Pharmacy Tech Topics™

VOLUME 25 NO. 4 | OCTOBER 2020

HIV TREATMENT AND PROPHYLAXIS

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Pharmacy Tech Topics™ (USPS No. 014-766) is published quarterly for $50 per year by the Illinois Council of Health-System Pharmacists, 4055 N. Perryville Road, Loves Park, IL 61111-8653. Phone 815-227-9292. Periodicals Postage Paid at Rockford, IL and additional mailing offices.

POSTMASTER: Send address changes to:
Pharmacy Tech Topics™, c/o ICHP, 4055 N. Perryville Road, Loves Park, IL 61111-8653

LEARNING OBJECTIVES

Upon completion of this module, the subscriber will be able to:

1. Identify modes of transmission of human immunodeficiency virus (HIV) and how to prevent transmission.
2. Identify first-line antiretroviral therapy for people living with HIV (PLWH) who are new (naïve) to treatment.
3. Recognize classes of antiretroviral agents and their associated side effects.
4. Identify potential drug-drug interactions between antiretroviral agents used to treat HIV and over the counter (OTC) products.
5. Recognize barriers to antiretroviral therapy initiation and adherence.

ACCREDITATION

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This module will provide 2.5 contact hours of continuing pharmacy education credit for pharmacy technicians.

ACPE Universal Activity Number: 0121-0000-20-004-H02-T | Type of Activity: Knowledge-based
Release Date: 10/1/20 | Expiration Date: 10/1/2023 (Must be completed by 9/30/2023 at 11:59PM CT)

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HIV: TREATMENT AND PROPHYLAXIS

Please refer to HIV Terminology in Appendix A **(page 19)** and HIV Medications in Appendix B **(page 20)** while reading through this module.

INTRODUCTION

Human Immunodeficiency Virus (HIV) is a virus responsible for attacking cells that assist the body in fighting infection.[1] If left untreated, HIV can lead to Acquired Immunodeficiency Syndrome (AIDS). There are 1.1 million Americans living with an HIV diagnosis in the United States (US) with approximately 38,000 individuals receiving a new diagnosis every year.[2] Still, 1 in 7 people are unaware of their HIV status which leads to the unknowing transmission of the virus.[2] Therefore, it is recommended that all persons 13 to 64 years of age receive at least one routine HIV test and those with risk factors for HIV (e.g., men who have sex with men [MSM]) get tested at least annually, but ideally once every 3 to 6 months based on their level of risk.[3]

HIV TRANSMISSION AND PREVENTION

HIV is typically transmitted parenterally (e.g., injection drug use) or sexually (e.g., condomless sex) **(Table 1)**. Unfortunately, there are various myths that HIV can be transmitted through sharing food or drink, saliva, sweat, tears, closed-mouth kissing, insects, pets, water, or air.[4,5]

Although blood transfusion carries the highest rate of infectivity, the risk of getting HIV through infusion is very low due to universal screening of blood products which must be tested for viruses. Within the US, the most common cause of HIV transmission is through receptive anal intercourse.[6] Due to the introduction of preventive efforts such as pre-exposure prophylaxis (PrEP), treatment as prevention (TasP), and the undetectable = untransmittable (U=U) movement, the incidence of HIV has remained stable in the US.

Pre-exposure Prophylaxis (PrEP)

PrEP is one way of preventing HIV transmission. This form of prevention currently requires a once daily oral tablet regimen. When daily adherence (compliance) is

Table 1. Approximate Probability (Chance) of Acquiring HIV from People Living with HIV (PLWH) by Exposure Act[4,5]

Type of Exposure	Risk per 10,000 Exposures
Parenteral	
Blood transfusion	9,250
Injection drug use with needle sharing	63
Needle-stick	23
Sexual	
Receptive anal intercourse	138
Insertive anal intercourse	11
Receptive penile-vaginal intercourse	8
Insertive penile-vaginal intercourse	4
Receptive or insertive oral intercourse	Low
Other	
Biting, spitting, throwing body fluids (semen/saliva), or sharing sex toys	Negligible

100%, PrEP reduces the risk of HIV transmission by 99%.[7] Currently, there are two formulations of PrEP available **(Table 2)**.[8,9] It is important to educate patients that PreP only prevents against HIV and not other sexually transmitted infections. Prior to starting PrEP, a patient must have a documented negative HIV test within the preceding 7 days and every 3 months thereafter. It is important that prescriptions for these medications are only written for 90 days and refills should require additional laboratory testing.[10]

Treatment as Prevention (TasP) and Undetectable = Untransmittable (U=U)

These two methods of prevention rely on an individual to be aware of their HIV status and receiving antiretroviral therapy (ART). Clinical trials have demonstrated efficacy in eliminating transmission of HIV from individuals who consistently have a viral load of less than 200 copies/mL. Remember, virologic suppression is defined as a viral load (how much virus is in the blood) below the limit of detection (commonly less than 20 copies/mL; also known as undetectable).[11]

Treatment as prevention (TasP) is a term used to describe a practice in reducing HIV transmission when a person living with HIV takes ART and reduces their viral load to an undetectable level. Once the person living with HIV reduces their viral load, they effectively reduce the risk of transmitting HIV through sex, needle sharing, and mother-to-child transmission.[11] This concept is the same as undetectable = untransmittable (U=U) since the goal of taking ART on a daily basis is to reduce a patient's viral load to an undetectable amount in the blood and, therefore, reduce the transmission potential of HIV.

