraindicated		
• Clozapine, olanzapine		Potential for ↑ antipsychotic		Potential for ↓ antipsychotic	Cobicistat-boosted PIs: potential for ↑ antipsychotic Ritonavir-boosted PIs: potential for ↓		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
					olanzapine and ↑/↓ clozapine		
• Modafinil	Dolutegravir, raltegravir Potential for ↓ bictegravir	Potential for ↓ elvitegravir	Potential for ↓ NNRTI	Potential for ↓ NNRTI	Potential for ↓ PIs	Potential for ↓ TAF	

Legend:

No dose adjustment required.

Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.

Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Benzodiazepines	Inhibition of CYP3A4 (midazolam, triazolam)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Contraindicated. Use alternate benzodiazepine.	
	Inhibition of mixed CYP (Alprazolam, bromazepam, buspirone, clonazepam, estazolam, eszopiclone, flurazepam, diazepam, nitrazepam, zolpidem, zopiclone)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir.	Adjust benzodiazepine dose according to response/toxicity. Other benzodiazepines may be used without dose adjustment.	Benzodiazepine toxicity: ataxia, dizziness, drowsiness, fatigue, muscle weakness, slowed reaction
	Lorazepam, oxazepam, temazepam	May be used with all ARVs	May use without dose adjustment	
Antidepressants	Inhibition of mixed CYP pathways (citalopram, escitalopram, fluoxetine, sertraline, venlafaxine, desvenlafaxine, trazodone, mirtazapine)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Adjust antidepressant dose according to response/toxicity. Other antidepressants may be used without dose adjustment.	Antidepressant toxicity: anticholinergic effects, orthostatic hypotension, tachycardia, agitation, headache, somnolence, dizziness, diarrhea, excessive sweating, weight gain.
	Induction of mixed CYP pathways pathways (fluoxetine, sertraline, trazodone, reboxetine, mirtazapine)	Efavirenz, etravirine, nevirapine	Adjust antidepressant dose according to response. Other antidepressants may be used without dose adjustment.	Antidepressant efficacy
	Induction of CYP2B6 (Bupropion)	Ritonavir-boosted protease inhibitors, efavirenz, nevirapine	Adjust antidepressant dose according to response (maximum 300 mg daily).	Antidepressant efficacy
	Induction of CYP3A4 (St. John's wort)	Dolutegravir, Bictegravir, elvitegravir/cobicistat, all PIs and NNRTIs and Tenofovir Alafenamide	Contraindicated with most antiretrovirals	

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Antipsychotics	Inhibition of mixed CYP pathways (aripiprazole, buspirone, lurasidone, modafinil, quetiapine, pimozide, paliperidone, risperidone, ziprasidone)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Adjust antipsychotic dose according to response/toxicity.	Antipsychotic toxicity: somnolence, sweating, chest pain, tachycardia, dizziness, insomnia, headache, nausea, diarrhea, dry mouth, numbness, weight gain
	Induction of mixed CYP pathways (aripiprazole, buspirone, lurasidone, modafinil, quetiapine, pimozide, paliperidone, risperidone, ziprasidone)	Efavirenz, etravirine, nevirapine	Adjust antipsychotic dose according to response	Antipsychotic efficacy
	Induction of CYP1A2 (Clozapine, olanzapine)	Ritonavir-boosted protease inhibitors	Adjust antipsychotic dose according to response.	Antipsychotic efficacy
Modafinil	Induction of CYP3A4	Most ARVS except for dolutegravir, raltegravir, TDF and abacavir.	Consider non-interacting ARV regimen if possible.	Antiretroviral efficacy

