Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) in the Long Term Care Setting

### Part 2: HIV Medications



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# **Overview - Part 2: HIV Medications**

- Principles for treating the elderly for HIV
- Medications commonly used
  - Decrease in viral load and decreased risk of transmission
  - Risk of resistance inherent in treatment
- Storage
- Administration
- Common timing related concerns
- Compliance
  - Timing/scheduling medication pass
  - Process controls that can help compliance in LTC



Antiretroviral Therapy (ART)

# ART is now recommended for all HIV-infected patients



# HIV and the Older Patient (Last updated March 27, 2012; last reviewed March 27, 2012)

### Key Considerations When Caring for Older HIV-Infected Patients

- Antiretroviral therapy (ART) is recommended in patients >50 years of age, regardless of CD4 cell count (BIII), because the risk of non-AIDS related complications may increase and the immunologic response to ART may be reduced in older HIV-infected patients.
- ART-associated adverse events may occur more frequently in older HIV-infected adults than in younger HIV-infected individuals. Therefore, the bone, kidney, metabolic, cardiovascular, and liver health of older HIV-infected adults should be monitored closely.
- The increased risk of drug-drug interactions between antiretroviral (ARV) drugs and other medications commonly used in older HIVinfected patients should be assessed regularly, especially when starting or switching ART and concomitant medications.
- HIV experts and primary care providers should work together to optimize the medical care of older HIV-infected patients with complex comorbidities.
- · Counseling to prevent secondary transmission of HIV remains an important aspect of the care of the older HIV-infected patient.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

*Rating of Evidence: I* = *Data from randomized controlled trials; II* = *Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III* = *Expert opinion* 

Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents <a href="https://aidsinfo.nih.gov/guidelines">https://aidsinfo.nih.gov/guidelines</a>



# Antiretroviral Therapy (ART), Highly Active Antiretroviral Therapy (HAART), Combination Antiretroviral Therapy (cART)



- MAINTAIN HEALTHY LIFESTYLE
  - EXERCISE
  - PROPER NUTRITION
  - REST
  - AVOID TOBACCO, ALCOHOL AND DRUG USE
- REGULAR EXAMINATIONS BY:
  - HIV SPECIALIST
  - PHYSICIAN WHO HAS COORDINATED CARE WITH AN HIV OR INFECTIOUS DISEASE SPECIALIST



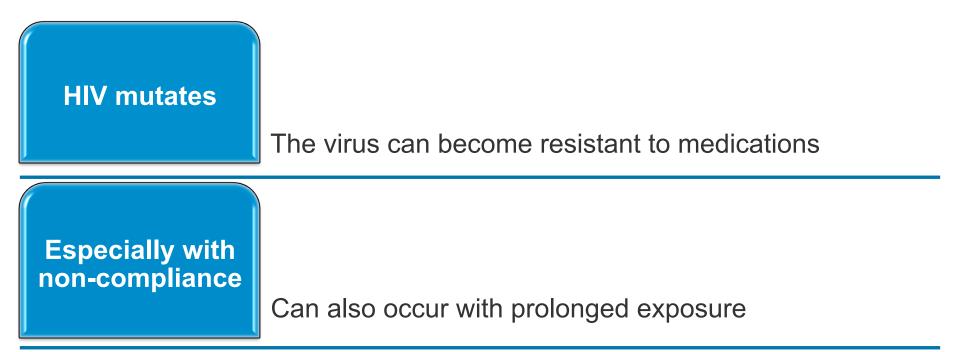
# Antiretroviral Therapy (ART)