Table 2. HIV Prevention Medications (PrEP)[8,9]

	Tenofovir alafenamide (TAF)/emtricitabine (FTC)	Tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC)
Brand name	DESCOVY	TRUVADA
PrEP indications	Men, transgender females (not approved for use in women)	Men and women
Use in kidney dysfunction	Yes	No
Food requirements	Can be taken with or without food	
Able to be crushed or split	• Crushing or splitting tablets has not been studied and is not recommended • TAF is soluble in water but has a bitter and burnt aromatic flavor profile • FTC is soluble in water	• May split tablets • May crush and stir into water, grape juice, or orange juice.
Drug interactions	Coadministration not recommended: • Rifabutin, Rifampin, Rifapentine • St. John's Wort • Tipranavir/Ritonavir Alternative recommended (Avoid Use): • Carbamazepine • Oxcarbazepine • Phenobarbital • Phenytoin	Avoid: • Adefovir • High dose NSAIDs Caution: • Medications competing for renal excretion
Side effects	• New or worsening kidney problems, including kidney failure (less likely than TDF) • Severe liver problems (immediately alert provider if patient complains of yellowing of skin or eyes, tea-colored urine, light stool color, ongoing loss of appetite) • Diarrhea • Headache • Fatigue • Nausea • Stomach pain	• New or worsening kidney problems, including kidney failure • Severe liver problems (immediately alert provider if patient complains of yellowing of skin or eyes, tea-colored urine, light stool color, ongoing loss of appetite) • Bone problems or increased bone fractures • Headache • Stomach pain • Decreased weight

NSAIDs = non-steroidal anti-inflammatory drugs (e.g., ibuprofen, naproxen, etc.)

Post-Exposure Prophylaxis (PEP)

Post-Exposure Prophylaxis, or PEP, is different than PrEP as it requires an individual who is HIV-negative to take full ART regimen for 28 days due to a potential or known exposure to someone living with HIV. PEP must be started within 72 hours after a possible exposure to HIV, but evidence shows that treatment should be started as soon as possible for the best outcomes.[12] There are two classifications for PEP, occupational (i.e., job-related for health care personnel) and non-occupational exposures (e.g., sexual or injection drug use). Occupational transmission is extremely rare, with only 1 case reported since 1999 due to the effective administration and timing of prophylaxis.[13] Healthcare personnel reporting contact with infectious blood, tissue, or body fluids in people living with HIV (PLWH) should be offered PEP if they meet criteria in **Table 3**.[14] It is important to note that fluids such as feces, gastric or nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are only considered infectious if they contain blood. Intact skin acts as a barrier against HIV transmission. Therefore, contamination of intact skin (i.e., no visible cuts or open wounds) with blood or other potentially contaminated fluids is not considered an exposure and does not require PEP.

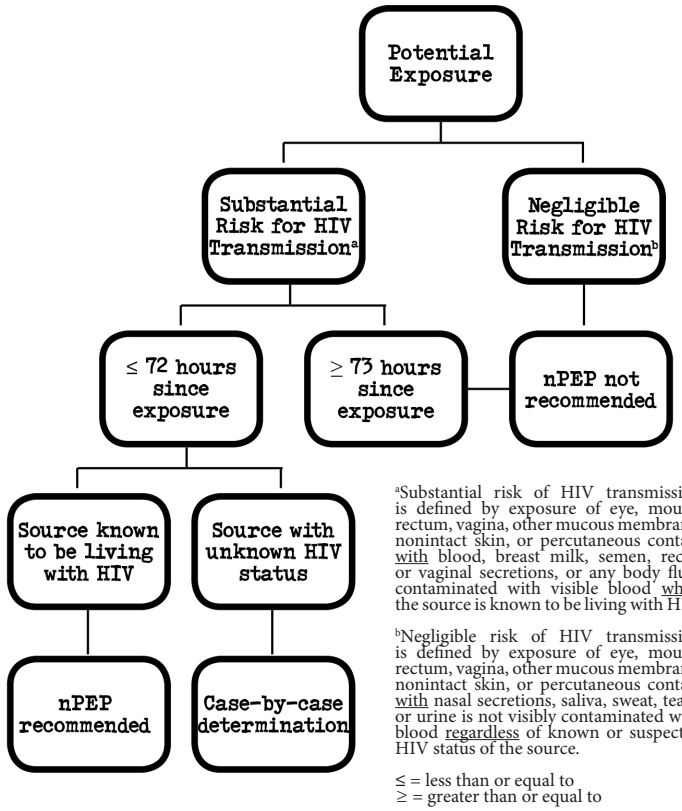
Non-occupational PEP (nPEP) should be started if a person who is HIV-negative may have been exposed to HIV during sex or while injecting drugs (**Table 3**) (**Figure 1**).[15,16] Non-occupational PEP (nPEP) should only be used in emergency situations and patients should be educated about necessary condom use and other safe sex practices, or using clean drug equipment when injecting drugs. If you notice a patient receiving frequent PEP, they should be educated about the benefits of PrEP.

HIV testing must be performed prior to initiating PEP to confirm an HIV-negative result. Additional testing for HIV should occur 4 – 6 weeks, 3 months, and 6 months after the exposure.[15] Individuals starting PEP are offered a 3-drug regimen taking into consideration kidney function, childbearing potential, pregnancy status, potential for drug-drug interactions, and the potential for medication resistance (drug no longer works). The preferred PEP regimen is tenofovir disoproxil fumarate/emtricitabine once daily plus dolutegravir 50 mg by mouth once daily or raltegravir 400 mg by mouth twice daily for 28 days (**Table 4 - See page 6**).[15] Although the adult and adolescent (13 years and older) guidelines recommend either dolutegravir or raltegravir, both integrase strand transfer inhibitors (INSTIs), there are specific considerations for dolutegravir in women of childbearing potential (**Table 4 - See page 6**).[15] Additionally, drug characteristics, potential side effects, and drug interactions are described in **Table 5 on page 7**.