TRANSPLANT MEDICATIONS:
IMMUNOSUPPRESSANTS

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
IMMUNOSUPPRESSANTS					
• Azathioprine *(Imuran)*					
• Cyclosporine *(Neoral)*		Potential for ↑ immunosuppressant		Potential for ↓ immunosuppressant	Potential for ↑ immunosuppressant
• Sirolimus *(Rapamune)*		Potential for ↑ immunosuppressant		Potential for ↓ immunosuppressant	Potential for ↑ immunosuppressant
• Mycophenolate mofetil *(CellCept, Myfortic)*				Potential for ↓ immunosuppressant	Cobicistat-boosted PIs: OK Ritonavir-boosted PIs: potential for ↓ immunosuppressant
• Tacrolimus *(Prograf, Advagraf)*		Potential for ↑ immunosuppressant		Potential for ↓ immunosuppressant	Potential for ↑ immunosuppressant

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Cyclosporine, sirolimus, tacrolimus	Substrates of CYP3A4 and Pgp. Concentrations may be increased by inhibitors and decreased by inducers.	Ritonavir- or cobicistat boosted regimens may increase immunosuppressants.	If possible switch to non-interacting antiretroviral such as doravirine, rilpivirine, or an unboosted INSTI. Otherwise, significant dose reduction of immunosuppressant may be required.	Monitor drug concentrations of immunosuppressant and dose accordingly.
		NNRTIs efavirenz, etravirine, nevirapine may decrease immunosuppressants	Consider changing to non-inducing NNRTI such as doravirine or rilpivirine, or an unboosted INSTI	Monitor drug concentrations of immunosuppressant and dose accordingly.
Mycophenolate	Substrate of UGT1A4, 1A9 Ritonavir and some NNRTIs may induce UGT enzymes.	Ritonavir-boosted PIs or enzyme inducing NNRTIs (efavirenz, etravirine, nevirapine) may decrease MMF	Consider changing to non-inducing NNRTI such as doravirine or rilpivirine, an INSTI, or a cobicistat-boosted PI.	Monitor drug concentrations of immunosuppressant and dose accordingly.

Legend:		No dose adjustment required.
		Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
		Contraindicated/avoid combination.

RECREATIONAL DRUGS:

AMYL NITRATE, AMPHETAMINES, CANNABIS, COCAINE/CRACK, GHB, HALLUCINOGENS, KETAMINE, HEROIN, NALOXONE

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
AMYL NITRATE					
• Poppers, ames					
AMPHETAMINES					
• MDMA/ecstasy, crystal, molly		Potential for ↑ recreational drug			Potential for ↑ recreational drug
CANNABIS (THC), CANNABIDIOL (CBD) *Note that oral cannabis oils or dried cannabis may include THC/CBD in various ratios					
• Marijuana, weed		Potential for ↑ THC & CBD		Potential for ↑ THC and ↓ CBD	Potential for ↑ THC Potential for ↑/↓ CBD
COCAINE					
• crack, base		Potential for ↑ recreational drug	Potential QT prolongation (rilpivirine)	Potential for ↑ levels of hepatotoxic metabolite	Potential for ↑ recreational drug
GAMMA-HYDROXYBUTYRATE					
• GHB, date rape drug, Geeb, liquid X		Potential for ↑ recreational drug			Potential for ↑ recreational drug

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
HALLUCINOGENS					
• LSD, acid • PCP, angel dust		Potential for ↑ recreational drug		Potential for ↓ recreational drug	Potential for ↑ recreational drug
KETAMINE					
• Special K, vitamin K, KitKat		Potential for ↑ recreational drug		Potential for ↓ recreational drug	Potential for ↑ recreational drug
HEROIN					
• Smack, H, tar, junk		Potential for ↑ recreational drug		Potential for ↓ morphine (converted from heroin) with efavirenz	Potential for ↑ recreational drug
NALOXONE					
• Narcan					Ritonavir-boosted PIs: potential for ↓ naloxone Cobicistat-boosted PIs

