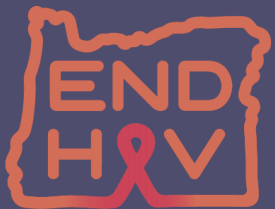


Approach to Antiretroviral Drug Interactions

Devon Flynn, PharmD, MPH, BCPS, AAHIVP
HIV Clinic Pharmacist, OHSU
Faculty, Oregon AETC



Disclosures

- none

What words come to mind
when you hear or see something
about antiretroviral drug
interactions?

Goals

- Review types of drug-drug interactions
- Identify common classes of non-ARV medications involved in drug interactions with ARVs
- Discuss the approach to assessment and management of interactions
- Identify resources to check for ARV-drug interaction information

FO

- FO is a 39 yr old person with HIV
 - She presents to pick up the following:
 - Abacavir / lamivudine / dolutegravir (Triumeq) 1 tab daily - refill
 - Prenatal vitamin 1 tab daily – new Rx per OB
 - Ferrous sulfate 325 mg 1 tab every other day – new Rx per OB
 - She also asks for advice for something for heartburn that has been bothering her more often
- ▶ What interaction(s) concern is/are there?
 - ▶ What are options to address any interaction(s)?

Types of Drug-Drug Interactions

- **Overlapping Toxicities**

- QT prolongation
- Nephrotoxicity
- Metabolic effects
- Hepatotoxicity
- Myelosuppression

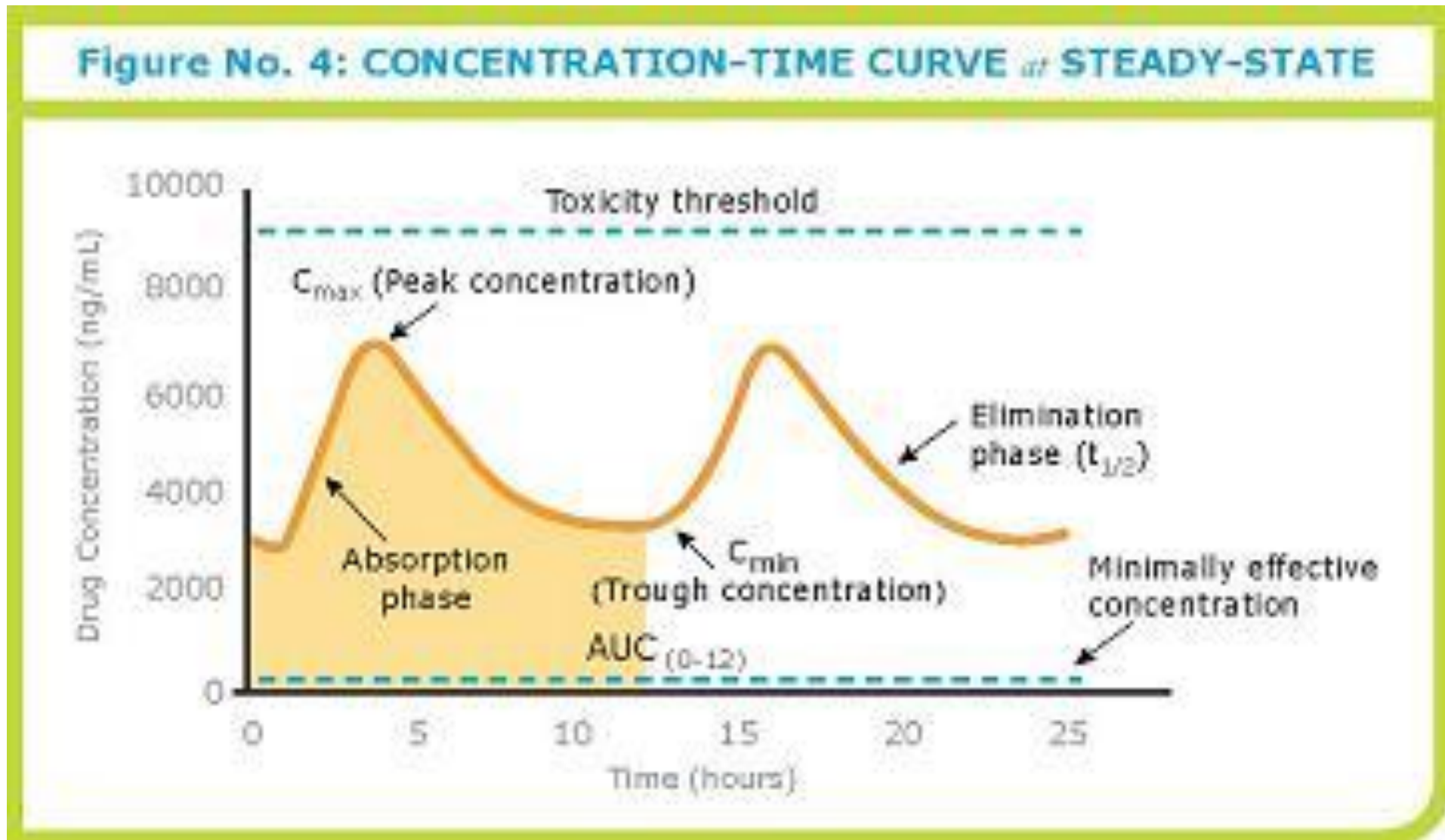
- **Drug-Disease Interactions**

- Cardiovascular disease effects; modifiable risks
- Metabolic effects
- Mental health effects