Table 3. Indications for PEP[14,15]

Non-occupational	Occupational
• Exposure to HIV during sex (condomless sex with someone living with HIV, unknown HIV status, or condom break during sex) • Victim of sexual assault • Sharing drug paraphernalia while injecting drugs (e.g., needles, syringes, or any other equipment)	• Percutaneous injury (e.g., needlestick or cut with sharp instrument used on a patient) • Contact with mucous membrane or nonintact skin (e.g., exposed skin with open wounds or abrasions) • Body fluids associated with transmission of HIV (e.g., blood, semen, vaginal secretions, body fluids with visible blood) • Potentially infectious body fluids (actual risk unknown) such as cerebrospinal, synovial (joint), pleural (lung), peritoneal (abdominal cavity), pericardial (around the heart), and amniotic (placental) fluids • Direct contact with HIV in a research laboratory

Figure 1. Algorithm for Treatment of Possible Nonoccupational HIV Exposure.[15]



[a]Substantial risk of HIV transmission is defined by exposure of eye, mouth, rectum, vagina, other mucous membrane, nonintact skin, or percutaneous contact with blood, breast milk, semen, rectal or vaginal secretions, or any body fluid contaminated with visible blood when the source is known to be living with HIV.

[b]Negligible risk of HIV transmission is defined by exposure of eye, mouth, rectum, vagina, other mucous membrane, nonintact skin, or percutaneous contact with nasal secretions, saliva, sweat, tears, or urine is not visibly contaminated with blood regardless of known or suspected HIV status of the source.

≤ = less than or equal to
≥ = greater than or equal to

Table 4. Preferred and Alternative Antiretroviral Medications for PEP[15]

Age	Preferred Medications	Alternative Medications
≥ 13 years, including pregnant women and women of childbearing potential, with normal kidney function (CrCL ≥ 60 mL/min)	Tenofovir disoproxil fumarate 300 mg/ emtricitabine 200 mg (TRUVADA) once daily ***plus*** raltegravir (ISENTRESS) 400 mg PO BID	Tenofovir disoproxil fumarate 300 mg/ emtricitabine 200 mg (TRUVADA) once daily ***plus*** darunavir (PREZISTA) 800 mg once daily ***and*** ritonavir (NORVIR) 100 mg PO once daily
≥ 13 years, if benefits outweigh risk in pregnant women and women of childbearing potential, with normal kidney function (CrCL ≥ 60 mL/min)	Tenofovir disoproxil fumarate 300 mg/ emtricitabine 200 mg (TRUVADA) once daily ***plus*** dolutegravir (TIVICAY) 50 mg PO daily	
≥ 13 years with abnormal kidney function (CrCL < 60 mL/min)	Dose adjusted zidovudine and lamivudine ***plus*** raltegravir (ISENTRESS) 400 mg BID ***OR*** dolutegravir (TIVICAY) 50 mg PO daily	Dose adjusted zidovudine and lamivudine ***plus*** darunavir (PREZISTA) 800 mg once daily ***and*** ritonavir (NORVIR) 100 mg PO once daily
2 – 12 years	Age and weight-based tenofovir disoproxil fumarate (VIREAD) ***plus*** emtricitabine (EMTRIVA), ***and*** raltegravir (ISENTRESS)	Age and weight-based zidovudine and lamivudine ***plus*** raltegravir ***OR*** lopinavir/ ritonavir
		Age and weight-based tenofovir disoproxil fumarate (VIREAD) ***plus*** emtricitabine (EMTRIVA), ***and*** lopinavir/ritonavir (KALETRA)
3 – 12 years	Age and weight-based tenofovir disoproxil fumarate (VIREAD) ***plus*** emtricitabine (EMTRIVA), ***and*** raltegravir (ISENTRESS)	Age and weight-based tenofovir disoproxil fumarate (VIREAD) ***plus*** emtricitabine (EMTRIVA), ***plus*** darunavir ***and*** ritonavir
4 weeks – < 2 years	Age and weight-based zidovudine oral solution ***plus*** lamivudine oral solution ***and*** raltegravir ***OR*** lopinavir/ritonavir oral solution	Age and weight-based zidovudine oral solution ***plus*** emtricitabine oral solution ***and*** raltegravir ***OR*** lopinavir/ritonavir oral solution

≥ = greater than or equal to, CrCL = creatine clearance, < = less than, PO = by mouth, BID = twice a day

INITIATING ANTIRETROVIRAL THERAPY IN A TREATMENT-NAÏVE INDIVIDUAL

HIV attacks and destroys CD4 cells (infection-fighting cells) of the immune system leading to infections and cancers related to HIV if left untreated (**Table 6 on page 8; Figure 1 on page 5**).[17,18,19] Treatment of HIV involves medications that slow the replication and progression of the virus thus reducing morbidity (illness) and mortality (death). Noted benefits to ART include sustained viral suppression (undetectable viral load), reduced risk of drug resistance, better overall health, improved quality of life, and decreased risk of transmission. There is no cure for HIV. Taking ART as prescribed reduces the amount of virus (also known as viral load) in a patient's blood and bodily fluids. It also reduces the risk of transmission to others, and improves patient outcomes by helping to increase the CD4-count (also known as T-cells). The goal of ART is to reduce the viral load to a level that is undetectable, meaning that the level of HIV in the blood is too low to be detected by laboratory tests. Typically, an undetectable viral load is associated with less than 20 copies/mL of HIV in the blood. Once starting ART, it usually takes 3 to 6 months to become undetectable.

