A MANAGEMENT TOOL FOR HIV DRUG-DRUG INTERACTIONS

The Canadian HIV/AIDS Pharmacists Network (CHAP)

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 created 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.

Neither CHAP, Toronto General Hospital, St. Michael's Hospital, University of Toronto, Windsor Regional Hospital, Regina General Hospital, Centre Hospitalier de l'Université de Montréal , nor the authors are responsible for deletions or inaccuracies in information or for claims of injury resulting from any such deletions or inaccuracies. Mention of specific drugs, drug doses or drug combinations within this tool does not constitute endorsement by CHAP, the authors or their affiliated institutions.

Acknowledgements:

The development team on behalf of the Canadian HIV/AIDS Pharmacists Network (CHAP) includes:

- Linda Robinson, BSc.Phm., AAHIVE, Windsor Regional Hospital
- Michael Stuber, BSP, Regina General Hospital
- Rachel Therrien, B.Phm., M.Sc., Centre Hospitalier de l'Université de Montréal (CHUM)
- Alice Tseng, Pharm.D., FCSHP, AAHIVP, Toronto General Hospital

and Gordon Arbess, MD, CCFP, Department of Community & Family Medicine, St. Michael's Hospital, Faculty of Medicine, University of Toronto.

Print production of this tool was made possible through an unrestricted educational grant from Merck Canada.

CARDIOVASCULAR DRUGS:
ANTIHYPERTENSIVES AND DIGOXIN

	ACEI	ARBs		BETA-BLOCKERS		CALCIUM CHANNEL BLOCKERS (CCB)	DIURETICS		DIGOXIN
	Benazepril, enalapril, lisinopril, perindopril, ramipril, etc.	Eprosartan, olmesartan, telmisartan, valsartan	Candesartan, irbesartan, losartan	Atenolol, nadolol	Acebutolol, bisoprolol, labetalol, metoprolol, pindolol, propranolol	Amlodipine, diltiazem, felodipine, nifedipine, verapamil	Furosemide, hydrochloro-thiazide, spironolactone	Indapamide	
INTEGRASE INHIBITORS									
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√	√	√
• ELVITEGRAVIR / COBICISTAT (Stribild, Genvoya)	√	√	⚠ Potential for ↑ / ↓ ARB	√	⚠ Potential for ↑ beta-blocker	⚠ Potential for ↑ CCB. Consider 50% dose ↓ or start with lowest dose possible	√	⚠ Potential for ↑ indapamide	⚠ Potential for ↑ digoxin
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√	√	√
PROTEASE INHIBITORS									
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	√	⚠ Potential for ↑ / ↓ ARB	√	⚠ Potential for ↑ beta-blocker	⚠ Potential for ↑ CCB. Consider 50% dose ↓	√	⚠ Potential for ↑ indapamide	⚠ Potential for ↑ digoxin

	ACEI	ARBs		BETA-BLOCKERS		CALCIUM CHANNEL BLOCKERS (CCB)	DIURETICS		DIGOXIN
	Benazepril, enalapril, lisinopril, perindopril, ramipril, etc.	Eprosartan, olmesartan, telmisartan, valsartan	Candesartan, irbesartan, losartan	Atenolol, nadolol	Acebutolol, bisoprolol, labetalol, metoprolol, propranolol, pindolol	Amlodipine, diltiazem, felodipine, nifedipine, verapamil	Furosemide, Hydrochloro-thiazide, spironolactone	Indapamide	
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS									
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	√	⚠ Potential for ↑ / ↓ ARB	√	√	⚠ Potential for ↓ CCB	√	⚠ Potential for ↓ indapamide	√

NOTES

CARDIOVASCULAR DRUGS:
ANTIHYPERTENSIVES AND DIGOXIN

Mechanism of Drug Interactions, Management and Monitoring

	ACEI	ARBs	BETA-BLOCKERS	CALCIUM CHANNEL BLOCKERS (CCB)		DIURETICS	DIGOXIN
MECHANISM OF INTERACTION	Renally cleared	Conversion via 2C9 to active metabolite (losartan), Substrate of 2C9 (candesartan, irbesartan)	Mixed CYP substrates (acebutolol, bisoprolol, labetalol, metoprolol, pindolol, propranolol)	Inhibition of CYP3A4	Induction of CYP3A4	Mixed CYP substrates (indapamide)	Inhibition of P-glycoprotein
MAIN INTERACTING ARVs	No significant interactions predicted	Elvitegravir (induction), efavirez, etravirine (inhibition)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir and most NNRTIs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir
MANAGEMENT	Use standard drug doses	Adjust candesartan, irbesartan, losartan dose according to response/ toxicity. Other ARBs may be used without dose adjustment	Adjust beta-blocker dose according to response/ toxicity. Other beta-blockers (atenolol, nadolol) may be used without dose adjustment.	Consider 50% dose reduction in CCB	Adjust CCB dose according to efficacy/ toxicity	Adjust indapamide dose according to response/ toxicity. Other diuretics may be used without dose adjustment.	Adjust digoxin dose according to response/ toxicity
MONITORING		ARB efficacy and toxicity	Beta-blocker toxicity: heart rate, blood pressure, shortness of breath	CCB toxicity: heart rate, blood pressure, shortness of breath, dizziness	CCB efficacy	Indapamide toxicity: dizziness, headache, hyperglycemia, hypokalemia	Digoxin concentrations, toxicity (arrhythmias, ventricular tachycardia, bradycardia, AV block, anorexia, nausea, blurred/ yellow vision, headache)

CARDIOVASCULAR DRUGS:
ANTIPLATELETS AND ANTICOAGULANTS

	ANTIPLATELETS				ANTICOAGULANTS			
	ASA	CLOPIDOGREL (Plavix)	PRASUGREL (Effient)	TICAGRELOR (Brilinta)	DABIGATRAN (Pradaxa)	RIVAROXABAN (Xarelto)	APIXABAN (Eliquis)	WARFARIN (Coumadin)
INTEGRASE INHIBITORS								
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√	√
• ELVITEGRAVIR / COBICISTAT (Stribild, Genvoya)	√	√	√	X Potential for ↑ ticagrelor and toxicity	⚠ Potential for ↑ dabigatran and toxicity	X Potential for ↑ rivaroxaban and toxicity	X Potential for ↑ apixaban and toxicity	⚠ Potential for ↓ warfarin
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√	√
PROTEASE INHIBITORS								
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	√	√	X Potential for ↑ ticagrelor and toxicity	⚠ Potential for ↑ dabigatran and toxicity	X Potential for ↑ rivaroxaban and toxicity	X Potential for ↑ apixaban and toxicity	⚠ Ritonavir-boosted PIs: potential for ↓ warfarin Cobicistat-boosted PIs: potential for ↑ warfarin concentrations

	ANTIPLATELETS				ANTICOAGULANTS			
	ASA	CLOPIDOGREL (Plavix)	PRASUGREL (Effient)	TICAGRELOR (Brilinta)	DABIGATRAN (Pradaxa)	RIVAROXABAN (Xarelto)	APIXABAN (Eliquis)	WARFARIN (Coumadin)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS								
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	√ Efavirenz, nevirapine ⚠ Etravirine: Potential for ↓ active metabolite of clopidogrel	√	X Potential for ↓ ticagrelor	√	X Potential for ↓ rivaroxaban	X Potential for ↓ apixaban	⚠ Efavirenz, etravirine: potential for ↑ warfarin concentrations Nevirapine: potential for ↓ warfarin concentrations
NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS								
• TENOFOVIR DISOPROXIL (Viread, Truvada, Atripla, Complera, Stribild)	⚠ Potential for renal toxicity with high dose or prolonged ASA use	√	√	√	√	√	√	√

CARDIOVASCULAR DRUGS:
ANTIPLATELETS AND ANTICOAGULANTS

Mechanism of Drug Interactions, Management and Monitoring

	ANTIPLATELETS				NOVEL ORAL ANTICOAGULANTS (NOACS)			WARFARIN	
MECHANISM OF INTERACTION	Inhibition of CYP3A4, P-gp (ticagrelor)	Induction of CYP3A4, P-gp (ticagrelor)	Inhibition of 2C19 (clopidogrel)	Combining nephrotoxic agents (ASA)	Inhibition of CYP3A4, P-gp (rivaroxaban, apixaban)	Induction of CYP3A4, P-gp (rivaroxaban, apixaban)	Inhibition of P-gp (dabigatran)	Induction of CYP2C9	Inhibition of CYP2C9
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs (efavirenz, etravirine, nevirapine)	Etravirine	Tenofovir disoproxil (TDF) containing regimens	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs (efavirenz, etravirine, nevirapine)	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Ritonavir boosted regimens, nevirapine, elvitegravir/ cobicistat	Efavirenz, etravirine
MANAGEMENT	Contraindicated. Prasugrel may be used	Avoid coadministration. Prasugrel may be used	Use with caution. May wish to consider alternatives to clopidogrel, such as prasugrel.	Avoid high-dose or prolonged ASA use if possible. Consider alternate HIV agent, such as abacavir or tenofovir alafenamide (TAF)	Apixaban and rivaroxaban are contraindicated	Avoid use. Consider alternative such as warfarin	Dabigatran monograph advises caution with P-gp inhibitors. Preliminary pharmacokinetic data suggest that a clinically significant interaction may not occur	Increase warfarin dose as needed to maintain therapeutic INR	Decrease warfarin dose as needed to maintain therapeutic INR
MONITORING	Ticagrelor toxicity: dyspnea, headache, epistaxis, chest pain, bleeding events	Ticagrelor efficacy	Antiplatelet activity	Monitor renal function. Assess OTC NSAID use.	Anticoagulant toxicity		Anticoagulant toxicity	Anticoagulant efficacy	Warfarin toxicity: bleeding, dizziness, headache, shortness of breath, hypotension

CARDIOVASCULAR DRUGS:
STATINS

	ATORVASTATIN (Lipitor)	ROSUVASTATIN (Crestor)	PITAVASTATIN (Livalo)	PRAVASTATIN (Pravachol)	LOVASTATIN (Mevacor)	SIMVASTATIN (Zocor)
INTEGRASE INHIBITORS						
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√
• ELVITEGRAVIR / COBICISTAT (Stribild, Genvoya)	⚠ Potential for ↑ statin	√	√	⚠ Potential for ↑ statin	X Potential for ↑ statin and toxicity	
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√
PROTEASE INHIBITORS						
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ Potential for ↑ statin. Use lowest statin dose possible (maximum 20 mg atorvastatin daily)	⚠ Potential for ↑ statin. Use lowest statin dose possible (maximum 10 mg rosuvastatin daily)	√	⚠ Potential for ↑ statin	X Potential for ↑ statin and toxicity	
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS						
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	⚠ Potential for ↓ statin	√	√	√	⚠ Potential for ↓ statin	⚠ Potential for ↓ statin

CARDIOVASCULAR DRUGS:
STATINS

Mechanism of Drug Interactions, Management and Monitoring

HMG-COA REDUCTASE INHIBITORS (Statins)	LOVASTATIN, SIMVASTATIN	ATORVASTATIN, PRAVASTATIN, ROSUVASTATIN	PITAVASTATIN
MECHANISM OF INTERACTION	Inhibition of CYP3A4	Inhibition of CYP3A4, OATP1B1, BCRP	Primarily cleared via UGT, OATP1B1
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	None
MANAGEMENT	Contraindicated. Use alternate statin.	Use lowest statin dose possible and titrate to effect	Most ARVs may be used
MONITORING	Statin toxicity: myalgia, rhabdomyolysis	Statin toxicity: myalgia, rhabdomyolysis	Statin toxicity: myalgia, rhabdomyolysis

NOTES

No dose adjustment required.