# ART can:

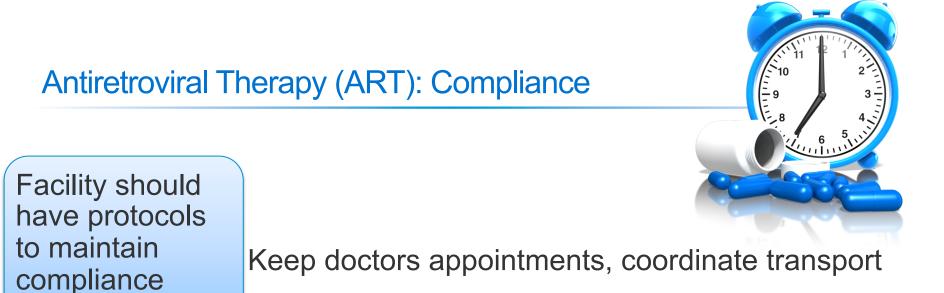
- ✓ Increase lifespan
- Decrease risk of developing illnesses
- Decrease (but not eliminate) the risk of spreading the disease











- Be aware of insurance coverage issues so medications are not missed
- Prior authorizations in HIV care specifically have been reported to cost over \$40 each in provider personnel time (a hidden cost) and have substantially reduced timely access to medications\*



Antiretroviral Therapy (ART): Compliance



Facility should have protocols to maintain compliance

If "self-administration" is occurring have a policy in place to ensure compliance

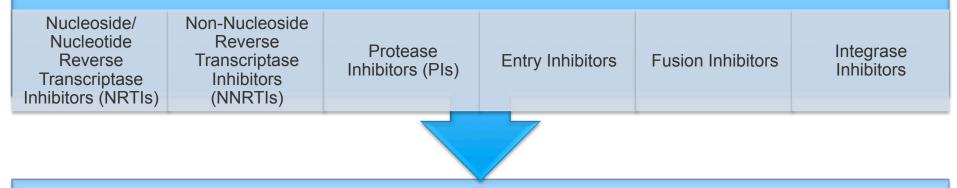
- Implement daily medication counts
- Document refusal of ART and communicate to prescriber
- If ART must be stopped for a procedure or a treatment, coordinate that in the plan of care and with primary and specialist physicians, document follow up and restarting the medication
- Avoid prolonged "hold" orders or misinterpreting discontinuation orders as permanent



# **Classes of HIV Medications**



### **Currently 6 different classes of HIV medications**



### Each class attacks the virus at different points in its life cycle

People generally are prescribed 3 different antiretroviral drugs from 2 different classes

### Often these medications are combined into 1 pill

Increases compliance

Can cause confusion

Spell out the name of all medications on the MAR and physicians orders

# Classes of HIV Medications: Combination therapy vs. Monotherapy

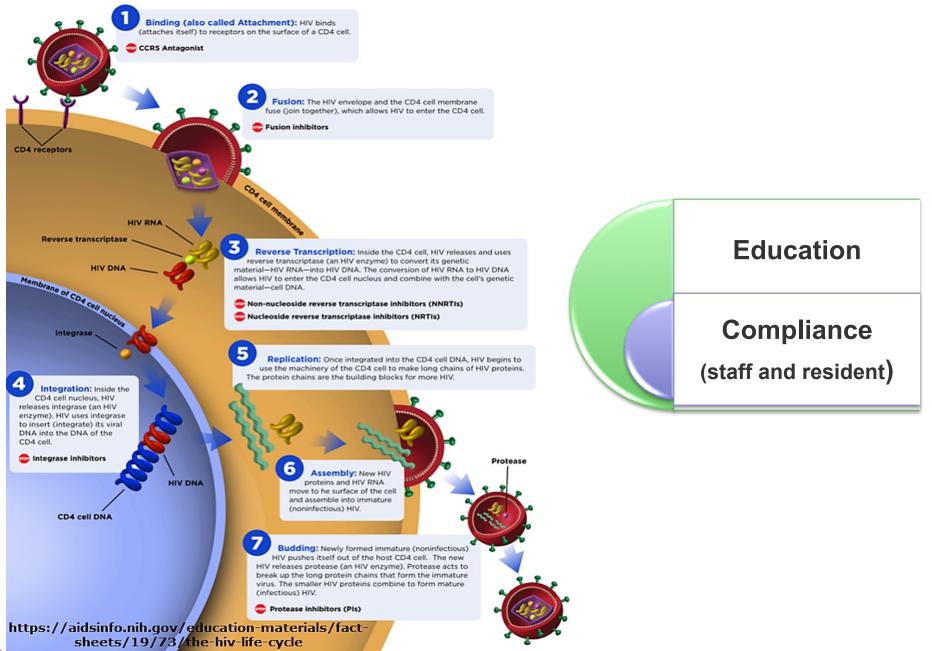
- Treating HIV with one pill containing multiple medications (e.g., fixed dose combination therapy) is acceptable
- Treating HIV with only one medication (monotherapy) is rarely acceptable
- Recommend checking this upon transitions in care (e.g., new admission, readmission from hospital, change of condition that resulted in a new provider consult)