All patients diagnosed with HIV or re-engaging in care should start ART as soon as possible, depending on the patient's willingness to do so.[11] Other factors to consider include, but are not limited to, affordability of medication (e.g., prescription insurance coverage, co-payments), comorbidities (other disease states), privacy, side effects, ability to comply with taking ART as prescribed, drug-drug interactions, living situation, and social support. Starting therapy in a patient newly diagnosed and who has never taken an ART for either treatment or PrEP is termed treatment-naïve. Patients who are re-engaging in care who previously took ART are considered treatment-experienced.

Currently, there are eight drug classes of antiretrovirals (ARVs) with more than 30 available medications.[19] These eight targets are where ARVs can interfere with the HIV lifecycle and prevent it from spreading. Currently recommended ART is composed of 2 – 3 medications consisting of 1-2 nucleoside(tide) reverse transcriptase inhibitors (NRTIs) + 1 integrase strand transfer inhibitor

Table 5. Formulations, Side Effects, Drug-Drug Interactions, and Contraindications with PEP.

Drug & Class	Available Formulations	Side Effects	Drug-Drug Interactions	Contraindications
Darunavir (DRV)/ritonavir (RTV) ***PI***	• 75, 150, 600, 800-mg tablets • 100-mg/mL oral suspension	• Diarrhea • Headache • Liver failure • Nausea • Rash	Numerous • Fluticasone (avoid use and use beclomethasone if possible) • Atorvastatin, pravastatin, rosuvastatin (start with low doses and increase based on response)	• Co-administration with RTV and certain sedative hypnotics, antiarrhythmics, sildenafil, or simvastatin
Dolutegravir (DTG) ***INSTI***	• 10, 25, 50-mg tablet	• Headache • Trouble sleeping	• Efavirenz • Fosamprenavir/RTV • Rifampin • Tipranavir/RTV • Products containing sucralfate, buffered medications, Al, Ca, Fe, Mg, or Zn as seen in antacids, laxatives, supplements, and MVI can reduce DTG absorption	• Dofetilide
Emtricitabine (FTC) ***NRTI***	• 200-mg capsule • 10-mg/mL solution	• Skin discoloration	---	• Lamivudine • For patients with chronic HBV, monitor closely after stopping medication – may cause worsening of acute hepatitis (inflammation of the liver)
Lamivudine (3TC) ***NRTI***	• 100, 150, and 300-mg scored tablets • 10-mg/mL oral solution	• Diarrhea • Headache • Nausea • Tiredness • Weakness	• Sorbitol-containing solutions	• Emtricitabine • For patients with chronic HBV, monitor closely after stopping medication – may cause worsening of acute hepatitis
Lopinavir (LPV)/RTV ***PI***	• 200/50 and 100/25-mg tablets • 80/20-mg/mL oral solution	• Diarrhea • Nausea/ vomiting	Numerous • Fluticasone (avoid use and use beclomethasone if possible) • Atorvastatin, pravastatin, rosuvastatin (start with low doses and increase based on response)	• Co-administration with RTV and certain sedative hypnotics, antiarrhythmics, sildenafil, or simvastatin
Raltegravir (RAL) ***INSTI***	• 400 and 800-mg tablets • 100-mg chewable, scored tablet • 25-mg chewable tablet	• Fatigue • Headache • Nausea	• Rifampin • Products containing sucralfate, buffered medications, Al, Ca, Fe, Mg, or Zn as seen in antacids, laxatives, supplements, and some MVI can reduce RAL absorption	• None
Ritonavir (RTV) ***PI***	• 100-mg tablets • 80-mg/mL oral solution	• Abdominal pain • Altered taste • Diarrhea • Dizziness • Headache • High blood sugars • Indigestion • Liver failure • Loss of appetite • Nausea/ vomiting • Numbness/ tingling • PR and QT prolongation • Weakness	Numerous • Fluticasone (avoid use and use beclomethasone if possible) • Atorvastatin, pravastatin, rosuvastatin (start with low doses and increase based on response)	• Co-administration with PI and certain sedative hypnotics, antiarrhythmics, sildenafil, or simvastatin
Tenofovir disoproxil fumarate (TDF) ***NRTI***	• 150, 200, 250, and 300-mg tablets • 40-mg/gm powder • FDC	• Diarrhea • Headache • Kidney injury • Nausea/vomiting • Weakness	NSAIDs (e.g., diclofenac, ibuprofen, naproxen)	• Adefovir • Do not give with acute or chronic kidney injury • For patients with chronic HBV, monitor closely after stopping medication – may cause worsening of acute hepatitis
Zidovudine (AZT) ***NRTI***	• 100-mg capsule • 300-mg tablet • 10-mg/mL oral syrup • 10-mg/mL intravenous infusion	• Anemia • Headache • Nausea/ vomiting • Tiredness • Trouble sleeping	• Ribavirin • Tolvaptan	

Al = aluminum; Ca = calcium; FDC = fixed-dose combination; Fe = iron; INSTI = integrase strand transfer inhibitor; Mg = magnesium; MVI = multivitamin; NRTI = nucleoside/tide reverse transcriptase inhibitor; NSAID = nonsteroidal anti-inflammatory drugs; PI = protease inhibitor; Zn = zinc
See appendices A and B for HIV abbreviations and medications.

(INSTI) (**Table 7 on page 10**).[11] The agents that are preferred for initial therapy are recommended due to their safety, efficacy, lack of food requirements, and reduced likelihood of drug interactions. Single tablet regimens (STRs) are preferred as a strategy to promote medication adherence.