Use combination with caution. Adjustment in drug dose or frequency, additional/more frequent monitoring, or use of an alternative agent 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)

	5 ALPHA REDUCTASE INHIBITORS		ALPHA 1 ADRENERGIC RECEPTOR BLOCKERS (non-selective)		ALPHA 1 ADRENERGIC RECEPTOR BLOCKERS (selective)			PDE5 INHIBITORS
	DUTASTERIDE (Avodart)	FINASTERIDE (Proscar)	DOXAZOSIN (Cardura)	TERAZOSIN (Hytrin)	ALFUZOSIN (Xatral)	SILODOSIN (Rapaflo)	TAMSULOSIN (Flomax CR)	TADALAFIL (Cialis) 5 mg daily dose ONLY*
INTEGRASE INHIBITORS								
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√	√
• ELVITEGRAVIR / COBICISTAT (Stribild, Genvoya)	⚠ Potential for ↑ dutasteride	√	⚠ Potential for ↑ doxazosin	⚠ Potential for ↑ terazosin	X Potential for ↑ alfuzosin concentrations and toxicity	⚠ Potential for ↑ silodosin. Use 4 mg dose and monitor for toxicity	⚠ Potential for ↑ tamsulosin. Use 0.4 mg dose and monitor for toxicity	Potential for ↑ tadalafil but dose adjustment not required (*for 5 mg daily dose only)
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√	√
PROTEASE INHIBITORS								
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ Potential for ↑ dutasteride	√	⚠ Potential for ↑ doxazosin	⚠ Potential for ↑ terazosin	X Potential for ↑ alfuzosin concentrations and toxicity	⚠ Potential for ↑ silodosin. Use 4 mg dose and monitor for toxicity	⚠ Potential for ↑ tamsulosin. Use 0.4 mg dose and monitor for toxicity	Potential for ↑ tadalafil but dose adjustment not required (*for 5 mg daily dose only)

	5 ALPHA REDUCTASE INHIBITORS		ALPHA 1 ADRENERGIC RECEPTOR BLOCKERS (non-selective)		ALPHA 1 ADRENERGIC RECEPTOR BLOCKERS (se lective)			PDE5 INHIBITORS
	DUTASTERIDE (Avodart)	FINASTERIDE (Proscar)	DOXAZOSIN (Cardura)	TERAZOSIN (Hytrin)	ALFUZOSIN (Xatral)	SILODOSIN (Rapaflo)	TAMSULOSIN (Flomax CR)	TADALAFIL (Cialis) 5 mg daily dose only*
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS								
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	⚠ Potential for ↓ dutasteride	√	⚠ Potential for ↓ doxazosin	⚠ Potential for ↓ terazosin	⚠ Potential for ↓ drug concentrations			⚠ Potential for ↓ drug concentrations

*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.

NOTES

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

Mechanism of Drug Interactions, Management and Monitoring

	5 ALPHA REDUCTASE INHIBITORS		ALPHA 1 ADRENERGIC BLOCKERS (non-selective)		ALPHA 1 ADRENERGIC BLOCKERS (selective)		PDE5 INHIBITOR TADALAFIL 5 mg daily dose ONLY*
MECHANISM OF INTERACTION	Inhibition of CYP3A4 (dutasteride)	Induction of CYP3A4 (dutasteride)	Inhibition of CYP3A4 (doxazosin, terazosin)	Induction of CYP3A4 (doxazosin, terazosin)	Inhibition of CYP3A4 (alfuzosin, silodosin, tamsulosin)	Induction of CYP3A4 (all)	Inhibition of CYP3A4 (tadalafil)
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs	May be used with all ARVs. *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
MANAGEMENT	Finasteride may be used	Finasteride may be used	Adjust dose according to efficacy/toxicity		Alfuzosin: consider low-dose silodosin or tamsulosin with monitoring or change antiretroviral regimen		Daily tadalafil 5 mg may be used without dose adjustment. May ↓ to 2.5 mg daily based on tolerability
MONITORING	Dutasteride toxicity: erectile dysfunction, decreased libido	Dutasteride efficacy	Toxicity: hypotension, dizziness, headache, asthenia, nasal congestion	Doxazosin & terazosin efficacy	Toxicity: hypotension, dizziness, headache, diarrhea, nasal congestion	Alfuzosin, silodosin, tamsulosin efficacy	Monitor for toxicity: headache, dyspepsia, flushing, back pain, nasal congestion

GENITOURINARY DRUGS:
PDE5 INHIBITORS FOR ERECTILE DYSFUNCTION (ED) OR PULMONARY ARTERIAL HYPERTENSION (PAH)

	TREATMENT OF ERECTILE DYSFUNCTION			TREATMENT OF PULMONARY ARTERIAL HYPERTENSION (PAH)	
	SILDENAFIL (Viagra)	TADALAFIL (Cialis)	VARDENAFIL (Levitra)	SILDENAFIL (Revatio)	TADALAFIL (Adcirca)
INTEGRASE INHIBITORS					
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√
• ELVITEGRAVIR / COBICISTAT (Stribild, Genvoya)	Potential for ↑ sildenafil. Decrease sildenafil dose to 25 mg every 48 hours	⚠ Potential for ↑ tadalafil. Decrease tadalafil dose to 10 mg every 72 hours, maximum 3 times per week	X Potential for ↑ vardenafil and toxicity	X Potential for ↑ sildenafil and toxicity	⚠ Potential for ↑ tadalafil. Start at tadalafil 20 mg daily and titrate to 40 mg daily based on tolerability
• RALTEGRAVIR (Isentress)	√	√	√	√	√
PROTEASE INHIBITORS					
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ Potential for ↑ sildenafil. Decrease sildenafil dose to 25 mg every 48 hours	⚠ Potential for ↑ tadalafil. Decrease tadalafil dose to 10 mg every 72 hours, maximum 3 times per week	X Potential for ↑ vardenafil and toxicity	X Potential for ↑ sildenafil and toxicity	⚠ Potential for ↑ tadalafil. Start at tadalafil 20 mg daily and titrate to 40 mg daily based on tolerability

GENITOURINARY DRUGS:
PDE5 INHIBITORS FOR ERECTILE DYSFUNCTION (ED) OR PULMONARY ARTERIAL HYPERTENSION (PAH)

	TREATMENT OF ERECTILE DYSFUNCTION			TREATMENT OF PULMONARY ARTERIAL HYPERTENSION (PAH)	
	SILDENAFIL (Viagra)	TADALAFIL (Cialis)	VARDENAFIL (Levitra)	SILDENAFIL (Revatio)	TADALAFIL (Adcirca)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS					
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	⚠ Potential for ↓ PDE5 concentrations			⚠ Potential for ↓ PDE5 concentrations	

NOTES

GENITOURINARY DRUGS:
PDE5 INHIBITORS FOR ERECTILE DYSFUNCTION (ED) OR PULMONARY ARTERIAL HYPERTENSION (PAH)

Mechanism of Drug Interactions, Management and Monitoring

	PDE5 INHIBITORS (SILDENAFIL, TADALAFIL, VARDENAFIL)	
MECHANISM OF INTERACTION	Inhibition of CYP3A4	Induction of CYP3A4
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs
MANAGEMENT	**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	Adjust dose according to efficacy/toxicity
MONITORING	PDE5 toxicity: headache, flushing, dyspepsia, nasal congestion, flushing, diarrhea, dizziness	PDE5 efficacy


No dose adjustment required.


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


Contraindicated/avoid combination.

PSYCHOTROPIC DRUGS:
SEDATIVES/HYPNOTICS, ANTIDEPRESSANTS, AND ANTIPSYCHOTICS

	SEDATIVES/HYPNOTICS			ANTIDEPRESSANTS				ANTIPSYCHOTICS		
	Lorazepam, oxazepam, temazepam	Alprazolam, bromazepam, buspirone, clonazepam, estazolam, flurazepam, diazepam, nitrazepam, zolpidem, zopiclone	Midazolam, triazolam	Most TCAs, duloxetine	Bupropion	St. John's wort	Most SSRIs (citalopram, escitalopram, fluoxetine, sertraline), venlafaxine, desvenlafaxine, trazadone, reboxetine, mirtazipine	Aripiprazole, lurasidone, quetiapine, pimozide, paliperidone, risperidone, ziprasidone	Clozapine, olanzapine	Modafinil
INTEGRASE INHIBITORS										
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	⚠ Use dolutegravir 50 mg b.i.d.	√	√	√	X Potential for ↓ antiretroviral, Avoid co-administration
• ELVITEGRAVIR / COBICISTAT (Stribild, Genvoya)	√	⚠ Potential for ↑ benzodiazepine	X Potential for ↑ benzodiazepine	√	√	X Potential for ↓ elvitegravir	⚠ Potential for ↑ antidepressant	⚠ Potential for ↑ antipsychotic Lurasidone & pimozide are contraindicated	⚠ Potential for ↓ antipsychotic	X Potential for ↓ elvitegravir
• RALTEGRAVIR (Isentress)	√	√	√	√	√	Raltegravir may be used without dose adjustment	√	√	√	X Raltegrevir may be used without dose adjustment