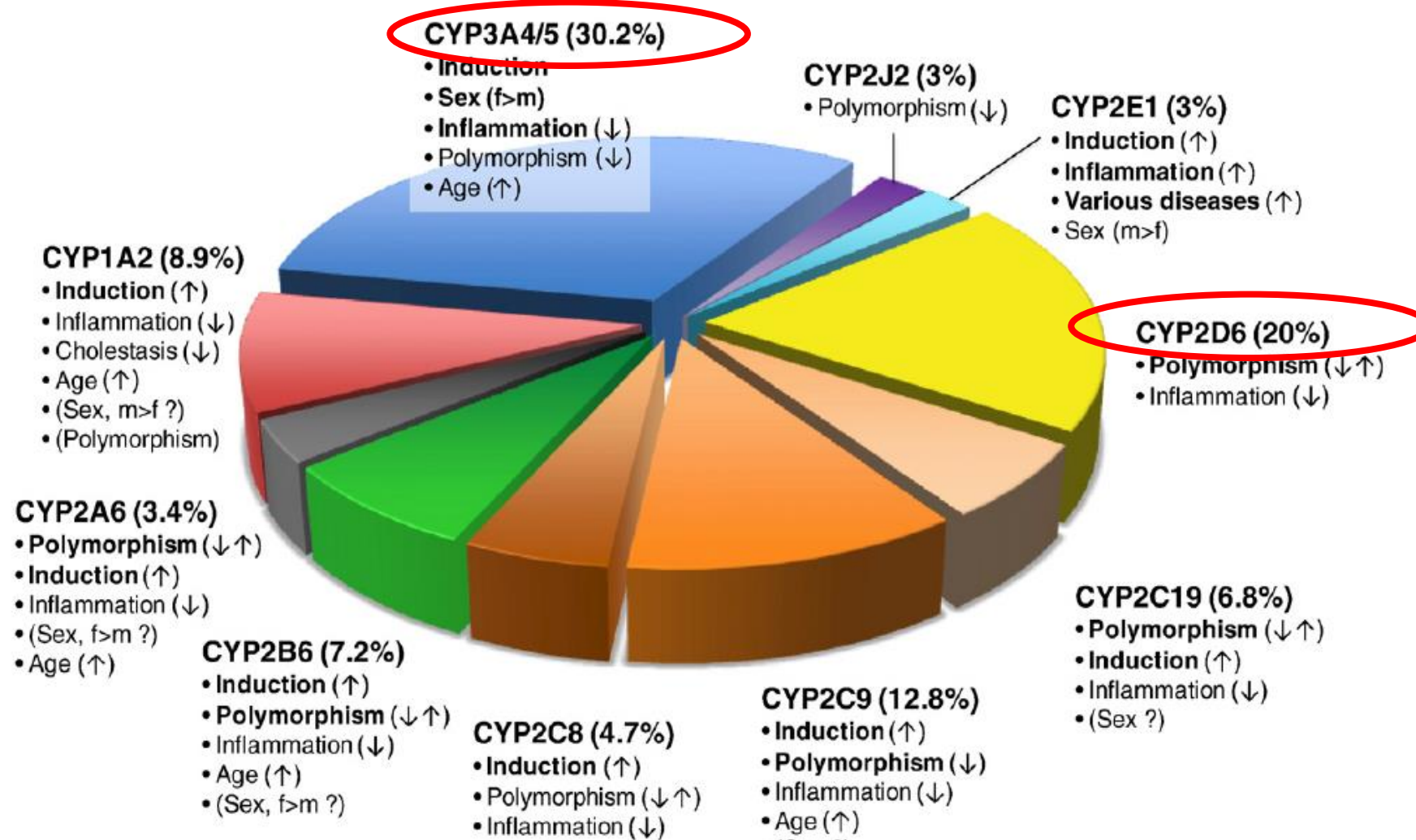
Types of Drug-Drug Interactions

- **Pharmacodynamic Interactions – alter drug *activity***
 - Can be additive, synergistic, or antagonistic
 - Ex: zidovudine-stavudine interaction (antagonistic)
- **Pharmacokinetic Interactions – alter drug *levels***
 - Absorption, Distribution, Metabolism, Excretion
 - Ex: etravirine – dolutegravir interaction

Pharmacokinetic Interaction Language



Cytochrome P450 Enzymes Involved in Drug Metabolism



Pharmacology & Therapeutics (2013) 138: 103-141.

CYP Involvement of ARVs

SUBSTRATES & <u>in</u> HIBITORS	SUBSTRATES & <u>in</u> DUCERS
<p>Protease Inhibitors (PIs):</p> <p>Atazanavir Nelfinavir Lopinavir/ritonavir Darunavir Saquinavir Fosamprenavir Indinavir</p>	<p>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):</p> <p>Efavirenz Etravirine Nevirapine</p>
<p>Pharmacokinetic “Boosters”:</p> <p>Cobicistat Ritonavir (also a protease inhibitor)</p>	<p>Protease Inhibitors (PIs): Tipranavir</p>
<p>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): Delavirdine</p>	