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Cannabidiol (CBD)	Substrate of CYP3A4, 2C19; inhibits CYP2C19	Cobicistat-boosted elvitegravir and PIs may increase CBD. Ritonavir-boosted PIs may increase or decrease CBD. Enzyme inducing NNRTIs (efavirenz, etravirine, nevirapine) may decrease CBD levels.	Warn patient of potential for increased or decreased CBD levels; CBD dose may need to be titrated.	Toxicity: CNS effects (sedation, confusion, impairment), heart rate, blood pressure.
Cannabis (THC)	Substrate of CYP2C9>3A4	Protease Inhibitors (PI) (with ritonavir or cobicistat), elvitegravir/cobicistat, etravirine and efavirenz may increase THC levels.	Warn patient of potential for increased THC levels; THC dose may need to be titrated.	Toxicity: as above.
Stimulants: Cocaine, amphetamines GHB	Inhibition of CYP3A4 (cocaine) and CYP 2D6 (amphetamines, GHB?) leading to increased levels of stimulant	Protease Inhibitors (PI) (with ritonavir or cobicistat) & Elvitegravir/cobicistat	Warn patient of potential for unpredictable increased levels of the recreational substance and provide harm reduction advice	Toxicity: Dehydration, dry mouth, teeth grinding, tense jaw, tachycardia. GHB: seizures, bradycardia, loss or consciousness
Hallucinogens: LSD, PCP (angel dust)	Mechanism unclear but potential for inhibition or induction of drug metabolism	PIs & elvitegravir/cobicistat may increase hallucinogen concentrations Enzme inducing NNRTIs (efavirenz, etravirine, nevirapine) may decrease levels	Warn patient of unpredictable increased levels of hallucinogen and provide harm reduction advice	Toxicity: Hallucinations, psychosis, flashbacks, seizures, hypertension.
Ketamine	Mechanism unclear but potential for inhibition or induction of drug metabolism	PIs & elvitegravir/cobicistat may increase ketamine Enzyme inducing NNRTIs (efavirenz, etravirine, nevirapine) may decrease levels	Warn patient of unpredictable increased levels and provide harm reduction advice	Toxicity: Nausea, vomiting, SOB, loss of coordination, cognitive decline

Class	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Heroin	Converted to morphine, which is glucuronidated (UGT2B7>UGT1A1) and a substrate of Pgp	PIs & elvitegravir/cobicistat may increase morphine Efavirenz may induce UGT and decrease morphine	Warn patient of unpredictable increased levels and provide harm reduction advice	Toxicity: decreased level of consciousness, miosis, respiratory depression. Acute symptoms may be reversed with naloxone.
Naloxone	Substrate of UGT2B7	Ritonavir-boosted PIs may induce UGT and decrease naloxone	Potential for decreased duration of naloxone efficacy	Monitor for duration of naloxone efficacy.

OVER-THE-COUNTER, COMPLEMENTARY AND ALTERNATIVE AGENTS

VITAMINS AND MINERALS, HERBAL PRODUCTS, APPEARANCE AND PERFORMANCE ENHANCING SUPPLEMENTS

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
VITAMINS AND MINERALS							
• Vitamin D				Potential for ↓ vitamin D			
• Cations such as calcium, magnesium, iron, aluminum, zinc, including supplements and multivitamins with high dose calcium, iron	↓ INSTI Raltegravir 600 mg HD tablets Raltegravir 400 mg OK with calcium	Potential for ↓ INSTI					
HERBAL PRODUCTS AND SUPPLEMENTS							
• Echinacea	Potential ↓ bictegravir Dolutegravir, raltegravir		Potential for ↓ NNRTI				

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
• Garlic	Potential for ↓ INSTI	Potential for ↓ INSTI	Potential for ↓ NNRTI	Potential for ↓ NNRTI	Potential for ↓ PI	Potential for ↓ TAF	
• Ginkgo biloba	Potential for ↓ bictegravir Dolutegravir, raltegravir		Potential for ↓ NNRTI	Potential for ↓ NNRTI	Always use boosted PI		
• Grapefruit juice			Potential for ↑ rilpivirine				
• Milk thistle • Saw palmetto							

APPEARANCE AND PERFORMANCE ENHANCING SUPPLEMENTS (APES)

• Creatine	Potential additive ↑ Scr without impacting renal function	Potential additive ↑ Scr without impacting renal function	Rilpivirine: potential additive ↑ Scr without impacting renal function		Potential additive ↑ Scr without impacting renal function		Tenofovir DF: Potential additive nephrotoxicity (rare)
• Testosterone (oral IM, topical)		Potential for ↑ testosterone		Potential for ↓ testosterone	Potential for ↑ testosterone		