In the absence of complete clinical data, BIKTARVY, TRUVADA or DESCOVY + TIVICAY can be started in most patients since these treatments are safe, effective, and have a high genetic barrier to resistance (meaning they are more forgiving if 100% medication adherence cannot be ensured).[11] Dolutegravir is now considered a preferred ARV drug throughout pregnancy and an alternative for women who are trying to conceive (become pregnant).[11] Although a first-line recommendation, the use of ISENTRESS with TRUVADA or DESCOVY is not typically started due to its higher pill count (burden) and lower genetic barrier to resistance with ISENTRESS.

In December 2019, the first 2-drug regimen (2DR) single tablet regimen (STR), dolutegravir/lamivudine (DOVATO), was added to the US national guidelines as a potential option to start in most people living with HIV. The use of DOVATO requires baseline resistance testing with an HIV-1 genotype, a pretreatment HIV-1 viral load of less than 500,000 copies/mL, and known hepatitis B virus (HBV) status. DOVATO should not be started in patients with HBV.[11] If a patient is unable to use a preferred regimen, there are alternative regimens that can be prescribed.[11]

The goal of ART is for the patient to be 100% adherent to (compliant with) ART and take the medication every day as prescribed in order to prevent transmission as well as the development of ARV resistance. Intermittent medication adherence (taking a medication every couple of days or skipping doses) allows the HIV virus to develop mutations since there is a low concentration of the ARV. As the HIV virus multiplies, it has the potential to change form (mutate).[20] If a mutation occurs, drug resistance may develop, causing HIV medications that were once effective in controlling a patient's virus to no longer be effective. This allows HIV to further mutate and causes the viral load to increase, which can cause transmission of the virus. Another factor to consider is that drug resistance can be transmitted from person to person (transmitted drug resistance). It is important to note that once a mutation develops, it does not go away and remains lifelong. Drug resistance testing can be performed to identify which ARVs are no longer effective. In addition to not taking any ARVs, if one ARV is missing from the patient's regimen because it is out of stock, the patient should be educated on the importance of not taking one medication without the other(s). This is yet another reason that fixed-dose combination (FDC) tablets and STRs are preferred.

Table 6. HIV Lifecycle[18]

1. & 2. Binding and fusion: HIV binds to a CD4 receptor and one of two co-receptors on the surface of a CD4+ T-lymphocyte. The virus fuses with the cell. After fusion, the virus releases RNA into the host cell.

Medications that work here:
Nucleoside Reverse Transcriptase Translocation Inhibitor (fostemsavir), Entry Inhibitor (maraviroc), Fusion Inhibitor (enfuvirtide), and Post-Attachment Inhibitor (ibalizumab-uiyk)

3. **Reverse transcription:** An HIV enzyme, reverse transcriptase, converts single-stranded HIV RNA to double-stranded HIV DNA.

What is the difference between NRTIs and NNRTIs?
NRTIs are nucleoside or nucelotide analogues and the virus grabs these phony building blocks vs. NNRTIs bind to the enzyme itself which prevent it from working.

Medications that work here:
NRTIs (abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir, zidovudine)
NNRTIs (doravirine, efavirenz, etravirine, nevirapine, rilpivirine)

4. **Integration:** The integrase enzyme incorporates HIV DNA within the host cell genome.

Medications that work here:
INSTIs (bictegravir, dolutegravir, elvitegravir, raltegravir)

5. **Transcription:** Host RNA polymerase synthesizes copies of the HIV genome, mRNA, and proteins.

6. **Assembly:** The HIV protease enzyme cleaves large polyproteins into mature, individual proteins.

Medications that work here:
PIs (atazanavir, darunavir, fosamprenavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir)

7. **Budding**: Newly assembled virus is released ("buds") from the host cell and starts the cycle of replication again.

Figure 2. HIV Life Cycle[18]