CYP Involvement of ARVs

SUBSTRATES	No CYP P450 Metabolism
<p>Integrase Inhibitors (InSTI): Dolutegravir (3A ~10%, UGT 90%)¹ Elvitegravir Bictegravir (3A ~40%; UGT 60%)¹</p>	<p>Integrase Inhibitors (InSTI): Raltegravir (UGT) Cabotegravir (UGT)</p>
<p>Entry Inhibitors (EI): Maraviroc Fostemsavir (~21%)</p>	<p>Entry Inhibitors (EI): Enfuvirtide Ibalizumab</p>
<p>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): Rilpivirine Doravirine</p>	<p>Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Abacavir Stavudine Didanosine Tenofovir (TAF minor 3A4) Emtricitabine Zidovudine (UGT) Lamivudine</p>

¹Pharmacotherapy (2019);39(5):576-598

FO

- FO is a 39 yr old person with HIV
 - She presents to pick up the following:
 - Abacavir / lamivudine / dolutegravir (Triumeq) 1 tab qday - refill
 - Prenatal vitamin – new Rx per OB
 - Ferrous sulfate 325 mg every other day – new Rx per OB
 - She also asks for advice for something for heartburn that has been bothering her more often
- ▶ What interaction(s) concern is/are there?
 - ▶ What are options to address any interaction(s)?

University of Liverpool Example

The screenshot shows the homepage of the HIV Drug Interactions website. The header is dark blue with the site logo on the left, the University of Liverpool crest and name in the center, and navigation buttons for 'Interaction Checker' and 'Apps' on the right. A secondary navigation bar below the header contains links for 'About Us', 'Interaction Checkers', 'Prescribing Resources', 'Videos', 'Site News', 'Contact Us', and 'Support Us'. A blue banner below the navigation bar highlights 'New Prescribing Resources' with a list of items: 'Dose dependent enzyme induction treatment selector, Rilpivirine (oral and IM) PK fact sheets, Cabotegravir (oral and IM) PK fact sheets'. The main content area features a large white box with the heading 'Interaction Checker' and a sub-heading 'Access our free, comprehensive and user-friendly drug interaction charts'. Below this are three white boxes: 'Educational Videos' (describing mini-lectures on pharmacology, HIV, and drug-drug interactions), 'Prescribing Resources' (listing interaction tables, treatment selectors, clinical prescribing resources, and pharmacokinetic fact sheets), and 'Twitter' (with the handle @hivinteractions and a call to follow for news and updates). At the bottom, there is a cookie consent banner and three buttons for 'Mobile Apps', 'Hepatitis Website', and 'Cancer Website'.

HIV Drug Interactions

UNIVERSITY OF LIVERPOOL

Interaction Checker →

Apps ▾

About Us Interaction Checkers Prescribing Resources Videos Site News Contact Us Support Us

New Prescribing Resources - Dose dependent enzyme induction treatment selector, Rilpivirine (oral and IM) PK fact sheets, Cabotegravir (oral and IM) PK fact sheets

Interaction Checker

Access our free, comprehensive and user-friendly drug interaction charts

Educational Videos

A series of mini-lectures on topics including pharmacology, HIV and drug-drug interactions

Prescribing Resources

Interaction tables, treatment selectors, clinical prescribing resources, and pharmacokinetic fact sheets

Twitter

@hivinteractions

Follow us on Twitter for interaction news and for the latest additions and changes to the website

Cookies help us deliver our services. By using our services, you agree to our use of cookies. [OK](#) [Learn more](#)

Mobile Apps Hepatitis Website Cancer Website

University of Liverpool Example

HIV Drugs	Co-medications	Drug Interactions
<input type="text" value="dol"/>	<input type="text" value="multi"/>	<input type="checkbox"/> Check HIV/ HIV drug interactions
<input type="button" value="X"/>	<input type="button" value="X"/>	<input type="button" value="Switch to table view"/>
<input type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	<input type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	<input type="button" value="Reset Checker"/>
<input checked="" type="checkbox"/> Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC) <input type="button" value="i"/>	<input checked="" type="checkbox"/> Iron supplements <input type="button" value="i"/>	Potential Interaction
<input checked="" type="checkbox"/> Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC) <input type="button" value="i"/>	<input checked="" type="checkbox"/> Multivitamins <input type="button" value="i"/>	Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC)
<input type="checkbox"/> Dolutegravir (DTG) <input type="button" value="i"/>	<input checked="" type="checkbox"/> Multivitamins <input type="button" value="i"/>	Iron supplements
<input type="checkbox"/> Dolutegravir/Lamivudine (DTG/3TC) <input type="button" value="i"/>		<input type="button" value="More Info"/> ^
<input type="checkbox"/> Dolutegravir/Rilpivirine (DTG/RPV) <input type="button" value="i"/>		Quality of evidence: Very Low <input type="button" value="i"/>
		Summary: Coadministration with dolutegravir/abacavir/lamivudine has not been studied. No interaction is expected with abacavir or lamivudine. Administration of an iron supplement (ferrous fumarate 324 mg) simultaneously under fed conditions or 2 hours after dolutegravir had no significant effect on dolutegravir exposure. However, when coadministered simultaneously in the fasted state, dolutegravir AUC and Cmax decreased by 54% and 57%, respectively. Administer Triumeq 2 hours before or 6 hours after taking supplements containing iron. The US product information for Triumeq

ARVs at Highest Risk for Drug Interactions

- **Protease Inhibitors and elvitegravir/cobicistat = regimens with a BOOSTER**
 - Often INcrease drug levels of other medications
 - Can be affected by other medications
 - Overlapping metabolic and/or cardiovascular effects
 - Overlapping hepatotoxicity