#### **The HIV Life Cycle**

HIV medicines in six drug classes stop 🚭 HIV at different stages in the HIV life cycle.



	FDA-Approved HIV Medicines			
Drug Class	Generic Name (Other names and acronyms)	Brand Name	FDA Approval Date	
Nucleoside Reverse Tran	scriptase Inhibitors (NRTIs)			
NRTIs block reverse transcriptase, an	<b>abacavir</b> (abacavir sulfate, ABC)	Ziagen	Dec.17, 1998	
enzyme HIV needs to make copies of itself	<b>didanosine</b> (delayed-release didanosine,	Videx	October 9, 1991	
	dideoxyinosine, enteric-coated didanosine, ddl, ddl EC)	Videx EC (enteric-coated)	October 31, 2000	
	emtricitabine (FTC)	Emtriva	July 2, 2003	
	lamivudine (3TC)	Epivir	Nov. 17, 1995	
	<b>stavudine</b> (d4T)	Zerit	June 24, 1994	
	tenofovir disoproxil fumarate (tenofovir DF, TDF)	Viread	October 26, 2001	
	<b>zidovudine</b> (azidothymidine, AZT, ZDV)	Retrovir	March 19, 1987	



https://aidsinfo.nih.gov/education-materials/fact-sheets/21/58/fda-approved-hiv-medicines

FDA-Approved HIV Medicines			
Drug Class	Class Generic Name (Other names and acronyms)		FDA Approval Date
Non-Nucleoside Reverse	Transcriptase Inhibitors (NNRTIs)		
NNRTIs bind to and later alter reverse transcriptase, an enzyme HIV needs to make copies of itself	<b>delavirdine</b> (delavirdine mesylate, DLV)	Rescriptor	April 4, 1997
	<b>efavirenz</b> (EFV)	Sustiva	Sept. 17, 1998
	etravirine (ETR)	Intelence	January 18, 2008
	<b>nevirapine</b> (extended-release nevirapine, NVP)	Viramune	June 21, 1996
		Viramune XR (extended release)	March 25, 2011
	<b>rilpivirine</b> (rilpivirine hydrochloride, RPV)	Edurant	May 20, 2011



	FDA-Approved HIV Medicines		
Drug Class	Generic Name (Other names and acronyms) Brand Name FDA A D		FDA Approval Date
Protease Inhibitors (PIs)			
PIs block HIV protease, an enzyme HIV needs to	<b>atazanavir</b> (atazanavir sulfate, ATV)	Reyataz	June 20, 2003
make copies of itself	<b>darunavir</b> (darunavir ethanolate, DRV)	Prezista	June 23, 2006
	<b>fosamprenavir</b> (fosamprenavir calcium, FOS-APV, FPV)	Lexiva	October 20, 2003
	<b>indinavir</b> (indinavir sulfate, IDV)	Crixivan	March 13, 1996
	<b>nelfinavir</b> (nelfinavir mesylate, NFV)	Viracept	March 14, 1997
	<b>ritonavir</b> (RTV)	Norvir	March 1, 1996
	<b>saquinavir</b> (saquinavir mesylate, SQV)	Invirase	December 6, 1995
	<b>tipranavir</b> (TPV)	Aptivus	June 22, 2005



https://aidsinfo.nih.gov/education-materials/fact-sheets/21/58/fda-approved-hiv-medicines