	SEDATIVES/HYPNOTICS			ANTIDEPRESSANTS				ANTIPSYCHOTICS		
	Lorazepam, oxazepam, temazepam	Alprazolam, bromazepam, buspirone, clonazepam, estazolam, flurazepam, diazepam, nitrazepam, zolpidem, zopiclone	Midazolam, triazolam	Most TCAs, duloxetine	Bupropion	St. John's wort	Most SSRIs (citalopram, escitalopram, fluoxetine, sertraline), venlafaxine, desvenlafaxine, trazadone, reboxetine, mirtazipine	Aripiprazole, lurasidone, quetiapine, pimozide, paliperidone, risperidone, ziprasidone	Clozapine, olanzapine	Modafinil
PROTEASE INHIBITORS										
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	⚠ Potential for ↑ benzodiazepine	X Potential for ↑ benzodiazepine	√	Cobicistat-boosted PIs: may be used without dose adjustment ⚠ Ritonavir-boosted PIs: potential for ↓ bupropion	X Potential for ↓ PIs	⚠ Potential for ↑ antidepressant	⚠ Potential for ↑ antipsychotic Lurasidone & pimozide are contraindicated	Cobicistat-boosted PIs: may be used without dose adjustment ⚠ Ritonavir-boosted PIs: potential for ↓ antipsychotic	X Potential for ↓ PIs
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS										
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	X Potential for ↓ rilpivirine	√	√	√	X Potential for ↓ rilpivirine

PSYCHOTROPIC DRUGS:
SEDATIVES/HYPNOTICS, ANTIDEPRESSANTS, AND ANTIPSYCHOTICS

	SEDATIVES/HYPNOTICS			ANTIDEPRESSANTS				ANTIPSYCHOTICS		
	Lorazepam, oxazepam, temazepam	Alprazolam, bromazepam, buspirone, clonazepam, estazolam, flurazepam, diazepam, nitrazepam, zolpidem, zopiclone	Midazolam, triazolam	Most TCAs, duloxetine	Bupropion	St. John's wort	Most SSRIs (citalopram, escitalopram, fluoxetine, sertraline), venlafaxine, desvenlafaxine, trazadone, reboxetine, mirtazipine	Aripiprazole, lurasidone, quetiapine, pimozide, paliperidone, risperidone, ziprasidone	Clozapine, olanzapine	Modafinil
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS										
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	⚠ Potential for ↓ benzodiazepine	⚠ Potential for ↓ benzodiazepine	√	Etravirine: may be used without dose adjustment ⚠ Efavirenz, nevirapine: Potential for ↓ bupropion	X Potential for ↓ NNRTI	⚠ Potential for ↓ antidepressant	⚠ Potential for ↓ antipsychotic	√	X Potential for ↓ NNRTI

PSYCHOTROPIC DRUGS:
SEDATIVES/HYPNOTICS, ANTIDEPRESSANTS, AND ANTIPSYCHOTICS

Mechanism of Drug Interactions, Management and Monitoring

	BENZODIAZEPINES			ANTIDEPRESSANTS				ANTIPSYCHOTICS		
MECHANISM OF INTERACTION	Inhibition of CYP3A4 (midazolam, triazolam)	Inhibition of mixed CYP (alprazolam, bromazepam, buspirone, clonazepam, estazolam, eszopiclone, flurazepam, diazepam, nitrazepam, zolpidem, zopiclone)	Lorazepam, oxazepam, temazepam	Inhibition of mixed CYP pathways (citalopram, escitalopram, fluoxetine, sertraline, desvenlafaxine, venlaxafine, trazadone, mirtazipine)	Induction of mixed CYP pathways (fluoxetine, sertraline, trazodone, reboxetine, mirtazapine)	Induction of CYP2B6 (bupropion)	Induction of CYP3A4 (St. John's wort)	Inhibition of mixed CYP pathways (aripiprazole, buspirone, lurasidone, modafinil, quetiapine, pimozide, paliperidone, risperidone, ziprasidone)	Induction of mixed CYP pathways (aripiprazole, buspirone, lurasidone, modafinil, quetiapine, pimozide, paliperidone, risperidone, ziprasidone)	Induction of CYP1A2 (clozapine, olanzapine)
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	May be used with all ARVs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs	Ritonavir-boosted protease inhibitors, efavirenz, nevirapine	Dolutegravir, elvitegravir/ cobicistat, all PIs and NNRTIs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs	Ritonavir-boosted protease inhibitors

PSYCHOTROPIC DRUGS:
SEDATIVES/HYPNOTICS, ANTIDEPRESSANTS, AND ANTIPSYCHOTICS

Mechanism of Drug Interactions, Management and Monitoring

	BENZODIAZEPINES			ANTIDEPRESSANTS				ANTIPSYCHOTICS		
MANAGEMENT	Contraindicated. Use alternate benzodiazepine	Adjust benzodiazepine dose according to response/toxicity. Other benzodiazepines may be used without dose adjustment	May use without dose adjustment	Adjust antidepressant dose according to response/toxicity. Other antidepressants may be used without dose adjustment	Adjust antidepressant dose according to response /toxicity. Other antidepressants may be used without dose adjustment	Adjust antidepressant dose according to response (maximum 300 mg daily)	Contraindicated with most antiretrovirals	Adjust antipsychotic dose according to response/toxicity	Adjust antipsychotic dose according to response	Adjust antipsychotic dose according to response
MONITORING		Benzodiazepine toxicity: ataxia, dizziness, drowsiness, fatigue, muscle weakness, slowed reaction		Antidepressant toxicity: anticholinergic effects, orthostatic hypotension, tachycardia, agitation, headache, somnolence, dizziness, diarrhea, excessive sweating, weight gain	Antidepressant efficacy	Antidepressant efficacy		Antipsychotic toxicity: somnolence, sweating, chest pain, tachycardia, dizziness, insomnia, headache, nausea, diarrhea, dry mouth, numbness, weight gain	Antipsychotic efficacy	Antipsychotic efficacy


No dose adjustment required.


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


Contraindicated/avoid combination.

CONTRACEPTIVES

	COMBINED ORAL CONTRACEPTIVES, PLAN B	DMPA (Depo-Provera)
INTEGRASE INHIBITORS		
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√
• ELVITEGRAVIR / COBICISTAT (Stribild, Genvoya)	⚠ Potential for ↓ ethinyl estradiol and ↑ norgestimate Use OC with minimum 30 mcg ethinyl estradiol	√ May increase progesterone levels
• RALTEGRAVIR (Isentress)	√	√
PROTEASE INHIBITORS		
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz)	⚠ Use OC with minimum 30 mcg ethinyl estradiol for atazanavir plus ritonavir Use OC with maximum 30 mcg ethinyl estradiol for atazanavir without ritonavir No data on use with Atazanavir plus cobicistat	X Not recommended by manufacturer Consider alternate method of contraception
• DARUNAVIR (Prezcobix, Prezista)	X Potential for ↓ ethinyl estradiol and norethindrone Use alternate/additional methods of contraception	√ May increase progesterone levels when used given with cobicistat
• LOPINAVIR (Kaletra)		√

CONTRACEPTIVES

	COMBINED ORAL CONTRACEPTIVES, PLAN B	DMPA (Depo-Provera)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS		
• RILPIVIRINE (Complera, Edurant)	√	√
• EFAVIRENZ (Sustiva, Atripla)	**X** Potential for failure of progesterone component; may need to increase progesterone dose when used for emergency contraception (Plan B)	√
• ETRAVIRINE (Intelence)	√	√
• NEVIRAPINE (Viramune)	⚠ Potential for ↓ ethinyl estradiol and norethindrone Use alternate/additional methods of contraception	√

CONTRACEPTIVES

Mechanism of Drug Interactions, Management and Monitoring

	COMBINED ORAL CONTRACEPTIVES, PLAN B	DMPA	
MECHANISM OF INTERACTION	Induction of CYP3A4, UGT	Inhibition of CYP3A4	Inhibition of CYP3A4
MAIN INTERACTING ARVs	Ritonavir-boosted protease inhibitors, elvitegravir/cobicistat, efavirenz	Atazanavir	Cobicistat-boosted protease inhibitors
MANAGEMENT	Use alternate non-hormonal methods of contraception. Plan B and efavirenz: may need to increase progesterone dose.	Consider alternate methods of contraception	
MONITORING	Monitor for loss of contraceptive efficacy		Monitor for progesterone-related side effects

NOTES


No dose adjustment required.


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


Contraindicated/avoid combination.

ANTIINFECTIVES:
AZOLE ANTIFUNGALS

	FLUCONAZOLE	ITRACONAZOLE	KETOCONAZOLE	POSACONAZOLE	VORICONAZOLE
INTEGRASE INHIBITORS					
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√
• ELVITEGRAVIR/ COBICISTAT (Stribild, Genvoya)	⚠ Potential for ↑ azole concentrations	⚠ Potential for ↑ azole concentrations. Potential for ↑ itraconazole concentrations. Use maximum itraconazole 200 mg daily	⚠ Potential for ↑ azole concentrations. Potential for ↑ ketoconazole concentrations. Use maximum 200 mg ketoconazole daily	⚠ Potential for ↑ azole concentrations	⚠ Potential for ↑ azole concentrations
• RALTEGRAVIR (Isentress)	√	√	√	√	√
PROTEASE INHIBITORS (BOOSTED WITH RITONAVIR OR COBICISTAT)					
• ATAZANAVIR (Evotaz, Reyataz)	√	⚠ Potential for ↑ itraconazole concentrations. Use maximum itraconazole 200 mg daily	⚠ Potential for ↑ ketoconazole concentrations. Use maximum 200 mg ketoconazole daily	⚠ ↑ Atazanavir concentrations. Monitor for toxicity	X Potential for ↓ voriconazole concentrations with ritonavir-boosted PIs and ↑ voriconazole concentrations with cobicistat-boosted PIs
• DARUNAVIR (Prezcobix, Prezista)	√	⚠ Potential for ↑ itraconazole concentrations. Use maximum itraconazole 200 mg daily	⚠ Potential for ↑ ketoconazole concentrations. Use maximum 200 mg ketoconazole daily	⚠ Possible ↑ in darunavir concentrations. Monitor for toxicity	X Potential for ↓ voriconazole concentrations
• LOPINAVIR (Kaletra)	√	⚠ Potential for ↑ itraconazole concentrations. Use maximum itraconazole 200 mg daily	⚠ Potential for ↑ ketoconazole concentrations. Use maximum 200 mg ketoconazole daily	⚠ Possible ↑ in lopinavir concentrations. Monitor for toxicity	X Potential for ↓ voriconazole concentrations