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
Anabolic steroids • Oral: oxandrolone, stanozolol • IM: nandrolone							
Selective androgen receptor modulators • Andarine, ostarine							
Selective estrogen receptor modulators (SERMS) • Clomiphene, tamoxifen	Potential for tamoxifen to ↓ bictegravir	Potential for ↑ tamoxifen, possibly ↓ elvitegravir Clomiphene OK	Potential for ↓ NNRTI Clomiphene OK	Potential for ↓ tamoxifen and possibly ↓ NNRTI Clomiphene OK	Potential for ↑ tamoxifen, possibly ↓ PI Clomiphene OK		
Aromatase inhibitors • Letrozole, anastrazole		Potential for ↑ aromatase inhibitor		Potential for ↓ aromatase inhibitor	Cobicistat-boosted PI: Potential for ↑ aromatase inhibitor Ritonavir-boosted PI: potential for ↑/↓ aromatase inhibitor		

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Cation-containing products, including supplements and multivitamins	Chelation and decreased absorption Many Multivitamins including once daily and especially those designed for women with extra Calcium and iron, and those used during pregnancy, contain enough cations to lead to chelation of the integrase inhibitors and limit their absorption. This results in lowered levels of the integrase inhibitor and could result in loss of virologic suppression.	All INSTIs	Management recommendations vary according to specific INSTI: • **Bictegravir:** Administer bictegravir and polyvalent cations simultaneously with food, or separate by 2 hours. • **Dolutegravir:** Administer dolutegravir and polyvalent cations simultaneously with food, or take dolutegravir 2 hours before or 6 hours after polyvalent cations. • **Elvitegravir/c :** Stagger administration by at least 2 hours from mineral supplements. • **Raltegravir:** ONLY 400 MG BID dose may be used with calcium carbonate; use with other polyvalent cations is not recommended. Do not use 600 mg HD tablet with any polyvalent cations.	In all cases, monitor for continued viral suppression.
Echinacea	May induce CYP3A4 (mild)	Bictegravir, doravirine, rilpivirine	Potential for decreased ARV concentrations, clinical significance unclear.	Antiretroviral efficacy.
Garlic	May induce CYP3A4, Pgp	All ARVs	Avoid ingestion of large amounts of garlic (fresh, cooked or supplements)	Antiretroviral efficacy.
Ginkgo Biloba	Ginkgo may induce CYP3A4	Bictegravir, unboosted atazanavir, NNRTIs	Do not use unboosted atazanavir with Ginkgo. Avoid Ginkgo with NNRTI or bictegravir; use alternate INSTI or boosted PI.	Antiretroviral efficacy.

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Grapefruit juice	May inhibit CYP3A4, Pgp	rilpivirine	Clinical significance unclear; caution may be warranted if patient is on other drugs which inhibit CYP3A4 and/or have QT-prolonging effect	
Creatine	Creatine is metabolized to creatinine, and may lead to higher serum creatinine without necessarily impacting renal function. Potential additive effect when combined with ARVs which inhibit renal tubular secretion of creatinine.	Cobicistat, ritonavir, dolutegravir, bictegravir, rilpvirine	Increases in serum creatinine secondary to inhibition of renal tubular transporters generally occur soon after starting these antiretrovirals and remain stable thereafter. Use of creatine supplements may enhance this effect. If additional significant increases in serum creatinine occur after patient is stable on antiretrovirals, explore other causes of potential nephrotoxicity.	Monitor renal function.
	Potential additive risk of renal toxicity.	Tenofovir disoproxil	Some cases of renal impairment after use of creatinine have been reported.	Monitor renal function.
Aromatase inhibitors (anastrozole, letrozole)	Anastrazole: substrate of CYP3A4, UGT Letrozole: substrate of CYP3A4, 2A6	Protease inhibitors, elvitegravir/cobicistat (inhibition of CYP3A4, ritonavir may induce UGT), NNRTIs (induction of CYP3A4)	Potential for increased or decreased concentrations of aromatase inhibitors.	Monitor for efficacy, toxicity of aromatase inhibitors.
Selective estrogen receptor modulators	Clomiphene: no metabolism/transporter effects. Tamoxifen: substrate and inducer of CYP3A4 Potential for increased tamoxifen with boosted regimens or decreased tamoxifen with enzyme inducing NNRTIs.	Bictegravir, elvitegravir/cobicistat, PIs, NNRTIs	Less interaction potential with clomiphene versus tamoxifen. If using tamoxifen, consider using an unboosted integrase inhibitor with minimal CYP3A4 involvement such as dolutegravir or raltegravir.	Efficacy/toxicity of tamoxifen. Antiretroviral efficacy.