FDA-Approved HIV Medicines			
Drug Class	Generic Name (Other names and acronyms)	Brand Name	FDA Approval Date
Fusion Inhibitors			
Fusion inhibitors block HIV from entering the CD4 cells of the immune system	<b>enfuvirtide</b> (T-20)	Fuzeon	March 13, 2003
Entry Inhibitors			
Entry inhibitors block proteins on the CD4 cells that HIV needs to enter the cells	maraviroc (MVC)	Selzentry	August 6, 2007
Integrase Inhibitors			
	dolutegravir (DTG)	Tivicay	August 13, 2013
Integrase inhibitors block HIV integrase, an enzyme HIV needs to make copies of itself	<b>elvitegravir</b> (EVG)	Vitekta	Sept. 24, 2014
	<b>raltegravir</b> (raltegravir potassium, RAL)	Isentress	October 12, 2007



https://aidsinfo.nih.gov/education-materials/fact-sheets/21/58/fda-approved-hiv-medicines

FDA-Approved HIV Medicines				
Drug Class	Drug Class Generic Name (Other names and acronyms)			
Pharmacokinetic Enhanc	er: cobicistat	•	-	
Cobicistat is used in HIV treatment to increase the effectiveness of another HIV medicine. It is included in an HIV regimen, not a treatment given by itself.	cobicistat (COBI)	Tybost	Sept. 24, 2014	
	atazanavir and cobicistat (atazanavir sulfate / cobicistat; ATV / COBI)	Evotaz	January 29, 2015	
	darunavir and cobicistat (darunavir ethanolate / cobicistat; DRV / COBI)	Prezcobix	January 29, 2015	
	elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate (QUAD, EVG / COBI / FTC / TDF)	Stribild	August 27, 2012	



FDA-Approved HIV Medicines				
Drug Class	Drug Class Generic Name (Other names and acronyms)			
Combination HIV Medicin	es			
Combination HIV medicines contain two or more HIV medicines from one or more drug classes	abacavir and lamivudine (abacavir sulfate / lamivudine, ABC / 3TC)	Epzicom	August 2, 2004	
	abacavir, dolutegravir, and lamivudine (abacavir sulfate / dolutegravir sodium / lamivudine, ABC / DTG / 3TC)	Triumeq	August 22, 2014	
	abacavir, lamivudine, and zidovudine (abacavir sulfate / lamivudine / zidovudine, ABC / 3TC / ZDV)	Trizivir	Nov. 14, 2000	
	efavirenz, emtricitabine, and tenofovir disoproxil fumarate (efavirenz / emtricitabine / tenofovir, efavirenz / emtricitabine / tenofovir DF, EFV / FTC / TDF)	Atripla	July 12, 2006	



FDA-Approved HIV Medicines			
Drug Class	Generic Name (Other names and acronyms)	Brand Name	FDA Approval Date
Combination HIV Medicin	es (continued)		
Combination HIV medicines contain two or more HIV medicines from one or more drug classes	emtricitabine, rilpivirine, and tenofovir disoproxil fumarate (emtricitabine / rilpivirine hydrochloride / tenofovir disoproxil fumarate, emtricitabine / rilpivirine / tenofovir, FTC / RPV / TDF)	Complera	August 10, 2011
	emtricitabine and tenofovir disoproxil fumarate (emtricitabine / tenofovir, FTC / TDF)	Truvada	August 2, 2004
	lamivudine and zidovudine (3TC / ZDV)	Combivir	Sept. 27, 1997
	<b>lopinavir and ritonavir</b> (ritonavir-boosted lopinavir, LPV/r, LPV / RTV)	Kaletra	Sept. 15, 2000



https://aidsinfo.nih.gov/education-materials/fact-sheets/21/58/fda-approved-hiv-medicines

### Classes of HIV Medications and HIV/AIDS Treatment in Older Adults: Omnicare Geriatric Pharmaceutical Care Guidelines



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# A MOST TRUSTED RESOURCE

#### Welcome to the Omnicare Geriatric Pharmaceutical Care Guidelines®

The Omnicare *Guidelines*<sup>®</sup> is the nationally recognized best practice for pharmacy care in seniors. This outcomes-based resource independently rates drug therapies specifically for their effectiveness and safety in an older adult population and provides the relative cost of each therapy.