	FLUCONAZOLE	ITRACONAZOLE	KETOCONAZOLE	POSACONAZOLE	VORICONAZOLE
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS					
• RILPIVIRINE (Complera, Edurant)	⚠ Potential for ↑ rilpivirine and ↓ azole concentrations. Use with caution and monitor for rilpivirine toxicity and breakthrough infections	⚠ Potential for ↑ rilpivirine and ↓ azole concentrations. Use with caution and monitor for rilpivirine toxicity and breakthrough infections	⚠ Potential for ↑ rilpivirine and ↓ azole concentrations. Use with caution and monitor for rilpivirine toxicity and breakthrough infections	⚠ Potential for ↑ rilpivirine and ↓ azole concentrations. Use with caution and monitor for rilpivirine toxicity and breakthrough infections	⚠ Potential for ↑ rilpivirine and ↓ azole concentrations. Use with caution and monitor for rilpivirine toxicity and breakthrough infections
• EFAVIRENZ (Sustiva, Atripla)	√	X Potential for ↓ azole concentrations	X Potential for ↓ azole concentrations	X Potential for ↓ azole concentrations	⚠ Potential for ↓ voriconazole and ↑ efavirenz concentrations. ↑ voriconazole to 400 mg q12 hours and ↓ efavirenz to 300 mg daily if therapy lasts more than a few days
• ETRAVIRINE (Intelence)	⚠ Possible ↑ etravirine concentrations. Monitor for side effects of etravirine	⚠ Possible ↑ etravirine and/or ↓ itraconazole concentrations. Consider dose increase of itraconazole	⚠ Possible ↑ etravirine and/or ↓ ketoconazole concentrations. Consider dose increase of ketoconazole	⚠ Possible ↑ etravirine concentrations. Monitor for side effects of etravirine	⚠ Possible ↑ etravirine and voriconazole concentrations. Monitor for side effects of etravirine. May need to dose adjust voriconazole
• NEVIRAPINE (Viramune)	⚠ Possible ↑ nevirapine concentrations. Monitor for adverse effects including hepatotoxicity	X Potential for ↓ azole concentrations	X Potential for ↓ azole concentrations	⚠ Possible ↑ nevirapine concentrations. Monitor for toxicity	X Potential for ↓ azole concentrations

ANTIINFECTIVES:
AZOLE ANTIFUNGALS

Mechanism of Drug Interactions, Management and Monitoring

	FLUCONAZOLE	ITRACONAZOLE, KETOCONAZOLE, POSACONAZOLE		VORICONAZOLE		
MECHANISM OF INTERACTION	Inhibition of CYP3A4	Inhibition of CYP3A4 (antiretrovirals)	Substrate of CYP3A4, induction by most NNRTIs	Induction of CYP2C19 by some antiretrovirals; voriconazole also inhibits CYP3A4.	Inhibition of CYP2C19	Inhibition of CYP3A4 (antiretrovirals and voriconazole)
MAIN INTERACTING ARVS	Rilpivirine, etravirine, nevirapine, elvitegravir/cobicistat	Ritonavir and cobicistat-boosted PIs, elvitegravir/cobicistat	Efavirenz, etravirine, nevirapine	Ritonavir-boosted PIs, efavirenz	Etravirine	Cobicistat-boosted PIs and elvitegravir/cobicistat
MANAGEMENT	Use standard doses of both drugs	Use maximum 200 mg ketoconazole or itraconazole daily	Avoid efavirenz and nevirapine if possible. Use etravirine with caution and consider increasing azole dose if necessary	Ritonavir-boosted PIs: avoid coadministration. Efavirenz: increase voriconazole to 400 mg q12 hours and decrease efavirenz to 300 mg daily.		
MONITORING	Antiretroviral toxicity	Azole toxicity	Azole efficacy	Voriconazole efficacy	Etravirine toxicity	Voriconazole toxicity

ANTIINFECTIVES:
MACROLIDE ANTIBIOTICS

	AZITHROMYCIN	CLARITHROMYCIN	ERYTHROMYCIN
INTEGRASE INHIBITORS			
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√
• ELVITEGRAVIR/ COBICISTAT (Stribild, Genvoya)	√	⚠ Dose adjustment necessary with renal impairment	√
• RALTEGRAVIR (Isentress)	√	√	√
PROTEASE INHIBITORS			
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.:	√	⚠ Dose adjustment necessary	√
• ATAZANAVIR (Evotaz, Reyataz)	√	⚠ Dose adjustment necessary with renal impairment	√
• DARUNAVIR (Prezcobix, Prezista)			
• LOPINAVIR (Kaletra)	√	⚠ Dose adjustment necessary with renal impairment	√

	AZITHROMYCIN	CLARITHROMYCIN	ERYTHROMYCIN
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS			
• RILPIVIRINE (Complera, Edurant)	√	⚠ May increase rilpivirine levels: Potential QT prolongation	⚠ May increase rilpivirine levels: Potential QT prolongation
• EFAVIRENZ (Sustiva, Atripla)	√	⚠ No dose adjustment needed. Potential for ↓ clarithromycin and ↑ 14-OH metabolite concentrations and increased risk of rash	√
• ETRAVIRINE (Intelence)	√	⚠ Potential for ↓ clarithromycin and ↑ 14-OH metabolite concentrations	√
• NEVIRAPINE (Viramune)	√	⚠ Potential for ↓ clarithromycin and ↑ clarithromycin metabolite concentrations. Potential for ↑ nevirapine concentrations	√

ANTIINFECTIVES:
MACROLIDE ANTIBIOTICS

Mechanism of Drug Interactions, Management and Monitoring

	AZITHROMYCIN	CLARITHROMYCIN		CLARITHROMYCIN, ERYTHROMYCIN
MECHANISM OF INTERACTION	Substrate of CYP3A4 (minor)	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.	Induction of CYP3A4 resulting in decreased clarithromycin and increased CLA-14 OH metabolite, which has reduced activity against Mycobacterium avium complex (MAC)	Inhibition of CYP3A4 (clarithromycin, erythromycin)
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted PIs and elvitegravir/cobicistat	Elvitegravir/cobicistat and boosted protease inhibitors	Efavirenz, etravirine, nevirapine	Rilpivirine
MANAGEMENT	Use standard doses of both drugs	**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.	May wish to consider switching to azithromycin, particularly if treating MAC infection	Use with caution
MONITORING	Monitor for QT interval prolongation in patients with other pre-existing risk factors	Monitor patients for signs of clarithromycin toxicity including QT interval prolongation	Clarithromycin efficacy and potential rash	Monitor for QT interval prolongation in patients with other pre-existing risk factors

ANTIINFECTIVES:
MEDICATIONS FOR TUBERCULOSIS

	RIFAMPIN	RIFABUTIN	ISONIAZID	PYRAZINAMIDE	ETHAMBUTOL
INTEGRASE INHIBITORS					
• DOLUTEGRAVIR (Tivicay, Triumeq)	⚠ Decreased dolutegravir. Use dolutegravir 50 mg b.i.d.	√	√	√	√
• ELVITEGRAVIR/ COBICISTAT (Stribild, Genvoya)	X Potential for ↓ elvitegravir	X Potential for ↓ elvitegravir and ↑ rifabutin concentrations	√	√	√
• RALTEGRAVIR (Isentress)	⚠ Decreased raltegravir. Use raltegravir 800 mg b.i.d.	√	√	√	√
PROTEASE INHIBITORS					
• ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	X Potential for ↓ protease inhibitor concentrations	⚠ ↑ Rifabutin concentrations. Use rifabutin 150 mg daily with boosted protease inhibitors	√	√	√

	RIFAMPIN	RIFABUTIN	ISONIAZID	PYRAZINAMIDE	ETHAMBUTOL
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS					
• RILPIVIRINE (Complera, Edurant)	X Potential for ↓ rilpivirine concentrations	⚠ ↓ Rilpivirine concentrations; ↑ to rilpivirine 50 mg daily	√	√	√
• EFAVIRENZ (Sustiva, Atripla)	√	⚠ Potential for ↓ rifabutin concentrations. ↑ to rifabutin 450-600 mg daily or 600 mg three times weekly	√	√	√
• ETRAVIRINE (Intelence)	X Potential for ↓ etravirine concentrations	√	√	√	√
• NEVIRAPINE (Viramune)	X Potential for ↓ nevirapine concentrations	√	√	√	√

ANTIINFECTIVES:
MEDICATIONS FOR TUBERCULOSIS

Mechanism of Drug Interactions, Management and Monitoring

	RIFAMPIN Integrase Inhibitors			RIFABUTIN		
MECHANISM OF INTERACTION	Rifampin is a potent CYP3A4 inducer			Rifabutin is a substrate and moderate inducer of CYP3A4	Induction of CYP3A4 (rifabutin) and inhibition of CYP3A4 (protease inhibitors)	Induction of CYP3A4 (rifabutin and NNRTIs)
MAIN INTERACTING ARVs	Integrase inhibitors: dolutegravir, raltegravir, elvitegravir	Protease inhibitors (atazanavir, darunavir, lopinavir)	NNRTIs: rilpivirine, efavirenz, etravirine, nevirapine	Elvitegravir/cobicistat	All protease inhibitors	NNRTIs: rilpivirine, efavirenz
MANAGEMENT	Increase dolutegravir to 50 mg b.i.d. and consider alternate therapy if patient is integrase inhibitor experienced Increase raltegravir to 800 mg b.i.d. 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 elvitegravir/cobicistat**	**Do not coadminister** Increasing dosage of LPV/r to 800/200 b.i.d. overcomes induction effect of rifampin but may result in intolerable adverse effects	**Do not coadminster with rilpivirine, etravirine or nevirapine** due to failures of antiretroviral therapy **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	Consider increasing cobicistat to 150 mg b.i.d. with elvitegravir 150 mg daily and decrease rifabutin to 150 mg q2 days, but this may not be possible. **Avoid combination. Consider alternate integrase inhibitor if possible**	When administering rifabutin with a protease inhibitor reduce dose to 150 mg daily or 300 mg 3x/week	Increase dose of rilpivirine to 50 mg daily (regular dose 25 mg) Increase rifabutin to 450-600 mg daily or 600 mg 3x/week when given with efavirenz Nevirapine or etravirine may be used without dose adjustment