ARVs at Highest Risk for Drug Interactions

- **Most NNRTIs**

- Often DEcrease drug levels of other medications
- Can be affected by other medications
- Overlapping hepatotoxicity
- Overlapping mental health effects (EFV > RPV)

- Rilpivirine and doravirine – more *moderate* risk

ARVs at Moderate to Low Risk for Drug Interactions

- **Maraviroc**

- Can be affected by other medications
 - Dose adjusted based on concomitant ARVs or other medications

- **Fostemsavir**

- Can be affected by other medications

ARVs at Moderate to Low Risk for Drug Interactions

- **Integrase Inhibitors (InSTIs)**

- ALL ORAL InSTIs interact with polyvalent cations
 - Common OTC products: TUMS, Mylanta, Maalox, Multivitamins w/minerals, zinc supplements, etc
- All can be affected by moderate to strong CYP 3A4 or general inDUCERS
- Raltegravir at LOWEST risk for ARV-drug interactions
- Cabotegravir also LOWEST risk for ARV-drug interactions – **ORAL vs IM differ**
- Elvitegravir/cobicistat is on the highest risk of interactions list
 - Only available in a combination, single tablet regimen tablet
- Drug – Disease Interaction
 - Insulin resistance / diabetes?
 - Weight gain

ARVs at Lowest Risk for Drug Interactions

- **NRTIs**

- No CYP metabolism or effects
 - TAF
- Concerns:
 - Overlapping nephrotoxicity – tenofovir (TDF > TAF)
 - Overlapping hepatotoxicity – abacavir (caution, dose adjust)
 - Overlapping myelosuppression – zidovudine, stavudine

- **Enfuvirtide, Ibalizumab**

- No interactions

Approach to Assessing ARV-Drug Interaction Severity

- **What is the potential interaction?**

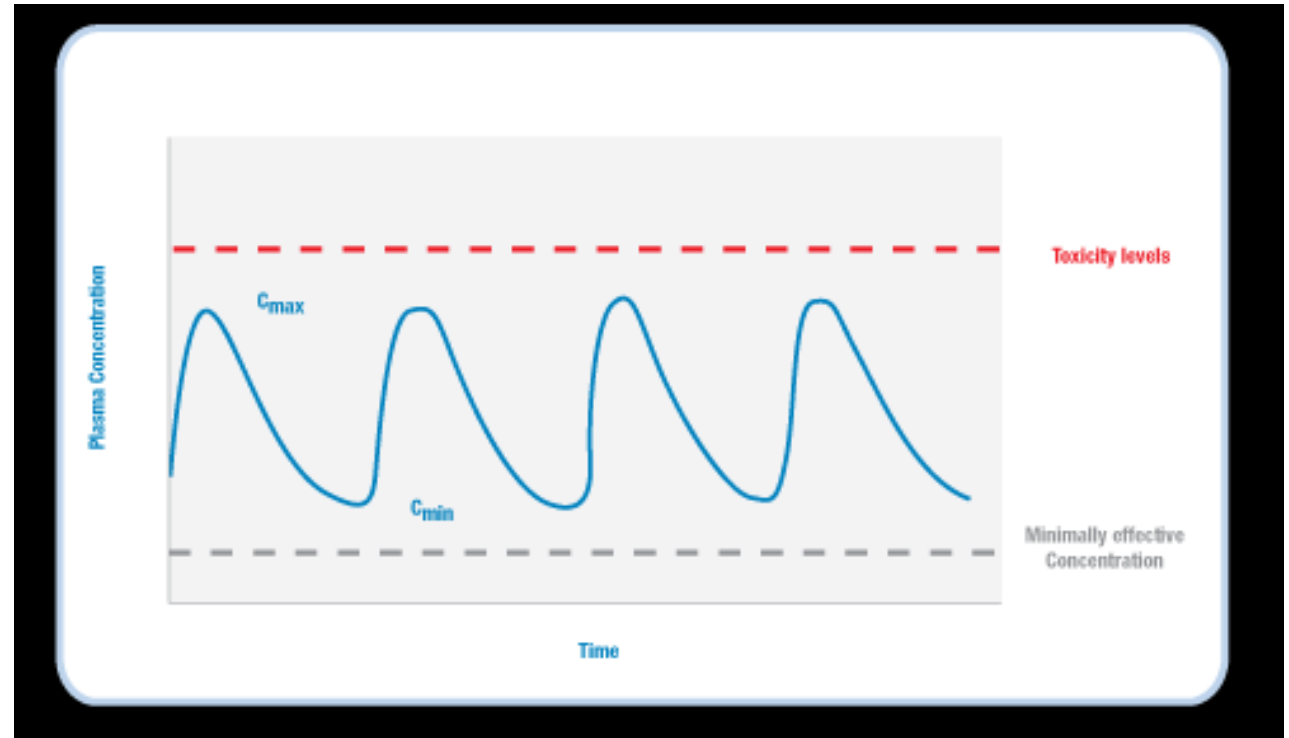
- Increase/decrease in ARV drug levels?
- Increase/decrease in the other medication?
- Is there data?
 - **NOTE: ritonavir effects \neq cobicistat effects**

- ▶ **Are there other contributing factors to possibly higher/lower drug levels?**

- ▶ Renal insufficiency?
- ▶ Hepatic insufficiency?
- ▶ Advanced age?
- ▶ Are there other routes of metabolism?