All clinical evaluations are performed by the Philadelphia College of Pharmacy at University of the Sciences in Philadelphia, and are approved by the national panel that comprises the Omnicare Pharmacy and Therapeutics Committee. In addition, the Omnicare *Guidelines*<sup>®</sup> is reviewed and endorsed by the American Geriatrics Society.

#### **Recent Updates**

> Allergic Rhinoconjunctivitis and Chronic Urticaria

My Quick References

> HIV/AIDS Management in Olde ..



### Classes of HIV Medications and HIV/AIDS Treatment in Older Adults: Omnicare Geriatric Pharmaceutical Care Guidelines

Table I. Preferred Regimens for ART-Naïve Patients Regardless of Baseline Viral Load or CD4 Count

Regimen	Components	Usual Dosage Range (mg) and Adjustments for Organ Dysfunction	Rationale	Considerations for Older Adult Patients
NNRTI- Based Regimen	EFV/TDF/FTC* (ATRIPLA®) <sup>70-75</sup>	600/300/200 → Once-daily regimen (1 tablet total) Renal: Split components in patients with creatinine clearance (CrCl) <50 mL/min; consider another NRTI instead of TDF Hepatic: Split components in moderate/severe hepatic impairment;	Once daily Very low pill burden Well tolerated Active against HBV EFV is the preferred NNRTI because of virologic efficacy and tolerability Resistance mutations and cross- resistance	TDF can cause renal failure (RF) → not recommended w/CrCl <50 mL/min TDF/FTC can decrease BMD Neuropsychiatric effects with EFV EFV not recommended in patients with Child-Pugh Class B, C hepatic impairment Lower genetic barrier to resistance than



Omnicare Geriatric Pharmaceutical Care Guidelines: HIV/AIDS Management in Older Adults

# Medication Information and HIV/AIDS Treatment in Older Adults: Omnicare Geriatric Pharmaceutical Care Guidelines



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#### **Detailed Findings**

Introduction Epidemiology Detection Multi-Morbidities Goals of Treatment Baseline Evaluation Initiate Therapy

- Resistance Testing Response to HAART HAART New Agents
- Non-preferred Agents
- Major Drug-Drug
- Immunizations
- Lifestyle
- End-of-Life
- Preferred Agents

