

THE ART OF HIV MANAGEMENT: AN ANTIRETROVIRAL THERAPY REVIEW

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Disclosure

- The speaker has no actual or potential conflicts of interest in relation to this presentation.

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Objectives

- **Pharmacists**
 - Identify recommended initial antiretroviral therapy (ART) regimens for most treatment naïve people with HIV
 - Evaluate common drug-drug interactions between ART and other medications
 - Describe the role pharmacist in various setting can play in HIV patient care
- **Pharmacy Technicians**
 - Identify commonly prescribed antiretroviral therapy (ART) regimens
 - Identify medications that contain tenofovir disoproxil fumarate vs tenofovir alafenamide
 - Describe the role pharmacy technicians can play in HIV patient care

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Which of the following best describes your role in pharmacy?

- Pharmacy technician
- Pharmacist in community setting
- Pharmacist in hospital setting
- Pharmacist in outpatient clinic
- Pharmacist in academia
- Pharmacy resident
- Pharmacy student
- Other

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Have you ever filled an antiretroviral prescription, verified an order, or managed a patient with HIV?

Yes

No

Unsure

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HIV in United States


- At the end of 2016, an estimated 1.1 million people aged 13 and older had HIV infection
- Approximately 38,700 Americans became newly infected in 2016
- 52% of these new infections were in the South
- 1 in 7 individuals living with HIV are unaware of their status

1. <https://www.cdc.gov/hiv/statistics/overview/index.html>,
2. <https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics>

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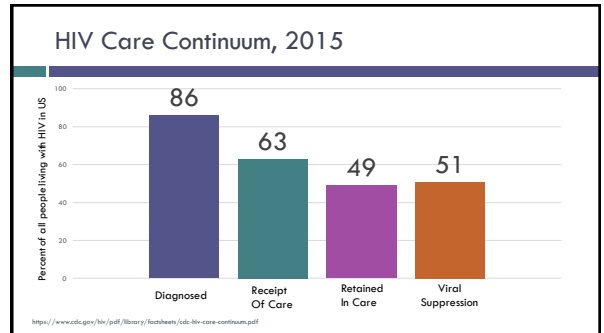
HIV in New Mexico—2016

- 3,442 people were living with HIV infection
- 134 new HIV diagnosis is adults and adolescents
- 54 people were newly classified as having stage-3 HIV infection (AIDS)
- 34 people had HIV infection progress to stage-3



<https://mhba.nmhs.org/data/view/Infections/2139/>

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HIV Transmission Risk

Potentially infectious	NOT infectious
<ul style="list-style-type: none"> Blood Breast milk Tissue Semen Vaginal secretions Visibly bloody fluids Other bodily fluids 	<ul style="list-style-type: none"> Urine Saliva Sweat Tears Nasal secretions Sputum Vomitus Stool

<https://www.hiv.gov/hiv-basics/overview/about-hiv-and-aids/how-to-hiv-transmitted>

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Estimated Per-Act Probability of Acquiring HIV from an Infected Source

Type of Exposure	Risk per 10,000 Exposures
Parenteral	
Blood Transfusion	9,250
Needle-Sharing During Injection Drug Use	63
Percutaneous (Needle-Stick)	23
Sexual	
Receptive Anal Intercourse	138
Insertive Anal Intercourse	11
Receptive Penile-Vaginal Intercourse	8
Insertive Penile-Vaginal Intercourse	4
Receptive Oral Intercourse	Low
Insertive Oral Intercourse	Low

<https://www.cdc.gov/hiv/risk/estimates/likelihoods.html>

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Treatment as Prevention

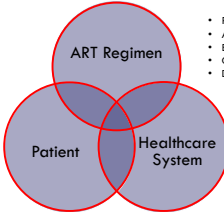


- People with HIV who maintain an undetectable viral load for at least 6 months do not transmit HIV through condomless sex.

^{1.} <https://www.preventionresearch.org/consensus>
^{2.} <https://www.cdc.gov/hiv/risk/art/inda.html>

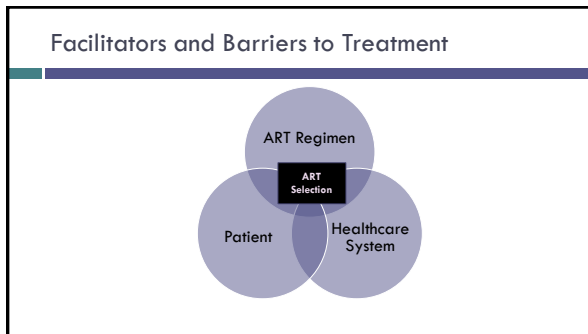
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Facilitators and Barriers to Treatment