Approach to **Assessing** ARV-Drug Interaction Severity

- **What are the risks of higher/lower drug levels?**
 - Therapeutic index and resistance potential of the ARV
 - Therapeutic index and toxicity/side effect potential of the other medication



CI

- CI is a 55 yr old person with HIV
 - CI presents with a new prescription for:
 - emtricitabine / tenofovir alafenamide / **Bictegravir** (Biktarvy) 1 tab daily
 - You review the current medications:
 - Emtricitabine / tenofovir alafenamide / **elvitegravir / cobicistat** (Genyova) 1 tab daily with food
 - Apixaban 2.5 mg bid
 - Atorvastatin 20 mg qday
 - Lisinopril 10 mg qday
- ▶ What is the assessment of the ARV-drug interaction with CI's regimen?
 - ▶ What is the potential interaction?
 - ▶ Are there other contributing factors to changes in drug PK (levels)?
 - ▶ What are the potential consequences of this interaction?
 - ▶ How can this ARV-drug interaction be managed?

DHHS Guidelines Example

Limitations to Treatment Safety and Efficacy +

Drug-Drug Interactions -

Overview

PI Drug Interactions

NNRTI Drug Interactions

NRTI Drug Interactions

INSTI Drug Interactions

CCR5 Antagonist Drug Interactions

Interactions Between PIs and NNRTIs

Interactions Between INSTI & NNRTI or PI

Conclusion

Appendix A: Key to Acronyms +

Anticoagulants			
Apixaban	BIC, DTG, RAL	↔ apixaban expected	No dose adjustment needed.
	EVG/c	↑ apixaban expected	Do not coadminister in patients who require apixaban 2.5 mg twice daily. Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily.
Betrixaban	BIC, DTG, RAL	↔ betrixaban expected	No dose adjustment needed.
	EVG/c	↑ betrixaban expected	Administer initial single dose of betrixaban 80 mg, followed by betrixaban 40 mg once daily.
Dabigatran	BIC, DTG, RAL	↔ dabigatran expected	No dose adjustment needed.
	EVG/c	↑ dabigatran expected With COBI 150 mg Alone: <ul style="list-style-type: none"> Dabigatran AUC ↑ 110% to 127% 	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran.

Approach to **Managing** ARV-Drug Interaction Potential

- Are there other ARV or general medication options?
 - ARV treatment, tolerance, and resistance histories
- Dose adjustment
 - For the ARV and/or the other medication
- Adjust frequency of monitoring
 - HIV VL, ECG, SCr, LFTs
- Minimize other contributing medications
- Therapeutic Drug Monitoring (TDM)

Common ARV Interactions

- **OTHER ARVS**
- **Minerals (InSTIs) – di- and poly- valent cations**
 - Iron, zinc, calcium, magnesium, copper, aluminum, etc
- **Acid Suppressants**
- Antidepressants / Antipsychotics
- Statins
- Anticoagulants / Antiplatelets
- Corticosteroids
- Antifungals
- Oral Contraceptives
- Pain Medications / Substance Abuse Treatments

Drug Classes w/ARV Contraindications

- Statins: lovastatin, simvastatin
- Benzodiazepines: triazolam, midazolam (oral)
- Cardiac Glycosides
- Anticoagulants / Antiplatelets
- Ergot Derivatives
- Anti-epileptics: phenobarbital, phenytoin, carbamazepine, oxcarbamazepine
- Anti-mycobacterials: rifampin, rifapentine
- Other: cisapride, alfuzosin

Mental Health Medications

- Antidepressants
 - SSRI – some are substrates, some inhibit CYP enzymes
 - SNRI – some are substrates of CYP enzymes
 - Overlapping QT prolongation
- Antipsychotics
 - Atypical – some are substrates of CYP enzymes
 - Typical
 - Overlapping QT prolongation
 - Overlapping metabolic side effects possible

Overlapping Toxicity Potential

QT Prolongation	
HIV Medications	Mental Health Medications
<p>Protease Inhibitors: Atazanavir Lopinavir/ritonavir Ritonavir Saquinavir</p> <p>Non-Nucleoside Reverse Transcriptase Inhibitors: Rilpivirine</p> <p>Entry Inhibitors: fostemsavir</p> <p>Pharmacokinetic “Boosters”: Ritonavir Cobicistat (possible)</p>	<p>Antidepressants: Citalopram Escitalopram Fluoxetine Paroxetine Sertraline Venlafaxine Mirtazapine Trazodone Tricyclic Antidepressants</p> <p>Typical Antipsychotics: Haloperidol Thioridazine</p> <p>Other: Lithium Methadone</p> <p>Atypical Antipsychotics: Aripiprazole Asenapine Clozapine Iloperidone Olanzapine Paliperidone Quetiapine Risperidone Ziprasidone</p>

University of Liverpool Example

The screenshot shows the homepage of the HIV Drug Interactions website. The header is dark blue with the site logo on the left, the University of Liverpool crest and name in the center, and navigation buttons for 'Interaction Checker' and 'Apps' on the right. Below the header is a light blue navigation bar with links for 'About Us', 'Interaction Checkers', 'Prescribing Resources', 'Videos', 'Site News', 'Contact Us', and 'Support Us'. A bright blue banner below the navigation bar contains text about new prescribing resources. The main content area features a large white box with the title 'Interaction Checker' and a description. Below this are three white boxes: 'Educational Videos', 'Prescribing Resources', and 'Twitter'. At the bottom, there is a cookie consent banner and a row of three buttons: 'Mobile Apps', 'Hepatitis Website', and 'Career Website'.