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
	Potential for decreased ARV concentrations via CYP3A4 induction by tamoxifen.			

Legend:		
		No dose adjustment required.
		Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
		Contraindicated/avoid combination.

MISCELLANEOUS DRUGS:
COLCHICINE AND ERGOT ALKALOIDS

	INSTIs		NNRTIs		PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
COLCHICINE					
• Colchicine *(various generics)*		Potential for ↑ colchicine Combination contraindicated in renal or hepatic impairment		Potential for ↓ colchicine	Potential for ↑ colchicine Combination contraindicated in renal or hepatic impairment
ERGOT ALKALOIDS					
• dihydroergotamine, ergonovine, ergotamine, methylergonovine *(Cafergot, Migranal, D.H.E. 45, Ergotrate, Methergine, Migergot, Ergomar)*		Potential for ↑ ergot		Potential for ↓ ergot	Potential for ↑ ergot

Legend:

- No dose adjustment required.
- Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.
- Contraindicated/avoid combination.

Mechanism of Drug Interactions, Management and Monitoring

	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Colchicine	Inhibition of P-gp, CYP3A4	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Adjust colchicine dose and monitor for toxicity. For treatment of gout flares: use colchicine 0.6 mg x 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. For prophylaxis of gout flares: use colchicine 0.3 mg once daily or every other day. For treatment of familial Mediterranean fever: Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID. **Combination is contraindicated in patients with renal or hepatic impairment. Life-threatening and fatal colchicine toxicity has been reported in such situations**	Colchicine toxicity: diarrhea, cramping, nausea, abdominal pain, vomiting, peripheral leukocytosis. Life-threatening complications associated with overdose include multi-organ failure, respiratory depression, and cardiovascular collapse
	Induction of P-gp, CYP3A4	NNRTIs efavirenz, etravirine, nevirapine	Consider switching to non-inducing NNRTI such as doravirine or rilpivirine if possible. Do not exceed maximum recommended dose of colchicine: • Gout flares: 1.8 mg over 1 hour period • Familial Mediterranean fever: 2.4 mg daily	Colchicine efficacy and toxicity
Ergot alkaloids	Inhibition of CYP3A4	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	**Coadministration is contraindicated**	Ergot toxicity: arterial vasoconstriction, peripheral vascular ischemia, gangrene
	Induction of CYP3A4	NNRTIs efavirenz, etravirine, nevirapine	Consider switching to non-inducing NNRTI such as doravirine or rilpivirine if possible. Do not exceed maximum recommended dose of ergot alkaloid	Ergot efficacy and toxicity