#### **Tables**

Table I. Regimens for ART-Naive Patients

Table II. Regimens for Pre-ART Plasma HIV

#### HIV/AIDS Management in Older Adults

Updated: June 2015

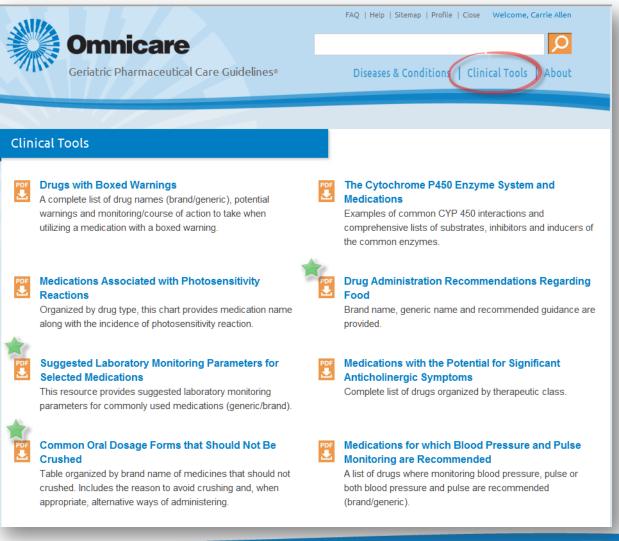
#### **Resistance Testing**

<u>HIV</u> drug resistance testing should be performed in all patients diagnosed with <u>HIV</u> during their initial visit even if therapy initiation has to be postponed. If therapy is being postponed, resistance testing can be repeated when drug therapy is initiated. Resistance testing should also be done prior to regimen changes if the change is due to virologic failure. Patients must have viral loads of  $\geq$ 500 copies/mL, since below that level, resistance testing cannot be measured. Optimal testing occurs with viral loads of >1000 copies/mL; however, patients with viral loads between 500 and 1000 copies/mL should still undergo resistance testing even with the risk of inconclusive results. If the reduction of viral load after the start of <u>HAART</u> is lower than expected, resistance testing also may be considered at that point.<sup>33</sup>

Resistance testing by genotype rather than by phenotype is preferred for initial evaluation. Phenotype testing is generally recommended for patients with resistance to multiple agents or drug classes. Phenotype testing is more expensive and has a longer turnaround time, making it less preferred. Genotype testing is more sensitive in detecting mixed wild-type/resistant virus. Most genotype testing evaluates present mutations in the reverse transcriptase or PI genes. If other drug classes are a concern for resistance, a supplemental test may need to be ordered. Interpreting resistance test results requires an experienced practitioner; therefore, it may be prudent to consult an infectious disease specialist for guidance, particularly if the patient's virus is highly resistant.<sup>49-51</sup>



# Medication Information and HIV/AIDS Treatment in Older Adults: Omnicare Geriatric Pharmaceutical Care Guidelines





Drug Class	Generic Name (Other names and acronyms)	Administration Tips and Common Concerns
Nucleoside/Nucleot	ide Reverse Trans	criptase Inhibitors (NRTIs)
<ul> <li>Class disadvantages:</li> <li>Lactic acidosis with hepatic steatosis</li> <li>Dyslipidemia</li> <li>Liver damage</li> </ul>	<b>abacavir</b> (abacavir sulfate, ABC)	Abacavir hypersensitivity reaction (HSR): 5 to 8% of patients ; usually observed during the first 6 weeks HLA-B*5701 allele is present in patients who are at risk of developing a HSR to abacavir, <b>contraindicated</b> if positive Risk of MI - use with caution in those with high risk for cardiovascular disease
	emtricitabine (FTC) lamivudine (3TC)	Hyperpigmentation (not harmful)
		Diarrhea, nausea, insomnia, headaches



https://aidsinfo.nih.gov/education-materials Table 14 ART Adverse Effects Omnicare Geriatric Pharmaceutical Care Guidelines: HIV/AIDS Management in Older Adults

Drug Class	Generic Name (Other names and acronyms)	Administration Tips and Common Concerns
Nucleoside/Nucleot	ide Reverse Trans	criptase Inhibitors (NRTIs) - continued
<ul> <li>Class disadvantages:</li> <li>Lactic acidosis with hepatic steatosis</li> <li>Dyslipidemia</li> <li>Liver damage</li> </ul>	<b>tenofovir disoproxil fumarate</b> (tenofovir DF, TDF)	Can be administered with or without food Can decrease bone mineral density Can cause renal impairment Renal dosing adjustments are required Use with caution in pre-existing renal insufficiency
	<b>zidovudine</b> (azidothymidine, AZT, ZDV)	Bone marrow suppression, lipoatrophy, lactic acidosis, myopathy



https://aidsinfo.nih.gov/education-materials Table 14 ART Adverse Effects Omnicare Geriatric Pharmaceutical Care Guidelines: HIV/AIDS Management in Older Adults

Drug Class	Generic Name (Other names and acronyms)	Administration Tips and Common Concerns	
Non-Nucleoside Rev	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
Class disadvantages:	<b>efavirenz</b> (EFV)	Neuropsychiatric and central nervous system (CNS) related side effects	
<ul> <li>Greater risk for resistance than some other classes</li> </ul>		Administer at bedtime on an empty stomach Avoid administering with high fat meals; as this increases absorption of EFV, and increases the risk of CNS side effects	
<ul> <li>Risk of cross- resistance</li> <li>Skin rash</li> </ul>		St. John's Wort may decrease EFV: combination not recommended	