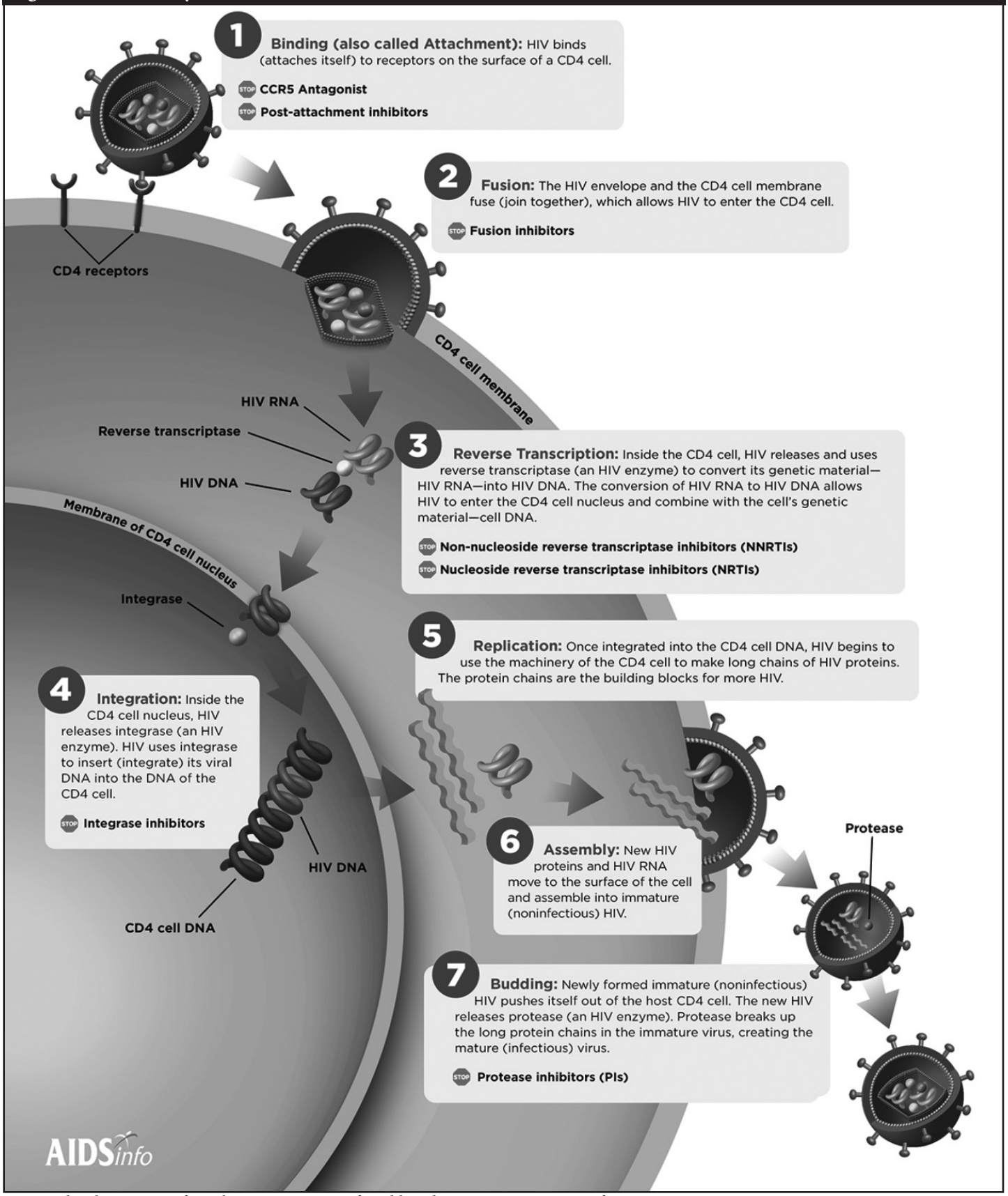


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Table 7. Recommended Initial Regimens for Most People Living with HIV[11]

	Generic Components	Brand Name	Dosing	Additional Considerations
1 INSTI + 1-2 NRTIs	Bictegravir 50 mg (BIC)/ emtricitabine 200 mg (FTC)/ tenofovir alafenamide 25 mg (TAF)	BIKTARVY[a]	1 tablet by PO daily	• Also treats HBV • Do not crush or split
	Dolutegravir 50 mg (DTG)/ abacavir 600 mg (ABC)/ lamivudine 300 mg (3TC)	TRIUMEQ[a]	1 tablet PO daily	• HLA-B*5701 test (check for HSR) must be negative
	DTG 50 mg /3TC 100 mg	DOVATO[a]	1 tablet PO daily	• First 2-drug regimen approved for initial therapy • Baseline viral load must be less than 500,000 copies/mL • Should not be used in patients with HBV or unknown HBV serologies • Genotype must be drawn prior to initiation • May be split in half or crushed and added to a small amount of semi-solid food or liquid; consume immediately
	DTG 50 mg + tenofovir disoproxil fumarate 300 mg (TDF)/FTC 200 mg	TIVICAY + TRUVADA	TIVICAY: 1 tablet (50 mg) PO daily TRUVADA: 1 tablet PO daily	• Dosage reduction in renal impairment (kidney disease) • Also treats HBV
	DTG 50 mg + TAF 25 mg/ FTC 200 mg	TIVICAY + DESCOVY	TIVICAY: 1 tablet (50 mg) PO daily DESCOVY: 1 tablet PO daily	• Also treats HBV • Improved kidney and bone markers compared to TDF
	Raltegravir 400 mg (RAL) tabs + TDF 300 mg/FTC 200 mg **or** TAF 25 mg/FTC 200 mg	ISENTRESS + TRUVADA OR DESCOVY	RAL 400 mg PO twice daily + TRUVADA **or** DESCOVY 1 tablet PO daily	• Also treats HBV
	RAL High dose (HD) 600 mg tabs + TDF 300 mg/FTC 200 mg **or** TAF 25 mg/FTC 200 mg	ISENTRESS HD + TRUVADA OR DESCOVY	RAL HD 1200 mg (2 x 600 mg tabs) PO once daily + TRUVADA **or** DESCOVY 1 tablet PO daily	

Note: PO = oral; lamivudine (3TC) can be substituted for emtricitabine (FTC) and vice versa, for all regimens, if not in a fixed-dose-combination, [a] = single-tablet regimen (STR). See appendices A and B for HIV abbreviations and medications.

ANTIRETROVIRAL THERAPY SIDE EFFECTS

Side effects have been reported with all ARVs. Prior to newer ARVs coming to the market, side effects were a common reason for switching or discontinuing therapy and medication nonadherence.[21] Thanks to modern treatment options, most side effects due to HIV medications are manageable and are rarely serious. Clinical trials generally report that less than 10% of ART-naïve patients enrolled in studies have treatment-limiting adverse events.[22]

In addition, ARVs can interact with other medications the patient is taking leading to side effects. It is for this reason that it is important to ask the patient what other prescription, over-the-counter (OTC), and supplements that they are taking to minimize the risk of drug-drug interactions. Overall, the benefits of ART far outweigh the risk of most side effects. In the event the patient does have side effects, symptoms can be managed or the patient can be switched to another ARV or alternative regimen. Refer to **Table 8 on pages 12 & 13** for common and serious side effects associated with ARVs.

It is crucial to educate the patient that side effects such as diarrhea, headache, nausea or vomiting, and/or rash may be common at the start of ART but tend to go away after the first 7 – 14 days of treatment.[11] It is important to stress that the patient should continue the regimen if the side effects are not severe and not to self-discontinue ART without first speaking to their prescriber's office. If the side effects are bothersome to the patient, many can be managed based on the patient's symptom(s).