	RIFAMPIN Integrase Inhibitors			RIFABUTIN		
MONITORING	Watch for virologic breakthrough and efficacy of antiretroviral		Monitor for virologic response and efavirenz drug levels with TDM if available		Rifabutin toxicity	Virologic response to antiretrovirals and antimycobacterial effect of rifabutin

NOTES

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

ACID SUPPRESSING DRUGS

	ANTACIDS Mg, Al or Ca CONTAINING ANTACIDS (Tums, Maalox)	H_2RAs (Famotidine, Nizatidine, Ranitidine)	PROTON PUMP INHIBITORS (PPI) (Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole)	
INTEGRASE INHIBITORS				
• DOLUTEGRAVIR (Tivicay, Triumeq)	⚠ ↓ Dolutegravir	√	√	
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	⚠ ↓ Elvitegravir	√	√	
• RALTEGRAVIR (Isentress)	X ↓ Raltegravir	√	√	
PROTEASE INHIBITORS				
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz)	⚠ ↓ Atazanavir	⚠ ↓ Atazanavir	⚠ ↓ Atazanavir with low dose PPI	X ↓ Atazanavir with high PPI
• DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	√	√	

	ANTACIDS Mg, Al or Ca CONTAINING ANTACIDS (Tums, Maalox)	H_2RAs (Famotidine, Nizatidine, Ranitidine)	PROTON PUMP INHIBITORS (PPI) (Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS			
• RILPIVIRINE (Complera, Edurant)	⚠ ↓ Rilpivirine	⚠ ↓ Rilpivirine	**X** ↓ Rilpivirine
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	√	√

NOTES

ACID SUPPRESSING DRUGS

Mechanism of Drug Interactions and Management

ACID SUPPRESSING DRUGS	ANTACIDS			H_2RAs		PROTON PUMP INHIBITORS
MECHANISM OF INTERACTION	**Integrase Inhibitors:** chelation leading to poor absorption	**Atazanavir:** increase in gastric pH leads to poor absorption	**Rilpivirine:** increase in gastric pH leads to poor absorption	**Atazanavir:** increase in gastric pH leads to poor absorption	**Rilpivirine:** increase in gastric pH leads to poor absorption	**Atazanavir, rilpivirine:** increase in gastric pH leads to poor absorption
MANAGEMENT	**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	**Atazanavir:** Administer 2 hours before or 1 hour after antacids	**Rilpivirine:** Administer antacids at least 2 hours before or 4 hours after rilpivirine	**Atazanavir:** Give simultaneously with or 10 hours after H2RA. If also on tenofovir-containing regimen, increase to atazanavir 400 mg and ritonavir 100 mg in experienced patients.	**Rilpivirine:** Give rilpivirine 4 hours before or 12 hours after H_2RA	**Atazanavir:** Coadministration is not recommended If unavoidable increase atazanavir dose to 400 mg with 100 mg of ritonavir Do not exceed doses of omeprazole 20 mg or comparable **Rilpivirine:** contraindicated with PPIs

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

RECREATIONAL DRUGS
(SEE "ANALGESICS" FOR OPIOID INTERACTIONS AND "PSYCHOTROPICS" FOR BENZODIAZEPINE INTERACTIONS)

	AMYL NITRATE (poppers)	CANNABIS (marijuana)	COCAINE (crack)	AMPHETAMINES (MDMA or Ecstasy, Crystal)	HALLUCINOGENS (LSD and PCP, "angel dust")	GHB ("date rape drug")	Ketamine (Special K)
INTEGRASE INHIBITORS							
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	√	√	⚠ Potential ↑ in levels of recreational drugs. See Management and Monitoring**				
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√
PROTEASE INHIBITORS							
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	√	⚠ Potential ↑ in levels of recreational drugs. See Management and Monitoring**				

RECREATIONAL DRUGS
(SEE "ANALGESICS" FOR OPIOID INTERACTIONS AND "PSYCHOTROPICS" FOR BENZODIAZEPINE INTERACTIONS)

	AMYL NITRATE (poppers)	CANNABIS (marijuana)	COCAINE (crack)	AMPHETAMINES (MDMA or Ecstasy, Crystal)	HALLUCINOGENS (LSD and PCP, "angel dust")	GHB ("date rape drug")	Ketamine (Special K)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS							
• EFAVIRENZ (Atripla, Sustiva) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√		⚠ Potential ↑ in levels of hepatotoxic metabolite	√	√ ↓ Ketamine levels	√	√ ↓ LSD and PCP levels
• RILPIVIRINE (Complera)	√		⚠ Potential QT prolongation	√	√	√	√

NOTES

RECREATIONAL DRUGS
(SEE "ANALGESICS" FOR OPIOID INTERACTIONS AND "PSYCHOTROPICS" FOR BENZODIAZEPINE INTERACTIONS)

Mechanism of Drug Interactions, Management and Monitoring

	STIMULANTS: Cocaine, amphetamines GHB	HALLUCINOGENS: LSD, PCP (angel dust)	KETAMINE
MECHANISM OF INTERACTION	Inhibition of CYP3A4 (cocaine) and CYP 2D6 (amphetamines, GHB?) leading to increased levels of stimulant	Mechanism unclear but potential for inhibition or induction of drug metabolism	Mechanism unclear but potential for inhibition or induction of drug metabolism
MAIN INTERACTING ARVs	Protease Inhibitors (PI) (with ritonavir or cobicistat) & Elvitegravir/cobicistat (Stribild)	PIs & Stribild may increase hallucinogen concentrations. Most NNRTIs may decrease levels	PIs & Stribild may increase ketamine concentrations. Most NNRTIs may decrease levels
MANAGEMENT**	Warn patient of potential for unpredictable increased levels of the recreational substance and provide harm reduction advice	Warn patient of unpredictable increased levels of hallucinogen and provide harm reduction advice	Warn patient of unpredictable increased levels and provide harm reduction advice
MONITORING**	**Toxicity:** Dehydration, dry mouth, teeth grinding, tense jaw, tachycardia **GHB:** seizures, bradycardia, loss of consciousness	**Toxicity:** Hallucinations, psychosis, flashbacks, seizures, hypertension	**Toxicity:** Nausea, vomiting, SOB, loss of coordination, cognitive decline

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

ANALGESICS (PAIN KILLERS)

	NARCOTICS					NON-NARCOTIC ANALGESICS	
	Morphine; Hydromorphone (Dilaudid®) (+heroin and cocaine)	Codeine; Oxycodone (Percocet®); Hydrocodone (Hycodan®)	Methadone	Tramadol	Fentanyl	Acetaminophen (Tylenol) & ASA (Aspirin)	Other Anti-Inflammatory Medications (NSAIDS) E.g.; Aleve, Advil, Motrin, Voltaren, Celebrex
INTEGRASE INHIBITORS							
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild)	√	⚠ ↑ oxycodone ↑ hydrocodone	√	⚠ ↑ tramadol	X ↑ fentanyl*	√	⚠ Increased risk of renal toxicity if combined with Stribild (tenofovir effect)
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√
PROTEASE INHIBITORS (PI)							
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	⚠ ↑ oxycodone ↑ hydrocodone	√	⚠ ↑ tramadol	X ↑ fentanyl* should not be used with CYP3A4 inhibitors unless the patient is very closely monitored and a reduction in fentanyl dose is often required	√	√

	NARCOTICS					NON-NARCOTIC ANALGESICS	
	Morphine; Hydromorphone (Dilaudid®) (+heroin and cocaine)	Codeine; Oxycodone (Percocet®); Hydrocodone (Hycodan®)	Methadone	Tramadol	Fentanyl	Acetaminophen (Tylenol) & ASA (Aspirin)	Other Anti-Inflammatory Medications (NSAIDS) E.g.; Aleve, Advil, Motrin, Voltaren, Celebrex
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI)							
• EFAVIRENZ (Atripla, Sustiva) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	⚠ ↓ Oxycodone ↓ hydrocodone	⚠ Potential for ↓ methadone and withdrawal symptoms (efavirenz, nevirapine)	⚠ ↓ Tramadol	⚠ ↓ Fentanyl	√	⚠ Increased risk of renal toxicity if combined with Atripla or Complera (tenofovir effect)
• RILPIVIRINE (Edurant, Complera)	√	√	√	√	√	√	
NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTI)							
• TENOFOVIR DISOPROXIL (Viread, Truvada, Atripla, Stribild, Complera)	√	√	√	√	√	√	⚠ Increased risk of renal toxicity
• Other NRTIs	√	√	√	√	√	√	√

ANALGESICS (PAIN KILLERS)

Mechanism of Drug Interactions, Management and Monitoring

	MORPHINE DERIVATIVES	CODEINE DERIVATIVES & TRAMADOL & *FENTANYL	METHADONE	NSAIDS
MECHANISM OF INTERACTION	Mostly UGT metabolized; renal elimination	CYP2D6 and 3A4 metabolism Inhibition CYP3A4 Induction	CYP3A4 and 2D6 metabolism induction	Combining nephrotoxic agents
MAIN INTERACTING ARVs	None	Cobicistat and Protease Inhibitors NNRTIs	Efavirenz and Nevirapine	Tenofovir-containing regimens
MANAGEMENT**	None	Possible increases in narcotic levels Possible decrease in narcotic level	Possible decrease in methadone levels potentially leading to withdrawal or loss of pain control	Consider alternative pain control Consider alternative ARV regimen
MONITORING**	None	Monitor for increase opioid side effects; symptoms of overdose *The Duragesic (fentanyl) monograph states: "The concomitant use of CYP3A4 inhibitors and DURAGESIC MAT is not recommended, unless the patient is closely monitored" Monitor pain symptoms and adjust narcotic doses incrementally as needed	Monitor for symptoms of opiate withdrawal or increase in pain and increase methadone dose by 10 mg increments	Monitor Renal function Assess OTC NSAID use

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

ANTICONVULSANTS

	CARBAMAZEPINE (Tegretol)	CLOBAZAM (Frisium)	GABAPENTIN (Neurontin) & PREGABALIN (Lyrica)	LAMOTRIGINE (Lamictal)	LEVETIRACETAM (Keppra)	PHENYTOIN (Dilantin) & PHENOBARBITAL	TOPIRAMATE (Topamax)	VALPROATE (Epival, Depakene)
INTEGRASE INHIBITORS								
• DOLUTEGRAVIR (Tivicay, Triumeq)	⚠ ↓DTG and RAL ↑Dolutegravir dose to 50 mg b.i.d.	√	√	√	√	⚠ ↓DTG and RAL ↑Dolutegravir dose to 50 mg b.i.d.	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	X ↓Elvitegravir concentrations	⚠ Potential ↑ clobazam	√	√	√	X ↓Elvitegravir concentrations	√	√
• RALTEGRAVIR (Isentress)	No guidelines available for raltegravir dose adjustment.	√	√	√	√	No guidelines available for raltegravir dose adjustment.	√	√