HIV Drug Interactions

UNIVERSITY OF LIVERPOOL

Interaction Checker →

Apps ↓

About Us Interaction Checkers Prescribing Resources Videos Site News Contact Us Support Us

New Prescribing Resources - Dose dependent enzyme induction treatment selector, Rilpivirine (oral and IM) PK fact sheets, Cabotegravir (oral and IM) PK fact sheets

Interaction Checker

Access our free, comprehensive and user-friendly drug interaction charts

Educational Videos

A series of mini-lectures on topics including pharmacology, HIV and drug-drug interactions

Prescribing Resources

Interaction tables, treatment selectors, clinical prescribing resources, and pharmacokinetic fact sheets

Twitter


@hivinteractions


Follow us on Twitter for interaction news and for the latest additions and changes to the website


Cookies help us deliver our services. By using our services, you agree to our use of cookies. [OK](#) [Learn more](#)


Mobile Apps Hepatitis Website Career Website


University of Liverpool Example


Treatment Selectors (by therapeutic indication) 


Analgesics
Updated March 2021 

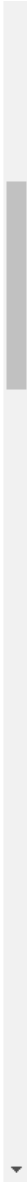
Anticoagulants & Antiplatelets
Updated March 2021 

Antidepressants
Updated March 2021 

Anti-Diabetics
Updated October 2019 

Anti-Malarials
Updated March 2021 

Antipsychotics
Updated March 2021 



Mental Health Medications

- SSRI (least to most interaction potential):

- Citalopram, escitalopram
- paroxetine, sertraline
- fluoxetine
- fluvoxamine

- SNRI (least to most interaction potential):

- Duloxetine, milnacipran, desvenlafaxine
- levomilnacipran
- venlafaxine

Antidepressant Treatment Selector

Charts revised March 2021. Full information available at www.hiv-druginteractions.org

For personal use only. Not for distribution. For personal use only. Not for distribution. For personal use only. Not for distribution. For personal use only. Not for distribution.

	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	MVC	BIC/F/TAF	DTG	EVG/c/F/TAF	EVG/r/F/TDF	RAL	ABC	FTC or 3TC	FTAF	TDF	ZDV
Selective Serotonin Reuptake Inhibitors																					
Citalopram	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Escitalopram	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Fluoxetine	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Fluvoxamine	↑	↑	↑	↑	↑	↔	↔	↔	↑	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Paroxetine	↑?	↑?	↑?	↑?	↑?	↔	↔	↔	↔	↔	↔	↔	↔	↑?	↑?	↔	↔	↔	↔	↔	↔
Sertraline	↑	↑?	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑?	↑?	↔	↔	↔	↔	↔	↔
Serotonin and Norepinephrine Reuptake Inhibitors																					
Duloxetine	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Milnacipran	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Venlafaxine	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↓	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Tricyclic Antidepressants																					
Amitriptyline	↑	↓	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Clomipramine	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Desipramine	↑	↓	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Doxepin	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Imipramine	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Nortriptyline	↑	↓	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Trimipramine	↑	↓	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Tetracyclic Antidepressants																					
Maprotiline	↑	↓	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Mianserin	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Mirtazapine	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Other																					
Agomelatine	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Bupropion	↔	↓	↔	↓	↓	↔	↓	↓	↓	↔	↔	↔	↔	↑?	↑?	↔	↔	↔	↔	↔	↔
Lamotrigine	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Nefazodone	↑	↑	↑	↑	↑	↔	↑	↑	↑	↑	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔
Reboxetine	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
St John's wort	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
Tranlycypromine	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Trazodone	↑	↓	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Vortioxetine	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔

Colour Legend

- No clinically significant interaction expected.
- These drugs should not be coadministered.
- Potential interaction which may require a dose adjustment or close monitoring.

Text Legend

- ↑ Potential increased exposure of the antidepressant
- ↓ Potential decreased exposure of the antidepressant
- ↔ No significant effect
- ↑ Potential increased exposure of HIV drug
- ↓ Potential decreased exposure of HIV drug
- ▼ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered with atazanavir or lopinavir; caution is advised with rilpivirine as supratherapeutic doses of rilpivirine (75 and 300 mg once daily) were shown to prolong the QT interval.

Mental Health Medications

- ▶ Antipsychotics (least to most interaction potential):
 - ▶ Atypical
 - ▶ Asenapine > olanzapine, paliperidone
 - ▶ aripiprazole, iloperidone, risperidone
 - ▶ quetiapine, ziprasidone
 - ▶ Not recommended with boosters: lurasidone
 - ▶ Clozapine - lower risk of ARV interactions; less preferred due to monitoring requirements
 - ▶ Typical
 - ▶ Haloperidol, thioridazine, loxapine, perphenazine, fluphenazine
 - ▶ Not recommended with boosters: pimoziide

Antipsychotic Treatment Selector

Charts revised March 2021. Full information available at www.hiv-druginteractions.org

For personal use only. Not for distribution. For personal use only. Not for distribution. For personal use only. Not for distribution. For personal use only. Not for distribution.