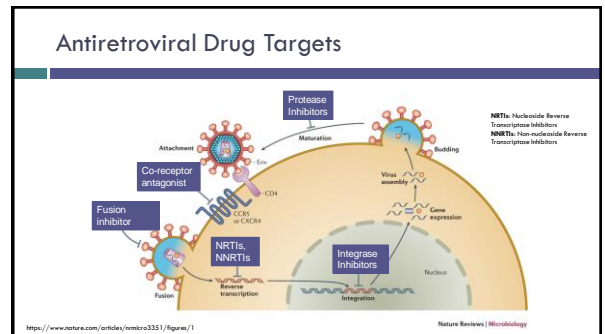


- Facilitators:**
 - Social issues
 - Finances
 - Housing
 - Access to food
 - Transportation
 - Social support
 - Comorbidities
 - Psychosocial issues
 - Stigma
- Barriers:**
 - Pill burden
 - Adverse effects
 - Barrier to resistance
 - Cost/coverage
 - Drug interactions
 - Insurance
 - Access to services
 - Formularies
 - Prior authorizations
 - Restrictions to specialty pharmacies
 - Stigma/discrimination
 - Cultural competency

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Antiretroviral Regimen Selection

- 2 to 3 drug regimen from at least 2 different drug classes
- Factors to be considered for ART selection
 - Pretreatment HIV VL and CD4 count
 - HIV genotype drug resistance testing
 - ART history
 - HLA-B*5701 status
 - Patient preference
 - Anticipated adherence to regimen
 - Comorbidities
 - Drug interactions
 - Adverse effects
 - Pill burden
 - Cost/ insurance coverage

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Treatment Goals

- Maximally and durably suppress plasma HIV RNA
 - Undetectable HIV viral load
- Restore and preserve immunologic function
 - Improve and maintain high stable CD4 count
- Reduce HIV-associated morbidity and prolong duration & quality of survival
- Prevent HIV transmission

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Predictors of Virologic Success

- Low baseline viremia
- High potency of the ART regimen
- Tolerability of the regimen
- Convenience of the regimen
- Excellent adherence to the regimen

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Recommended Initial Regimen for Most People with HIV

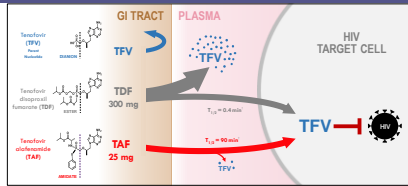
1 INSTI + 2 NRTIs

- Bictegravir/emtricitabine/TAF
- Dolutegravir/lamivudine/abacavir*
- Dolutegravir + emtricitabine/TDF **OR** emtricitabine/TAF
- Raltegravir + emtricitabine/TDF **OR** emtricitabine/TAF

INSTI= Integrase Strand Transfer Inhibitor
NRTI= Nucleoside Reverse Transcriptase Inhibitor
TDF=tenofovir disoproxil fumarate
TAF=tenofovir alafenamide
*Only for patients HLA-B*5701 negative

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Tenofovir Disoproxil Fumarate VS Tenofovir Alafenamide



1. Lee W, et al. *Antiviral Agents Chem* 2005;9(15):1898-1906. 2. Bika G, et al. *Antiviral Agents Chem* 2007;11(12):543-555. 3. Bakshi D, et al. *Antiviral Chem* 2013;10(2):419-46. 4. Rana P, et al. *J Acquir Immune Defic Syndr* 2013; 63:449-5. 5. Sun F, et al. *JACS* 2014. 2014;7(1):123-30. 6. Sun F, et al. *Chem* 2015;33(5):2006-15.

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Recommended Initial ART Regimens

- Bictegravir/emtricitabine/TAF (Biktarvy[®])
 - Dolutegravir/lamivudine/abacavir (Triumeq[®])
 - Dolutegravir (Tivicay[®]) + emtricitabine/TDF (Truvada[®]) OR emtricitabine/TAF (Descovy[®])
 - Raltegravir (Isentress[®]) 400mg BID + Truvada[®] OR Descovy[®]
 - Raltegravir (Isentress HD[®]) 1200mg daily + Truvada[®] OR Descovy[®]
- https://aidsinfo.nih.gov/guidelines/html/11/initial-and-adjunctive-therapy/11_what-to-start

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Which of the following is an antiretroviral regimen recommended by the DHHS Guidelines as an initial regimen for most people with HIV?

- darunavir + ritonavir + emtricitabine/tenofovir alafenamide
- elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
- bictegravir/emtricitabine/tenofovir alafenamide
- rilpivirine/dolutegravir

Visit the presentation to see full content. Select the correct answer. Select the correct answer. Visit the presentation to see full content.