ANTICONVULSANTS

	CARBAMAZEPINE (Tegretol)	CLOBAZAM (Frisium)	GABAPENTIN (Neurontin) & PREGABALIN (Lyrica)	LAMOTRIGINE (Lamictal)	LEVETIRACETAM (Keppra)	PHENYTOIN (Dilantin) & PHENOBARBITAL	TOPIRAMATE (Topamax)	VALPROATE (Epival, Depakene)
PROTEASE INHIBITORS								
• Cobicistat-boosted PIs: ATAZANAVIR (Evotaz) DARUNAVIR (Prezcobix)	X ↓ PI concentrations, ↑ carbamazepine concentrations	⚠ Potential ↑ clobazam	√	√	√	X ↓ PI concentrations	√	√
• RITONAVIR (Norvir)-boosted PIs: • ATAZANAVIR (Evotaz,Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ ↑ carbamazepine concentrations potential ↓ PI concentrations (lopinavir, daily darunavir – b.i.d. darunavir OK)	⚠ Potential ↑ clobazam	√	⚠ ↓ lamotrigine concentrations	√	X ↓ PI concentrations unpredictable ↑ or ↓ in anticonvulsant levels		⚠ ↓ valproate concentrations

	CARBAMAZEPINE (Tegretol)	CLOBAZAM (Frisium)	GABAPENTIN (Neurontin) & PREGABALIN (Lyrica)	LAMOTRIGINE (Lamictal)	LEVETIRACETAM (Keppra)	PHENYTOIN (Dilantin) & PHENOBARBITAL	TOPIRAMATE (Topamax)	VALPROATE (Epival, Depakene)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI)								
• RILPIVIRINE (Complera, Edurant)	X ↓ Rilpivirine Phenytoin/ Phenobarbital	√	√	√	√	X ↓ Rilpivirine ++	√	√
• EFAVIRENZ (Sustiva, Atripla) NEVIRAPINE (Viramune) ETRAVIRINE (Intelence)	⚠ ↓ Clobazam Efavirenz/ Nevirapine X ↓ Etravirine Clobazam	⚠ Potential ↓ Clobazam ** Etravirine	√	⚠	√	⚠ Potential ↓ nevirapine and/or anticonvulsants X ↓ Efavirenz, Etravirine ++	√	√

ANTICONVULSANTS

Mechanism of Drug Interactions, Management, and Monitoring

	GABAPENTIN, PREGABALIN, TOPIRAMATE, LEVETIRACETAM	CARBAMAZEPINE	PHENOBARBITAL, PHENYTOIN	LAMOTRIGINE, VALPROATE	CLOBAZAM
MECHANISM OF INTERACTION	Primarily excreted unchanged in urine	CYP3A4 substrate and inducer of CYP3A, 2C19, UGT. Potential for decreased antiretrovirals or increased carbamazepine	Substrate of 2C9, 2C19 and potent inducers of CYP3A4, 2C9/19, UGT. Potential for decreased antiretrovirals or decreased anticonvulsants	Primarily cleared via UGT Lamotrigine: mild UGT inducer Valproate: Inhibitor of UGT, CYP2C9/19	CYP3A4 substrate. Potential for increased clobazam with boosted regimens and decreased concentrations with NNRTIs
MAIN INTERACTING ARVs	None	Ritonavir and cobicistat-boosted protease inhibitors or elvitegravir, dolutegravir, raltegravir, rilpivirine	Ritonavir and cobicistat-boosted protease inhibitors or elvitegravir, dolutegravir, raltegravir, rilpivirine, efavirenz	Potential for decreased anticonvulsants due to UGT induction by ritonavir-boosted PIs and efavirenz	Ritonavir and cobicistat-boosted protease inhibitors or elvitegravir, Most NNRTIs (efavirenz, etravirine, nevirapine)
MANAGEMENT	None	Avoid with cobicistat-boosted PIs, rilpivirine, and elvitegravir/cobicistat. May need to reduce carbamazepine dose with ritonavir-boosted PIs Increase dolutegravir to 50 mg b.i.d.; use raltegravir with caution	Avoid these anticonvulsants if others are available and efficacious Increase dolutegravir to 50 mg b.i.d.; use raltegravir with caution	May have to increase dose of anticonvulsant if ARV regimen cannot be changed and/or if there is no other suitable anticonvulsant	Boosted regimens may increase clobazam and risk of toxicity, NNRTIs may decrease clobazam
MONITORING	None	Antiretroviral efficacy Carbamazepine concentrations and toxicity (somnolence,dizziness)	Antiretroviral efficacy Monitor for CBZ toxicity, loss of seizure control	Monitor for loss of seizure control	Monitor for signs of toxicity and reduce dose if necessary Monitor for loss of seizure control

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

HEPATITIS C TREATMENT

	DIRECT-ACTING AGENTS				OLDER TREATMENTS	
	Ledipasvir + Sofosbuvir (Harvoni)	Ombitasvir/ Paritaprevir/r +/-Dasabuvir (Holkira, Technivie)	Sofosbuvir (Sovaldi)	Daclatasvir (Daklinza)	Pegylated Interferon alpha 2a	Ribavirin
INTEGRASE INHIBITORS						
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genyova)	⚠ Potential: ↑ Tenofovir	X Potential increase in elvitegravir or paritaprevir	√	⚠ Potential: ↑ Daclatasvir Reduce dose to 30 mg daily	√	√
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√
PROTEASE INHIBITORS (PI)						
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ Potential: ↑ Tenofovir	X Ok with ATV 300 mg and possibly unboosted DRV but TDM of ARV levels highly suggested	√	⚠ ↑ Daclatasvir with boosted atazanavir; Reduce dose to 30 mg daily √ (darunavir, lopinavir)	√	√

HEPATITIS C TREATMENT

	DIRECT-ACTING AGENTS				OLDER TREATMENTS	
	Ledipasvir + Sofosbuvir (Harvoni)	Ombitasvir/ Paritaprevir/r +/-Dasabuvir (Holkira, Technivie)	Sofosbuvir (Sovaldi)	Daclatasvir (Daklinza)	Pegylated Interferon alpha 2a	Ribavirin
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI)						
• EFAVIRENZ (Atripla, Sustiva)	⚠ ↑ Tenofovir when using Atripla	X	√	⚠ ↓ Daclatasvir Increase dose to 90 mg daily	√	√
• ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)				X Etravirine and nevirapine ↓ Daclatasvir Levels +++		
• RILPIVIRINE (Edurant, Complera)	⚠ ↑ Tenofovir when using Complera	X ↑ Rilpivirine ++ Potential QT prolongation	√	√	√	√

	DIRECT-ACTING AGENTS				OLDER TREATMENTS	
	Ledipasvir + Sofosbuvir (Harvoni)	Ombitasvir/ Paritaprevir/r +/-Dasabuvir (Holkira, Technivie)	Sofosbuvir (Sovaldi)	Daclatasvir (Daklinza)	Pegylated Interferon alpha 2a	Ribavirin
NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTI)						
• TENOFOVIR DISOPROXIL (Viread, Truvada, Atripla, Stribild, Complera)	⚠ ↑ Tenofovir	√	√	√	√	√
• OTHER NRTIs e.g:. ABACAVIR (Ziagen or Kivexa), LAMIVUDINE, EMTRICITABINE, ZIDOVUDINE (Retrovir, Combivir)	√	√	√	√	√ Abacavir and Tenofovir and FTC and 3TC ok	
• ZIDOVUDINE (Retrovir, Combivir)	√	√	√	√	X Zidovudine Didanosine Stavudine	

HEPATITIS C TREATMENT

Mechanism of Drug Interactions, Management and Monitoring

	LEDIPASVIR + SOFOSBUVIR (HARVONI)	OMBITASVIR/PARITAPREVIR/R +/-DASABUVIR (HOLKIRA PAK) (TECHNIVIE)	DACLATASVIR (DAKLINZA)	PEGYLATED INTERFERON ALPHA 2A & RIBAVIRIN
MECHANISM OF INTERACTION	Ledipasvir is a mild inhibitor of PgP, BCRP, OATP1B1 and OATP1B2	Ritonavir boost already present. Combinations with CYP, PgP inhibitors and inducers will lead to unpredictable drug levels for all	Substrate of P-glycoprotein and CYP3A4	
MAIN INTERACTING ARVs	Boosted PIs, elvitegravir/cobicistat and NNRTIs when combined with tenofovir Increased tenofovir levels can potentially lead to renal toxicity	PIs, Efavirenz /Nevirapine Rilpivirine	Cobicistat PIs NNRTIs	Contraindicated with zidovudine due to increased toxicity
MANAGEMENT**	If pre-existing renal compromise, consider switching to non-tenofovir backbone or regimen. Otherwise, monitor renal function closely	Avoid with all boosted PIs or integrase inhibitors boosted with ritonavir or cobicistat. Avoid with all NNRTIs Best to combine with dolutegravir or raltegravir based regimens	Adjust daclatasvir dose accordingly. Best combined with dolutegravir-, raltegravir- or rilpivirine-based regimens.	