	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	MVC	BIC/F/TAF	DTG	EVG/c/F/TAF	EVG/c/F/TDF	RAL	ABC	FTC or 3TC	F/TAF	TDF	ZDV
Atypical Antipsychotics																					
Amisulpride	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Aripiprazole	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Asenapine	↑▼	↓▼	↑	↓▼	↓▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Clozapine	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Olanzapine	↔	↓	↔	↓	↓	↔	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Paliperidone	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Quetiapine	↑ ^b ▼	↑ ^b ▼	↑ ^b	↑ ^b	↑ ^b ▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑ ^b	↑ ^b	↔	↔	↔	↔	↔	↔ ^a
Risperidone	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Zotepine	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Phenothiazines																					
Chlorpromazine	↑▼	↑▼	↑	↑	↑▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Fluphenazine	↑▼	↑▼	↑	↑	↑▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Levomepromazine	↑▼	↑▼	↑	↑	↑▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Perazine	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Periclazine	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Perphenazine	↑▼	↑▼	↑	↑	↑▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Pimozide	↑▼	↑▼	↑	↑	↑▼	↔	↑ ^c	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Prochlorperazine	↑▼	↑▼	↑	↑	↑▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Thioridazine	↑▼	↑▼	↑	↑	↑▼	↓	↓	↓	↓	↓▼	↓	↓	↓	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Others																					
Haloperidol	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↑	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Iloperidone	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Pipotiazine	↑▼	↑▼	↑	↑	↑▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a
Sulpiride	↔▼	↔▼	↔	↔	↔▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Tiapride	↔▼	↔▼	↔	↔	↔▼	↔	↔	↔	↔	↔▼	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Ziprasidone	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔
Zuclopenthixol	↑▼	↑▼	↑	↑	↑▼	↔	↓	↓	↓	↔▼	↔	↔	↔	↑	↑	↔	↔	↔	↔	↔	↔ ^a

Colour Legend

- No clinically significant interaction expected.
- These drugs should not be coadministered.
- Potential interaction which may require a dose adjustment or close monitoring.
- Potential interaction predicted to be of weak intensity. No a priori dosage adjustment is recommended.

Text Legend

- ↑ Potential increased exposure of the antipsychotic
- ↓ Potential decreased exposure of the antipsychotic
- ↔ No significant effect
- ↑ Potential increased exposure of HIV drug
- ↓ Potential decreased exposure of HIV drug
- ▼ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered with atazanavir or lopinavir; caution is advised with rilpivirine as supratherapeutic doses of rilpivirine (75 and 300 mg once daily) were shown to prolong the QT interval.

Preferences to Minimize Potential for and/or Severity of Drug-ARV Interaction

- Mood Stabilizers
 - Lithium > valproate (divalproex), lamotrigine
 - Above are generally minimal risk
 - Lithium – tenofovir overlapping nephrotoxicity
 - **Valproate** –dolutegravir, 2 cases & retrospective data show decreased dolutegravir AUC possibly due to protein binding displacement or chelation
 - Lamotrigine – decreased levels with lopinavir/ritonavir

Acid Suppressants

- **Concerns: decreased ARV absorption, virologic failure, potentiation of ARV resistance**
- **ARVs of concern:**
 - **ALL Integrase Inhibitors – antacids only**
 - **Rilpivirine – all acid suppressants**
 - **Atazanavir +/- booster – all acid suppressants**
- **Acid Suppressant Medications**
 - **Antacids – Maalox, Mylanta, TUMS, etc**
 - **H2 Receptor Antagonists – ranitidine, famotidine, cimetidine, etc**
 - **Proton Pump Inhibitors – omeprazole, pantoprazole, lansoprazole, etc**

Acid Suppressants – Management Options

- Antacids
 - Contain polyvalent cations – magnesium, aluminum, calcium
 - Require dose spacing with ALL InSTIs (or food w/specific InSTI and mineral)
 - Require dose spacing with atazanavir +/- RTV/Cobi and rilpivirine
- H2 Receptor antagonists
 - Require dose spacing with atazanavir +/- RTV/Cobi and rilpivirine
- Proton Pump Inhibitors
 - Do NOT use with atazanavir (unboosted) or PI-experienced patients taking boosted atazanavir
 - Do NOT use with rilpivirine
 - Require dose spacing with atazanvir + ritonavir/cobicistat
 - Only ok if not PI-experienced

Pain Medications: Preferences to Minimize Potential for and/or Severity of Drug-ARV Interaction

- NSAIDS

- Potential overlapping nephrotoxicity with tenofovir (TDF > TAF) if used long term
- Prefer celecoxib, aspirin > other NSAIDs

- Opioids

- Levels may be increased by inhibitors, decreased by inducers
- Inhibition of 2D6 may decrease conversion to active metabolite (hydrocodone, tramadol, codeine)
- Prefer hydromorphone, morphine > oxycodone, hydrocodone, tramadol, codeine > Fentanyl

Substance Use Treatment Medications: Preferences to Minimize Potential for and/or Severity of Drug-ARV Interaction

- Substance Use Treatment

- Naltrexone > buprenorphine +/- naloxone > methadone

- Naltrexone

- Non-CYP metabolism
- Not expected to interact with ARVs
- Available as an oral tablet or IM injection

- Buprenorphine +/- naloxone

- INSTIs – elvitegravir/cobi increases levels, not likely clinically significant
- PIs – unboosted **ATV most profound effect do not use**; ATV/r, ATV/c, DRV/r, DRV/c increase levels, start low, may need to adjust buprenorphine dose if starting PI; LPV/r no effect
- NNRTIs – EFV > ETR decrease buprenorphine levels