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Other Common ART (NNRTI-Based)

- Rilpivirine (Edurant[®])
 - Must be taken with a full meal
 - Do not initiate in individuals with CD4 count <200 or HIV VL > 100,000
- Rilpivirine/emtricitabine/TDF (Complera[®])
- Rilpivirine/emtricitabine/TAF (Odefsey[®])

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Pharmacokinetic Enhancers (Boosters)

- Must be administered with most PIs and INSTI elvitegravir
- Allow higher drug exposure, lower pill burden, less frequent dosing
- Ritonavir and cobicistat work by inhibiting CYP3A4
- Cobicistat coformulated with newer regimens requiring a booster
- Cobicistat only approved from once a day PIs
- If PI is BID then ritonavir is administered BID



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Other Common ART (PI-Based)

- Darunavir (Prezista[®])
 - Should be taken with food
 - 600mg BID dosing in pregnancy or treatment experienced with darunavir resistance
- Darunavir (Prezista[®]) + ritonavir (Norvir[®]) + Truvada[®] OR Descovy[®]
- Darunavir/cobicistat (Prezcobix[®]) + Truvada[®] OR Descovy[®]
- Darunavir/cobicistat/emtricitabine/TAF (Symtuza[®])


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Other Common ART (INSTI-Based)

- Elvitegravir
 - Should be taken with food
 - Always administered with cobicistat
- Elvitegravir/cobicistat/emtricitabine/TDF (Stribild®)
 
- Elvitegravir/cobicistat/emtricitabine/TAF (Genvoya®)
 

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Other Common ART (2 drug NNRTI/INSTI)

- Rilpivirine/dolutegravir (Juluca®)
 
 - Indication: individual with HIV virologically suppressed on a stable ART regimen for ≥ 6 months with no history of treatment failure and no known resistance to the individual components
 - Must be taken with a full meal

Juluca (package insert). Research Triangle Park, NC: ViiV Healthcare; 2017

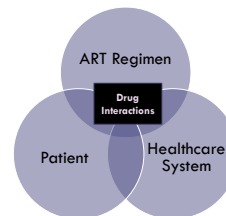
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Management of Treatment-Experienced Patients

- Based on ART history and resistance patterns
- Generally at least 2 to 3 active drugs if possible
- Often 2 NRTIs + another class
- May be NRTI sparing
- May require dose adjustment of ART agents

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Facilitators and Barriers to Treatment



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Complexity of ART

- Increased number of antiretroviral agents and combination products
- Patients may be unable to recall complex regimens
- Lack of medication knowledge by prescribers
- Non-HIV/ID providers are not well familiar with appropriate ART
- High adherence rates required for virologic suppression
- Drug resistance can drastically limit future ART options

Eggen KE, et al. Am J Pharmather 2013;47:933-40.

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Medication Errors in HIV-Infected Hospitalized Patients

- Occur in ~30% to 40% of patients
- Common Errors:
 - Improper antiretroviral regimens
 - Inappropriate dosing
 - Missing agents
 - Drug interactions
 - Omission of opportunistic infection prophylaxis

Eggen KE, et al. Am Pharmather 2013;47:933-40
Champion TD, et al. Pharm Pract 2015; 13:112

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Drug-Drug Interactions

- Pharmacokinetic (PK) drug interactions between ART and concomitant medications can cause increased or decreased drug exposures to either drug
- PK interactions can occur during absorption, metabolism, or elimination of ART
- Effects on ART drug levels can cause increased toxicities or decreased therapeutic response
- ART treatment failure is a possible result of drug interactions

<https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/367/overview>

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Resources for ART Drug Interactions

- Make sure references are updated on a regular basis and using most updated version
- Panel on Antiretroviral Guidelines for Adults and Adolescents (DHHS Guidelines)
 - <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/367/overview>
- University of Liverpool HIV Drug Interaction Checker
 - <https://www.hiv-druginteractions.org/>
- Other drug reference databases (Lexicomp, Clinical Pharmacology, Micromedex, etc.)

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NRTI Drug Interactions

- Minimal number of clinically significant drug interactions
- Do NOT coadminister emtricitabine and lamivudine
- Do NOT coadminister TDF and TAF
- Caution with other nephrotoxic drugs and TDF
- Avoid major CYP3A4 inducers with TAF
 - Carbamazepine
 - Oxcarbazepine
 - Phenytoin
 - Phenobarbital

<https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/286/nrti-drug-interactions>

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INSTI Drug Interactions

- Polyvalent cations (Al, Mg, Ca, Fe) may chelate with INSTIs
 - Each INSTI has specific separation recommended (most separate by >2hrs)
 - Avoid coadministration of raltegravir and aluminum or magnesium
- Max dose of metformin coadministered with dolutegravir is 1000mg Qday
- Elvitegravir/cobicistat has many drug interactions as both are major substrates of CYP 3A4 and cobicistat is a strong **CYP3A4 inhibitor**