	LEDIPASVIR + SOFOSBUVIR (HARVONI)	OMBITASVIR/PARITAPREVIR/R +/-DASABUVIR (HOLKIRA PAK) (TECHNIVIE)	DACLATASVIR (DAKLINZA)	PEGYLATED INTERFERON ALPHA 2A & RIBAVIRIN
MONITORING**	Monitor renal function when used with tenofovir: eGFR, serum creatinine and phosphate; urine creatinine and phosphate if assessing tubular damage	If adding unboosted atazanavir or darunavir, suggest measuring antiretroviral concentrations		

NOTES

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

DIABETES MEDICATIONS
ANTIHYPERGLYCEMIC DRUGS

	α GLUCOSIDASE INHIBITORS	BIGUANIDES	DPP-4 INHIBITORS			HUMAN GLUCAGON-LIKE PEPTIDE (GLP-1 AGONISTS)	
	Acarbose (Prandase, Glucobay)	Metformin (Glucophage, Glumetza, Avandamet, Janumet)	Linagliptin (Trajenta)	Saxagliptin (Onglyza) Saxagliptin/metformin (Kombiglyze)	Sitagliptin (Januvia) Sitagliptin/metformin (Janumet)	Exenatide (Byetta)	Liraglutide (Victoza)
INTEGRASE INHIBITORS							
• ELVITEGRAVIR/ COBICISTAT (Stribild, Genvoya)	√	√	√	√	√	√	√
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	⚠ ↑ Metformin	√	√	√	√	√
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√
PROTEASE INHIBITORS							
• DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	√	√	√	√	√	⚠ Potential for additive PR prolongation

	α GLUCOSIDASE INHIBITORS	BIGUANIDES	DPP-4 INHIBITORS			HUMAN GLUCAGON-LIKE PEPTIDE (GLP-1 AGONISTS)	
	Acarbose (Prandase, Glucobay)	Metformin (Glucophage, Glumetza, Avandamet, Janumet)	Linagliptin (Trajenta)	Saxagliptin (Onglyza) Saxagliptin/metformin (Kombiglyze)	Sitagliptin (Januvia) Sitagliptin/metformin (Janumet)	Exenatide (Byetta)	Liraglutide (Victoza)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS							
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√	⚠ Potential for additive PR prolongation
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	√	⚠ Potential for ↓ linagliptin	⚠ Potential ↓ saxagliptin	√	√	√

DIABETES MEDICATIONS
ANTIHYPERGLYCEMIC DRUGS

	MEGLITINIDES		SGLT2 INHIBITORS		SULFONYLUREAS	THIAZOLIDINEDIONES (TZDS)	
	Repaglinide (GlucoNorm)	Nateglinide (Starlix)	Canagliflozin (Invokana)	Dapagliflozin (Forxiga), empagliflozin (Jardiance)	Gliclazide (Diamicron) Glimepiride (Amaryl) Glyburide (Diabeta)	Pioglitazone (Actos)	Rosiglitazone (Avandia) Rosiglitazone/Metformin (Avandamet)
INTEGRASE INHIBITORS							
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√
• ELVITEGRAVIR/ COBICISTAT (Stribild, Genvoya)	⚠ Potential ↑ repaglinide	⚠ Potential ↓ nateglinide	√	√	⚠ Potential ↓ sulfonyurea	√	√
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√
PROTEASE INHIBITORS							
• RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ Potential ↑ repaglinide	⚠ Potential ↓/↑ nateglinide concentrations	⚠ Potential ↓ canagliflozin with ritonavir-boosted PIs	√	⚠ Potential ↓ sulfonyurea with ritonavir-boosted PIs	⚠ Potential ↑ pioglitazone	⚠ Potential ↑ rosiglitazone with atazanavir alone with 2C8 inhibition
			√ Cobicistat-boosted PIs: no interaction expected		√ Cobicistat-boosted PIs: no interaction expected	√	√

	MEGLITINIDES		SGLT2 INHIBITORS		SULFONYLUREAS	THIAZOLIDINEDIONES (TZDS)	
	Repaglinide (GlucoNorm)	Nateglinide (Starlix)	Canagliflozin (Invokana)	Dapagliflozin (Forxiga), empagliflozin (Jardiance)	Gliclazide (Diamicron) Glimepiride (Amaryl) Glyburide (Diabeta)	Pioglitazone (Actos)	Rosiglitazone (Avandia) Rosiglitazone/Metformin (Avandamet)
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS							
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	⚠ Potential ↓ repaglinide	⚠ Potential ↑ nateglinide with etravirine and efavirenz	⚠ Potential ↓ canagliflozin with efavirenz	√	⚠ Potential ↑ sulfonyurea with etravirine and efavirenz	⚠ Potential ↓ pioglitazone	√

Mechanism of Drug Interactions, Management and Monitoring

	METFORMIN	DPP-4 INHIBITORS		MEGLITINIDES		
MECHANISM OF INTERACTION	**Metformin:** excreted 100% as unchanged drug by glomerular filtration plus active tubular secretion via OCT2 and MATE-1-2K	**Linagliptin:** inhibition of CYP3A4 and P-gp **Saxagliptin:** inhibition of CYP3A4	**Linagliptin, saxagliptin:** induction of CYP3A4/P-gp	**Repaglinide:** inhibition OATP1B1 and CYP3A4	**Nateglinide:** induction CYP2C9	**Nateglinide:** inhibition CYP2C9
MAIN INTERACTING ARVs	Dolutegravir	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Elvitegravir	Efavirenz, etravirine
MANAGEMENT	Close monitoring is recommended when starting or stopping dolutegravir and metformin together If patient is already receiving dolutegravir, start with a low metformin dose and gradually increase. If patient is starting/stoping dolutegravir while receiving metformin, a dose adjustment may be necessary Choose an alternative antidiabetic agent or antiretroviral if high-dose metformin is not tolerated with dolutegravir, if it is considered necessary	May not be clinically significant, since linagliptin and saxagliptin have a large safety window No dose adjustment necessary	Adjust linagliptin and saxagliptin doses if needed	Adjust dose if needed	Adjust dose if needed	Adjust dose if needed
MONITORING	Metformin side effects (primarily gastrointestinal)	No monitoring suggested	Close monitoring of efficacy	Close monitoring of side effects	Antihyperglycemic efficacy	Close monitoring of side effects. May potentiate the hypoglycemic action

DIABETES MEDICATIONS
ANTIHYPERGLYCEMIC DRUGS

Mechanism of Drug Interactions, Management and Monitoring

	SGLT2 INHIBITORS	SULFONYLUREAS		THIAZOLIDINEDIONES		
MECHANISM OF INTERACTION	**Canagliflozin:** induction UGT	**Gliclazide, glimepiride and glyburide:** 2C9 induction	**Gliclazide, glimepiride and glyburide:** 2C9 inhibition	**Pioglitazone:** 3A4 inhibition	**Pioglitazone:** 3A4 induction	**Rosiglitazone:** 2C8 inhibition
MAIN INTERACTING ARVs	Ritonavir protease inhibitors boosted and efavirenz	Ritonavir PIs boosted Elvitegravir	Efavirenz and etravirine	Ritonavir and cobicistat PIs boosted Cobicistat elvitegravir boosted	Efavirenz, nevirapine and etravirine	Unboosted atazanavir
MANAGEMENT	Adjust dose as needed	Adjust dose as needed	Adjust dose as needed	Adjust dose as needed	Adjust dose as needed	Adjust dose as needed
MONITORING	Antihyperglycemic efficacy	Antihyperglycemic efficacy	Sulfonylurea side effects	Pioglitazone side effects	Antihyperglycemic efficacy	Rosiglitazone side effects

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

CORTICOSTEROID INTERACTIONS
(INHALED, INTRANASAL, INJECTABLE)

	INTRANASAL OR ORAL INHALATION					INJECTABLE
	Beclomethasone (Qvar) (Beconase)	Budesonide (Pulmicort/Symbicort) (Rhinocort)	Ciclesonide (Alvesco)	Fluticasone (Flovent/Advair) (Flonase/Avamys)	Mometasone (Asmanex/Zenhale) (Nasonex)	Triamcinolone
INTEGRASE INHIBITORS						
• DOLUTEGRAVIR (Tivicay, Triumeq)	√					√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	√	⚠ Potential ↑ systemic budesonide and risk of Cushing's syndrome and adrenal failure See management and monitoring	⚠ Potential ↑ ciclesonide. May be used with monitoring	X Potential ↑ systemic fluticasone and risk of Cushing's syndrome and adrenal failure Avoid combination	⚠ Potential ↑ systemic mometasone and risk of Cushing's syndrome and adrenal failure	⚠ Potential ↑ systemic triamcinolone and risk of Cushing's syndrome and adrenal failure
• RALTEGRAVIR (Isentress)	√					√

	INTRANASAL OR ORAL INHALATION					INJECTABLE
	Beclomethasone (Qvar) (Beconase)	Budesonide (Pulmicort/Symbicort) (Rhinocort)	Ciclesonide (Alvesco)	Fluticasone (Flovent/Advair) (Flonase/Avamys)	Mometasone (Asmanex/Zenhale) (Nasonex)	Triamcinolone
PROTEASE INHIBITORS						
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Evotaz, Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	⚠ Potential ↑ systemic budesonide and risk of Cushing's syndrome and adrenal failure See management and monitoring	⚠ Potential increased ciclesonide. May be used with monitoring	X Potential ↑ systemic fluticasone and risk of Cushing's syndrome and adrenal failure. Avoid combination.	⚠ Potential ↑ systemic mometasone and risk of Cushing's syndrome and adrenal failure	⚠ Potential ↑ systemic triamcinolone and risk of Cushing's syndrome and adrenal failure
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS						
• EFAVIRENZ (Atripla, Sustiva) • ETRAVIRINE (Intelence) • RILPIVIRINE (Complera) • NEVIRAPINE (Viramune)	√					√

CORTICOSTEROID INTERACTIONS
(INHALED, INTRANASAL, INJECTABLE)

Mechanism of Drug Interactions, Management and Monitoring

	BUDESONIDE FLUTICASONE, MOMETASONE (INHALED OR INTRANASAL)	CICLESONIDE (INHALED)	TRIAMCINOLONE INJECTION
MECHANISM OF INTERACTION	Inhibition of CYP3A4	Inhibition CYP3A4 of the active metabolite of the ciclesonide. Potential but does not seem to be clinically significant	Inhibition of CYP3A4
MAIN INTERACTING ARVs	Protease inhibitors (PI) with ritonavir or cobicistat, elvitegravir/cobicistat (Stribild)	Protease inhibitors (PI) with ritonavir or cobicistat, elvitegravir/cobicistat (Stribild)	Protease inhibitors (PI) with ritonavir or cobicistat, elvitegravir/cobicistat (Stribild)
MANAGEMENT	Prefer beclomethasone which does not interact because it is not metabolized by CYP3A4	Use with caution	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
MONITORING	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	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	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

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

CHEMOTHERAPY DRUGS

	BLEOMYCIN	CARBOPLATIN CISPLATIN CYTARABINE	CYCLOPHOSPHAMIDE	DACARBAZINE	DEXAMETHASONE	DOXORUBICIN	GEMCITABINE
INTEGRASE INHIBITORS							
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	√	√	⚠ ↑ Cyclophosphamide	√	⚠ ↑ Dexamethasone, potential for ↓ elvitegravir if chronic dexamethasone; intermittent dexamethasone is OK	⚠ ↑ Antineoplastic and cytotoxic properties	√
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√
PROTEASE INHIBITORS							
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	√	⚠ ↑ Cyclophosphamide	√	⚠ ↑ Dexamethasone, potential for ↓ protease inhibitor if chronic dexamethasone; intermittent dexamethasone is OK	⚠ ↑ Antineoplastic and cytotoxic properties	√