APPENDIX A
COMMONLY USED HIV MEDICATIONS AT A GLANCE

	GENERIC NAME	TRADE NAME	STRENGTH	DIN	USUAL DOSAGE
	Single Tablet Regimen (STR) Products				
	Efavirenz/ emtricitabine/ tenofovir DF	Atripla	600/200/300 mg tablet	02300699	1 tablet daily
	Bictegravir/ emtricitabine/ tenofovir alafenamide	Biktarvy	50/200/25 mg tablet	02478579	1 tablet daily
	Emtricitabine/ rilpivirine/ tenofovir DF	Complera	200/25/300 mg tablet	02374129	1 tablet daily
	Doravirine/ lamuvidine/ tenofovir DF	Delstrigo	100/300/300 mg tablet	02482592	1 tablet daily
	Dolutegravir/ lamivudine	Dovato	50/300 mg tablet	02491753	1 tablet daily
	elvitegravir/ cobicistat/ emtricitabine/ tenofovir alafenamide	Genvoya	150/150 mg/200/10 mg tablet	02449498	1 tablet daily
	Dolutegravir/ rilpivirine	Juluca	50/25 mg tablet	02475774	1 tablet daily
	Emtricitabine/ rilpivirine/tenofovir alafenamide	Odefsey	200/25/25 mg tablet	02461463	1 tablet daily
	elvitegravir/ cobicistat/ emtricitabine/ tenofovir DF	Stribild	150/150 mg/200/300 mg tablet	02397137	1 tablet daily
	Darunavir/ cobicistat/ emtricitabine/ tenofovir alafenamide	Symtuza	800/150/200/10 mg tablet	02473720	1 tablet daily
	Dolutegravir/abacavir/lamivudine	Triumeq	50/600/300 mg tablet	02430932	1 tablet daily
	Integrase Inhibitor				
	dolutegravir	Tivicay	50 mg tablet 10, 25 mg tablets	02414945 (50 mg) 02475774 (25 mg) 02461218 (10 mg)	50 mg daily (naïve) or BID (experienced)
 	raltegravir	Isentress HD Isentress	600 mg tablets 400 mg tablets	02465337 02301881	1200 mg daily 400 mg BID

	GENERIC NAME	TRADE NAME	STRENGTH	DIN	USUAL DOSAGE
	NRTIs: Combination Products				
	Abacavir, lamivudine	Kivexa	600/300 mg tablet	02269341	1 tablet daily
	Tenofovir disoproxil, emtricitabine	Truvada	300/200 mg tablet	02274906	1 tablet daily
	Tenofovir alafenamide, emtrictabine	Descovy	25/200 mg tablet 10/200 mg tablet	02454424 02454416	1 tablet daily
	NNRTIs (Non-Nucleoside Reverse Transcriptase Inhibitors)				
	doravine	Pifeltro	100 mg tablet	02481545	100 mg daily
	efavirenz	Sustiva	600 mg tablet	02246045	600 mg daily
	etravirine	Intelence	200 mg tablet	02375931	200 mg BID
	nevirapine	Viramune XR	400 mg tablet	02367289	200 mg daily x 14 days, then 400 mg daily
	rilpivirine	Edurant	25 mg tablet	02370603	25 mg daily
	Protease Inhibitors				
	atazanavir	Reyataz	150, 200, 300 mg capsule	02248610 (150 mg); 02248611 (200 mg); 02294176 (300 mg)	300 mg with 100 mg ritonavir QD
	darunavir	Prezista	600, 800 mg tablets	02324024 (600 mg); 02393050 (800 mg)	600 mg plus 100 mg ritonavir BID or 800/100 mg daily (naive subjects)
	darunavir/cobicistat	Prezcobix	800 mg/150 mg tablet	02426501	1 tablet daily
	lopinavir/ritonavir	Kaletra	200/50 mg tablet 100/25 mg tablet 80mg/20 mg per mL solution	02285533 02312301 02243644	400/100 mg BID or 800/200 mg QD (naïve subjects)
	ritonavir	Norvir	100 mg tablet	02357593	100-200 mg QD/BID as booster

APPENDIX B

COMMONLY USED HIV DRUG INTERACTION WEBSITES

URL	Authors
http://app.hivclinic.ca	Toronto General Hospital
https://www.hivmedicationguide.com/	Centre hospitalier de l'Université de Montréal (CHUM)
https://www.hiv-druginteractions.org	University of Liverpool
http://hivinsite.ucsf.edu/interactions	University of California, San Francisco

*please note: these drug interaction websites generally check for interactions between HIV medications and other drugs. Interactions between combinations of non-HIV drugs are not checked.

A MANAGEMENT TOOL FOR HIV DRUG-DRUG INTERACTIONS

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