<https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/287/insti-drug-interactions>

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NNRTI Drug Interactions

- Rilpivirine (RPV)
 - requires acidic environment for absorption
 - major substrate of CYP3A4
- Antacids: give at least 2 hours before or 4 hours after RPV
- H2 blockers: give H2 blocker at least 12 hours before or 4 hours after RPV
- Proton Pump Inhibitors: **CONTRAINDICATED. Do not coadminister**

<https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/285/nrti-drug-interactions>

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PI Drug Interactions

- Most PIs and boosters are major substrates of CYP 3A4 and strong CYP3A4 inhibitor = **MANY DRUG INTERACTIONS**
- Corticosteroids: coadministration can result in adrenal insufficiency and Cushing's syndrome
 - Inhaled or intranasal corticosteroids: beclomethasone & flunisolide safe
- Statins: lovastatin & simvastatin **contraindicated**
 - Atorvastatin and rosuvastatin may be titrated and based on PI have a max dose recommended
- **Contraindicated** with some hepatitis C direct-acting antiviral agents

<https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/284/pi-drug-interactions>

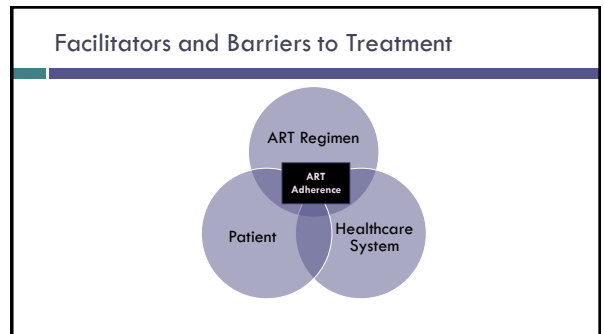
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Which of the following is a major drug-drug interaction with the entire integrase inhibitor class?

Proton pump inhibitors
H2-blockers
Polyvalent cations
Statins

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Medication Adherence

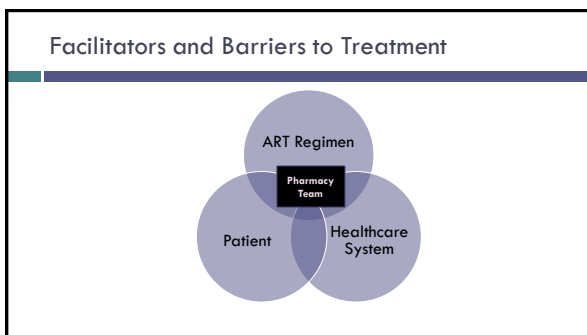
- Whether patients take their medications as prescribed and continue to take their medication correctly
- Reasons why medication adherence can be difficult
 - Medication side effects
 - Busy schedule
 - Dose schedule
 - Medication cost
 - Illness or depression
 - Alcohol or drug use
 - Homelessness
 - Fear of others finding out patient has HIV

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Medication Adherence Tools

Images illustrating medication adherence tools: a pill bottle with keys, a pill box, a blister pack, the Behavioral Health logo, a house icon, and a smartphone displaying a medication app interface.

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Pharmacist Role in HIV Care

- Adherence counseling (refill reminders, refill syncing, pill boxes, blister packs, alarms)
- Patient education (regarding dosing, adverse effects, drug interactions, missed doses)
- Maintain ART inventory
- Dispense complete regimens
- ART regimen selection
- Medication reconciliation at hospital admission and discharge
- ART safety monitoring (renal/hepatic dose adjustment, adverse effects, drug interactions)
- Opportunist infection prophylaxis and treatment monitoring
- Provider/pharmacy education
- Smoking cessation & other comorbidity management
- Referrals

1. Seibert P, et al. Patient Preference and Adherence 2012;6:297-322. 2. Schaefer JJ, et al. Am J Health-Syst Pharm. 2016;73:468-94.

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Pharmacy Technician Role in HIV Care

- Benefits investigation
- Help with prior authorization
- Help maintain inventory
- Copay assistance enrollment
- Refill reminders
- Avoid HIV disclosure

Gilbert EM, et al. Am J Health-Syst Pharm. 2016;73:57-63

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Which of the following is a possible role a pharmacist can take in HIV patient care?

- Counsel a patient on OTC medications to avoid with ART regimen
- Perform medication reconciliation upon admission to ensure ART appropriately restarted
- Sync a patient's refills to ensure they pick up a complete ART regimen
- All of the above

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Conclusion

- Only about 50% of individual living with HIV in the US are retained in care and have viral suppression
- There are numerous safe and effective ART agents available
- ART is complex in terms of increased numbers of agents and combinations, drug interactions, & high adherence rates required for virologic suppression
- Pharmacy teams in various settings can impact and improve HIV care

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