CHEMOTHERAPY DRUGS

	BLEOMYCIN	CARBOPLATIN CISPLATIN CYTARABINE	CYCLOPHOSPHAMIDE	DACARBAZINE	DEXAMETHASONE	DOXORUBICIN	GEMCITABINE
NNRTIs							
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√ Potential for ↓ rilpivirine if chronic dexamethasone; intermittent dexamethasone is OK	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	√	⚠ ↑ Cyclophosphamide neurotoxic metabolite	√	⚠ ↓ Dexamethasone	⚠ ↑ Antineoplastic and cytotoxic properties	√
NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS							
• TENOFOVIR DISOPROXIL (Viread, Truvada, Atripla, Complera, Stribild)	√	⚠ ↑ Renal toxicity	√	√	√	√	√

CHEMOTHERAPY DRUGS

	ETOPOSIDE	IFOSPHAMIDE	MELPHALAN, MESNA, METHOTREXATE, MELPHALAN	METHYLPREDNISOLONE, PREDNISONE	PROCARBAZINE	VINCRISTINE, VINBLASTINE
INTEGRASE INHIBITORS						
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	⚠ ↑ Etoposide	⚠ ↓ Ifosphamide activation	√	⚠ ↑ Steroid	√	⚠ ↑ Vinca alkaloid and risk of toxicity
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√
PROTEASE INHIBITORS						
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ ↑ Etoposide	⚠ ↓ Ifosphamide activation	√	⚠ ↑ Steroid	⚠ Possible ↑ active metabolite with ritonavir boosted PIs	⚠ ↑ Vinca alkaloid and risk of toxicity

CHEMOTHERAPY DRUGS

	ETOPOSIDE	IFOSPHAMIDE	MELPHALAN, MESNA, METHOTREXATE, MELPHALAN	METHYLPREDNISOLONE, PREDNISONE	PROCARBAZINE	VINCRISTINE, VINBLASTINE
NNRTIs						
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	⚠ ↓ Etoposide	⚠ ↑ Ifosphamide activation and potentially more neurotoxic metabolites	√	⚠ ↓ Steroid	√	⚠ Potential ↓ vinca alkaloid

CHEMOTHERAPY DRUGS

Mechanism of Drug Interactions, Management and Monitoring

	CYCLOPHOSPHAMIDE		CISPLATIN, CYTARABINE, CARBOPLATIN	DEXAMETHASONE		
MECHANISM OF INTERACTION	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 increase the active metabolite	Induction of CYP 3A4 may increase toxic metabolite	Potential additive toxicity with other agents such as tenofovir (renal toxicity)	Possibility of increased dexamethasone levels with CYP3A4 inhibitors	Possibility of decreased levels with CYP3A4 inducers	Induction of CYP3A4 (dexamethasone)
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	Tenofovir	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	PIs, NNRTIs, elvitegravir/ cobicistat, rilpivirine
MANAGEMENT	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring of the renal function or consider replacing tenofovir	No dose adjustment suggested	No dose adjustment suggested	Pulse dosing of dexamethasone is OK. Daily/chronic dexamethasone may decrease antiretroviral drugs and should be avoided if possible
MONITORING	Close monitoring of side effects	Close monitoring of side effects (neurotoxicity)	Close monitoring of the renal function (creatine, urine analysis)	Close monitoring of side effects		

CHEMOTHERAPY DRUGS

Mechanism of Drug Interactions, Management and Monitoring

	DOXORUBICINE		ETOPOSIDE		IFOSPHAMIDE	
MECHANISM OF INTERACTION	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	Enzyme inductors may increased reduction to free radicals via induction of cytochrome P450 which may increase both antineoplastic and cytotoxic properties	Possibility of increased levels with CYP3A4 inhibitors	Possibility of decreased levels with CYP3A4 inducers	Inhibition of CYP 3A4 may inhibit drug activation	Induction of CYP 3A4 may increase activation of ifosfamide but may also produce more potentially neurotoxic metabolites
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Éfavirenz, etravirine, névirapine	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine
MANAGEMENT	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents
MONITORING	Close monitoring efficacy and side effects	Close monitoring efficacy and side effects	Close monitoring of side effects (mucositis, myelosuppression and transaminitis)	Close monitoring of efficacy	Close monitoring of efficacy	Close monitoring of efficacy and side effects (neurotoxicity)

	METHYLPREDNISOLONE, PREDNISONE		PROCARBAZINE	VINBLASTINE, VINCRISTINE	
MECHANISM OF INTERACTION	Possible increased level with CYP3A4 inhibitors	Possible decreased level with CYP3A4 inducers	Possible increase of the metabolite active of procarbazine with ritonavir-boosted PI (CYP2B6, 1A) induction.	Possible increased level with CYP3A4 inhibitors	Possible decreased level with CYP3A4 inducers
MAIN INTERACTING ARVs	Ritonavir- and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	Ritonavir-boosted protease inhibitors	Ritonavir- and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine
MANAGEMENT	Not well studied. Dose modification could be suggested	Not well studied. Dose modification could be suggested	Not well studied. No dose adjustment suggested	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents
MONITORING	Close monitoring of corticosteroids side effects	None. Steroid efficacy?	None	Close monitoring of side effects (peripheral and autonomic neuropathy, myelosuppression)	Close monitoring of efficacy

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

MISCELLANEOUS DRUGS

	COLCHICINE	ERGOT ALKALOIDS (dihydroergotamine, ergonovine, ergotamine, methylergonovine, such as Cafergot, Migranal, D.H.E. 45*, Ergotrate, Methergine*, Migergot*, Ergomar*, and others)
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	⚠ Potential for ↑ colchicine	X Potential for ↑ ergot
	X Combination contraindicated in renal or hepatic impairment.	
• RALTEGRAVIR (Isentress)	√	√
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ Potential for ↑ colchicine	X Potential for ↑ ergot
	X Combination contraindicated in renal or hepatic impairment.	
• RILPIVIRINE (Complera, Edurant)	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	⚠ Potential for ↓ colchicine	⚠ Potential for ↓ ergot

Mechanism of Drug Interactions, Management and Monitoring

	COLCHICINE		ERGOT ALKALOIDS	
MECHANISM OF INTERACTION	Inhibition of P-gp, CYP3A4	Induction of P-gp, CYP3A4	Inhibition of CYP3A4	Induction of CYP3A4
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs	Ritonavir and cobicistat-boosted protease inhibitors and elvitegravir	Most NNRTIs
MANAGEMENT	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 daily or every other day For treatment of familial Mediterranean fever: Do not exceed colchicine 0.6 mg daily or 0.3 mg b.i.d. **Combination is contraindicated in patients with renal or hepatic impairment. Life-threatening and fatal colchicine toxicity has been reported in such situations**	Do not exceed maximum recommended dose of colchicine: • Gout flares: 1.8 mg over 1 hour period • Familial Mediterranean fever: 2.4 mg daily	**Coadministration is contraindicated**	Do not exceed maximum recommended dose of ergot alkaloid

Mechanism of Drug Interactions, Management and Monitoring

	COLCHICINE		ERGOT ALKALOIDS	
MONITORING	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.	Colchicine efficacy and toxicity	Ergot toxicity: arterial vasoconstriction, peripheral vascular ischemia, gangrene	Ergot efficacy and toxicity

NOTES

√ No dose adjustment required.

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

X Contraindicated/avoid combination.

NOTES

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	Atripla	600/200/300 mg tablet	02300699	1 tablet daily
	Emtricitabine/ rilpivirine/ tenofovir	Complera	200/25/300 mg tablet	02374129	1 tablet daily
	Elvitegravir/ cobicistat/ emtricitabine/ tenofovir alafenamide	Genvoya	150/150 mg/200/10 mg tablet	02449498	1 tablet daily
	Elvitegravir/ cobicistat/ emtricitabine/ tenofovir	Stribild	150/150 mg/200/300 mg tablet	02397137	1 tablet daily
	Abacavir/ dolutegravir/ lamivudine	Triumeq	abacavir 600 mg, dolutegravir 50 mg and lamivudine 300 mg	02430932	1 tablet daily
INTEGRASE INHIBITORS					
	Dolutegravir	Tivicay	50 mg tablet	02414945	50 mg daily (naïve) or b.i.d. (experienced)
	Raltegravir	Isentress	400 mg tablet	02301881	400 mg b.i.d.
NRTIS: COMBINATION PRODUCTS					
	Abacavir, lamivudine	Kivexa	600/300 mg tablet	02269341	50 mg 1 tablet daily
	Tenofovir, emtricitabine	Truvada	300/200 mg tablet	02274906	1 tablet daily

NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS					
	Tenofovir	Viread	300 mg tablet	02247128	300 mg daily
NNRTIS (NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS)					
	Efavirenz	Sustiva	600 mg tablet	02246045	600 mg daily
	Etravirine	Intelence	200 mg tablet	02375931	200 mg b.i.d.
	Nevirapine	Viramune XR	400 mg tablet	02367289	200 mg daily x 14 days, then 400 mg
	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 daily
	Atazanavir/ cobicistat	Evotaz	300 mg/150 mg tablet	02446731	1 tablet daily
	Darunavir	Prezista	600, 800 mg tablets	02324024 (600 mg); 02393050 (800 mg)	600 mg plus 100 mg ritonavir b.i.d. or 800/100 mg daily for naïve subjects
	Darunavir/ cobicistat	Prezcobix	800 mg/150 mg tablet	02426501	1 tablet daily
	Lopinavir/ ritonavir	Kaletra	200/50 mg tablet	022285533	400/100 mg b.i.d. or 800/200 mg daily (naïve subjects)
	Ritonavir	Norvir	100 mg tablet	02357593	100–200 mg daily/b.i.d. as booster

APPENDIX B:
COMMONLY USED HIV DRUG INTERACTION WEBSITES

URL	AUTHORS
http://app.hivclinic.ca	Toronto General Hospital
www.hivmedicationguide.com	Centre hospitalier de l'Université de Montréal (CHUM)
www.hiv-druginteractions.org	University of Liverpool
http://hivinsite.ucsf.edu/insite?page=ar-00-02	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

Printed with the assistance of an unrestricted educational grant from:

MERCK