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Drug Class	Generic Name (Other names and acronyms)	Administration Tips and Common Concerns
Non-Nucleoside Re	verse Transc	riptase Inhibitors (NNRTIs) - continued
Class disadvantages: • Greater risk for	<b>rilpivirine</b> (rilpivirine HCl, RPV)	Should be taken with a normal-to-high-calorie meal for adequate absorption (protein supplement drinks do not qualify)
resistance than Protease		Use of proton pump inhibitors (e.g., omeprazole) is <b>contraindicated</b>
<ul><li>Inhibitors (PIs)</li><li>Risk of cross-</li></ul>		Antacids and H2-Receptor Antagonists (e.g., ranitidine) may decrease its effects
<ul><li>resistance</li><li>Skin rash</li></ul>		Give 4 hr. before or 12 hr. after H2-receptor antagonists
		St. John's Wort decreases RPV avoid combination

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Omeprazole, ranitidine, and antacids examples of medications that are often obtained from central supply

This means there is **no** interaction check done by pharmacy

Always ask the pharmacist before giving OTC meds to people taking ART



Drug Class		
Protease Inhibitors (PIs)		
Class disadvantages:		
<ul> <li>Metabolic complications: dyslipidemia, insulin resistance,</li> </ul>		
hepatotoxicity		
<ul> <li>Significant GI effects: nausea, flatulence, diarrhea, dyspepsia</li> </ul>		

- Can recommend pre-treatment with simethicone for flatulence
- Can recommend other remedies for dyspepsia, nausea and diarrhea
  - Caution with antacids, PPI, and H2-Receptor Antagonists (H2RA; e.g., ranitidine)

https://aidsinfo.nih.gov/education-materials Table 14 ART Adverse Effects Omnicare Geriatric Pharmaceutical Care Guidelines: HIV/AIDS Management in Older Adults



Drug Class: Protease Inhibitors (PIs) Generic Name (Other names and acronyms)	Administration Tips and Common Concerns
atazanavir (atazanavir sulfate, ATV)	Always take with meals, to increase absorption Gastric upset Strict rules on separating timing from PPI (12 h), and H2RA (10 h) and reducing dose of the acid suppressing agent Administer ATV 2 hours before or 1 hour after taking antacids
<b>ritonavir</b> (RTV)	Gastric upset, metabolic concerns (including central obesity), musculoskeletal pain, parasthesias, peripheral neuropathy Note: many other PIs are given in combination with ritonavir, <u>example</u> : ritonavir-boosted atazanavir (ATZ/r)





Drug Class	Generic Name (Other names and acronyms)	Administration Tips and Common Concerns	
Integrase Inhibitors			
Class disadvantages: • Insomnia • GI effects	<b>dolutegravir</b> (DTG)	Administer with or without food Without food: take DTG 2 hours before or 6 hours after cation-containing antacids (e.g., Tums) or supplements (e.g., calcium)	
	<b>elvitegravir</b> (EVG)	Administer with food St. John's Wort may decrease EVG	
	<b>raltegravir</b> (raltegravir potassium, RAL)	Administer with or without food St. John's Wort may decrease RAL Depression Hypersensitivity reaction (HSR) has occurred when RAL + other drugs known to cause HSR. Stop all ARVs if HSR occurs and get a medical evaluation	



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Be aware of issues noted on the previous slides

Be prepared to counsel patients, anticipate their needs, and to be supportive





Collaborate with the resident, prescribers, coworkers, and pharmacists

Everyone should share information to avoid:

- Treatment failure and resistance
- Harmful adverse effects or intolerable side effects
- Permanent harm and debility
- Opportunistic infections
- Missed doses





# References

- Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents <u>https://aidsinfo.nih.gov/guidelines</u>
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