Substance Use Treatment Preferences to Minimize Potential for and/or Severity of Drug-ARV Interaction

- Substance Use Treatment

- Methadone

- InSTIs – elvitegravir/cobi may minimally increase methadone levels
 - PIs – may decrease methadone levels, not usually significant except possibly with LPV/r; w/cobicistat did not appear to be any changes however, US packaging recommends slow titration and possible dose adjustment when starting PI+cobi
 - **NNRTIs (EFV, NVP) decrease methadone levels, withdrawal symptoms may occur** – inform treatment center; etravirine may minimally increase levels or have no effect; rilpivirine minimal decrease

Antifungals

- Fluconazole
 - Cautions with nevirapine and tipranavir; no other significant ARV-interactions
- Itraconazole
 - PI's and EVG / Cobi – avoid doses > 200 mg/day unless guided by itraconazole drug levels
 - Efavirenz and nevirapine - Not recommended unless guided by itraconazole levels to ensure therapeutic levels
 - Etravirine - Itraconazole drug levels recommended; interaction not as well characterized
 - Maraviroc – dose as 150 mg bid with itraconazole

Antifungals

- Isavuconazole
 - PI's and EVG / coBI – monitor isavuconazole drug levels, monitor for ADEs and response
 - Efavirenz, nevirapine, etravirine – may lower isavuconazole, monitor drug levels
- Posaconazole
 - PI's and EVG / coBI – likely increase posaconazole levels and vice versa; monitor posaconazole levels and ADE of each medication
 - Efavirenz – not recommended, if used together, monitor posaconazole drug levels
 - Maraviroc – use 150 mg bid when with posaconazole
- Voriconazole
 - PI's and EVG / coBI – not recommended, if it's a must then monitor voriconazole levels
 - Efavirenz – contraindicated, nevirapine maybe check voriconazole level
 - Maraviroc – use the 150 mg bid dose

Quick Summaries

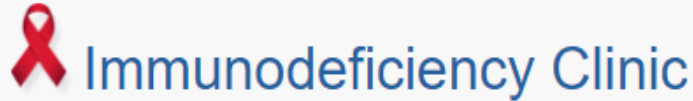
Interaction Concerns with Integrase Inhibitors (InSTIs)

- ALL InSTIs – Polyvalent Cations
 - Including, possibly liquid nutrition products (such as Ensure, Boost)
- Elvitegravir/cobicistat – *highest risk of interactions*
 - Similar interaction risks as PIs
 - Cobicistat effects NOT always the same as ritonavir effects
- Dolutegravir & Bictegravir – *moderate risk of interactions*
 - Caution, avoid, or dose adjust (DTG) with strong CYP 3A4 inducers
 - Metformin (DTG > BIC)
 - Do not use dofetilide
- Raltegravir & Cabotegravir – *lowest risk of interactions*
 - Caution, avoid, or dose adjust with UGT inducers (i.e. rifampin)
 - Oral CAB vs IM CAB

ARV-Drug Interaction Resources

- www.hivinfo.nih.gov
 - Within the HIV / AIDS Treatment Guidelines
 - Includes Data on Drug – Drug Interactions when available
- University of Liverpool
 - www.hiv-druginteractions.org
 - Also for Hep C (www.hep-druginteractions.org)
- Toronto General Hospital Immunodeficiency Clinic
 - <https://hivclinic.ca>
 - Tablet Crushing / Capsule Opening Information

Toronto Immunodeficiency Clinic



- HOME
- CLINIC ▾
- PATIENT ▾
- DRUG INFORMATION ▾
- RESEARCH ▾
- RESIDENCY ▾
- PHARMACY ORG ▾

NEW >

Immu



Immunodeficiency

- Drug Information Home
- Drug Interaction Tables
- Antiretroviral Interactions with Chemotherapy Regimens
- Pharmacologic Properties of Antiretrovirals
- Pharmacologic Properties of Hepatitis C Antivirals
- Additional Information for Healthcare Professionals
- Medication Fact Sheets
- Drug Reimbursement Information

Mobile App
Available Now

The **Immunodeficiency Clinic** provides specialized outpatient consultation to you and your family doctor on how to best manage your HIV care. We do this in an optimum facility where most needed HIV services are under one roof. Every time you are seen in the Clinic, a detailed letter will be sent to your family doctor by your Clinic physician. In addition, we may recommend additional care that is not available in the community, which may include the latest approaches in treatment, or counselling with one of our multidisciplinary team members.

Our care is based on the principles of accessibility, comprehensiveness, health promotion and patient satisfaction. If you are interested in an approach that has not been offered please let us know, to see if we can help you to access it. If you do not agree with a recommendation being made, please let us know and we can make alternate suggestions. Our goal is to empower you to meet your own personal health goals.

Services include medical specialists, nurses, pharmacists, social workers, dieticians, psychiatrists, and occupational



Quick Links

PATIENTS

[Directions to the Clinic](#)

[Your First Visit](#)

[Guide To Services](#)

HEALTHCARE PROFESSIONALS

ARV-Herb Interaction Resources

- Natural Medicines
 - The Natural Medicines Comprehensive Database
 - Naturalmedicines.therapeuticresearch.com
- The Memorial Sloan Kettering Cancer Center (About Herbs)
 - <https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs>

Let's end HIV in Oregon.

We can make it
happen.
The time is now.