Immune Reconstitution Inflammatory Syndrome (IRIS)

Healthcare providers should monitor for the development of non-specific side effects when starting ART such as Immune Reconstitution Inflammatory Syndrome (IRIS). This occurs when the immune system begins to recover following the start of ART. Immune Reconstitution Inflammatory Syndrome can be mild or life-threatening and is essentially an exaggerated inflammatory reaction. It can cause "unmasking," or a flare-up of an underlying, previously undiagnosed infection or a "paradoxical" reaction when there is worsening of a previously treated infection after ART is started.[17]

Another concern about ART are hypersensitivity reactions (HSRs). Although rare, HSRs can result in fever, rash, weakness, tiredness, nausea, headache, joint or muscle aches, chills, diarrhea, vomiting, or shortness of breath and typically worsen with each dose of the offending agent.[11] If a patient has this type of reaction, they should never be re-challenged with the offending agent.

For instance, the HLA-B*5701 test was developed to determine the risk for an HSR with abacavir. If the test is positive, abacavir should never be prescribed to the patient since having this gene is associated with life-threatening HSR. Therefore, abacavir-containing products (EPZICOM, TRIUMEQ, TRIZIVIR, and ZIAGEN) should never be prescribed and an allergy to abacavir should be noted in the patient's health record.[11]

Weight Gain

A side effect that has been receiving a lot of attention is the issue of weight gain with the Integrase strand transfer inhibitor (INSTI) class as well as TAF-based therapy.[11] Long-term consequences of weight gain on the development of hypertension, diabetes, and dyslipidemia in this population are unknown.

ANTIRETROVIRAL DRUG INTERACTIONS

Drug interactions, whether with other medications, supplements, foods, or disease states **(Table 9 on page 14)**, can lead to unwanted side effects. Routine medication reconciliations are of utmost importance; and updating a patient's medication record should occur with any medication change.[23] It is important to encourage the patient to be familiar with their medications (e.g., carry a list of medications or have them documented in their phone) and any OTC medications or supplements they may be taking. It is important to identify drug interactions since they can increase or decrease the effects of medications or cause adverse events. The NNRTI and PI classes of ARVs are notorious for causing drug-drug interactions and close attention should be paid to these classes of medications.

Notable ARV Interactions with OTC Medications/Supplements[11]

It is important to assess not only the potential for prescribed medication interactions but also interactions between ARVs and OTC medications and/or supplements. Perhaps the most notorious OTC supplement to interact with other medications is St. John's wort. This supplement has the potential to interact with all NNRTIs, NRTTIs, PIs, bictegravir, dolutegravir, elvitegravir/cobicistat, maraviroc, and tenofovir alafenamide by reducing the concentration of these ARVs in the blood. Therefore, St. John's wort should never be combined with these ARVs.[11]

Non-Nucleoside Reverse Transcriptase Translocation Inhibitors (NRTTIs)

Fostemsavir was recently approved for heavily treatment experienced patients living with HIV. This agent is a first in class medication that carries the potential for various drug interactions. St. John's wort is contraindicated with fostemsavir since it can decrease drug concentrations of fostemsavir.[11] Therefore, these two medications should never be used together.

Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTIs)

Post-marketing data revealed that tenofovir disoproxil fumarate (TDF) carries the potential to cause kidney damage and/or failure.[11] Therefore, use of TDF with concurrent or recent use of high-dose or multiple

Table 8. Common and/or Severe Side Effects by Antiretroviral (ARV) Class[11]

Side Effect	Fusion Inhibitor	Entry Inhibitor	Post-attachment Inhibitor (PAI)	Nucleoside/-tide Reverse Transcriptase Inhibitor (NRTI)
Bone Mineral Density Reduction	---	---	---	TDF > TAF
Bone Marrow Suppression	---	---	---	AZT: anemia, neutropenia
Heart Conduction Effects	---	---	---	---
Heart Disease	---	---	---	ABC: Some studies associate ABC with increased risk of heart attack
Gallstones and/or Kidney Stones	---	---	---	---
Diabetes Mellitus and insulin resistance	---	---	---	AZT
Dyslipidemia (cholesterol abnormalities)	---	---	---	AZT > ABC: ↑ TG, LDL TAF: ↑ TG, LDL, HDL
GI Effects	---	---	Diarrhea	AZT > other NRTIs: nausea/ vomiting
Injection Site Reactions	T20	---	---	---
Liver Effects	---	MVC: Liver damage + rash or hypersensitivity	---	TAF, TDF, 3TC, FTC: Severe flare in HBV liver disease with discontinuation AZT: Fatty liver disease
Hypersensitivity Reaction	---	MVC	---	ABC: Contraindicated if HLA-B*5701 is positive (median onset 9 days; most reactions occur within 6 weeks)
Lactic Acidosis (acid build up in body)	---	---	---	Older NRTIs (d4T, AZT, ddI)
Lipodystrophy (abnormal distribution of fat)	---	---	---	Lipoatrophy (loss of fat tissue) Exposure to d4T or AZT (d4T > AZT)
Myopathy (muscle weakness and pain)	---	---	---	AZT
Nervous System/ Psychiatric Effects	---	---	---	Exposure to ddI, ddC, or d4T: Irreversible peripheral neuropathy (numbness and tingling in hands and feet)
Rash	---	MVC	IBA	FTC: Hyperpigmentation (patches of skin becoming darker in color)
Kidney Effects			IBA: ↑ serum creatinine (marker of kidney function)	TDF: Kidney dysfunction (risk higher with concurrent use of COBI- or RTV-containing regimens) TAF: less impact on kidney function compared to TDF
Stevens-Johnson Syndrome/ Toxic Epidermal Necrosis (severe blistering/shedding of skin)	---	---	---	---
Weight Gain	---	---	---	TAF > TDF Associated with ART initiation and viral suppression

Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)	Integrase Strand Transfer Inhibitor (INSTI)	Protease Inhibitor (PI)	Non-nucleoside Reverse Transcriptase Translocation Inhibitor (NRTTI)
Observed after start of any ART (may be due to other ARVs used in combination)			---
---	---	---	---
RPV, EFV: QTc prolongation (arrythmia)	---	ATV/r, LPV/r: PR prolongation	---
---	---	Boosteda DRV, LPV/r: Some studies associate these drugs with cardiovascular (heart) events	---
---	---	ATV	---
---	---	LPV/r	---
EFV: ↑ TG, LDL, HDL	EVG/c: ↑ TG, LDL, HDL	All RTV or COBI-boosted PIs: ↑ TG, LDL, HDL LPV/r > DRV/r, ATV/r: ↑ TG	---
---	EVG/c: nausea, diarrhea	All PIs: diarrhea, nausea, vomiting LPV/r > DRV/r, ATV/r: diarrhea	Nausea
---	---	---	---
EFV: ↑ liver enzymes → fulminant hepatitis → liver failure or death NVP: Severe liver failure associated with skin rash or hypersensitivity	DTG: Co-infection with HBV or HCV may ↑ risk of liver damage	All PIs: drug-induced hepatitis and liver failure ATV: yellowing of the skin, eyes	FTR: ↑ liver enzymes
NVP: Syndrome of liver failure and rash with accompanying non-specific symptoms (risk in ARV-naïve women with pretreatment CD4 count > 250 and men with pretreatment CD4 count > 400. Risk is greater in women). Start with a lower dose of NVP for first 2 weeks.	RAL: Reported when given in combination with other drugs known to cause HSR DTG: Reported in < 1%	---	---
---	---	---	---
Lipohypertrophy (fat increase in the abdominal area) observed with EFV, PIs, and RAL			---
---	RAL, DTG	---	---
Neuropsychiatric Events: EFV > RPV, DOR, ETR EFV: Difficulty sleeping, drowsiness, abnormal dreams, dizziness, depression, psychosis, suicidality RPV: Depression, suicidality, sleep disturbances DOR: Dizziness, sleep disturbances, depression, suicidality	---	---	---
All NNRTIs	All INSTIs	ATV, DRV, LPV/r	FTR
RPV: Inhibits creatinine secretion (a marker of kidney function) without reducing kidney function	ATV, LPV/r: ↑ chronic kidney disease ATV: ↑ kidney stone or crystal formation COBI: Inhibits creatinine secretion without reducing kidney function	BIC, DTG, COBI boosting in EVG: Inhibits creatinine secretion without reducing kidney function	FTR: ↑ serum creatinine (marker of kidney function)
NVP > EFV, ETR, RPV	RAL	Some cases reported with DRV, LPV/r, and ATV	---
DOR > EFV Associated with ART initiation and viral suppression	INSTIs > other ARVs	Associated with ART initiation and viral suppression	---

Key: 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; AZT = zidovudine; BIC = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CVD = cardiovascular disease; d4T = stavudine; ddC = zalcitabine; ddI = didanosine; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EI = entry inhibitor; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; T20 = enfuvirtide; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides, >= greater than, ↑ = increased, < = less than

[a]Boosted= cobicistat and ritonavir interfere with the breakdown of certain protease inhibitors (i.e. darunavir, atazanavir, lopinavir) or integrase strand transfer inhibitor (elvitegravir) which allows the ARV being boosted to remain in the body longer at a higher concentration

Table 9. Definitions of Interactions	
Interaction	**Definition**
Drug-drug	Reaction between 2 or more drugs or supplements
Drug-food	Reaction between a drug and food or beverage
Drug-condition	Reaction that occurs when taking a drug and having a particular medical condition

nonsteroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen and naproxen) should be avoided since, when used together, this has the potential to cause further kidney damage or failure, especially with long-term use.[11] Although the risk for kidney damage appears to be less with tenofovir alafenamide (TAF), a risk still exists. If patients require NSAID agents, low doses should be recommended and kidney function should be checked routinely or acetaminophen use should be considered instead.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Rilpivirine interacts with acid suppressants since an acidic environment in the stomach is required for maximal absorption and activity of rilpivirine. Antacids (e.g., calcium carbonate containing products like TUMS, ROLAIDS, MYLANTA, MAALOX) and H2-receptor antagonists (e.g., famotidine, ranitidine, etc.) should be used with caution as co-administration may significantly decrease rilpivirine plasma concentrations due to an increase in gastric pH.[11]

Proton pump inhibitors, or PPIs (e.g., esomeprazole, lansoprazole, omeprazole, pantoprazole) are contraindicated to take with rilpivirine at the same time since it can cause loss of virologic suppression (increasing HIV-1 viral load) and possible development of resistance to rilpivirine or to the class of NNRTIs (**Table 10**).[11]

Integrase Strand Transfer Inhibitors (INSTIs)

The use of this ARV class has risen dramatically since all first-line therapies for ART initiation now include an INSTI. The most notable interaction with OTC agents is with polyvalent cations which include aluminum, calcium, iron, magnesium, and zinc. Essentially, if these cations are given with an INSTI, it can reduce the efficacy of the INSTI. For aluminum, magnesium, and calcium-containing antacids, as well as other polyvalent cation supplements, including multivitamins with minerals, administration requires separation from INSTIs (**Table 11**).

Table 10. Acid Suppressant Interactions with Rilpivirine[11]	
Acid Suppressing Agent	**Dosing Recommendation With Rilpivirine**
Antacids (containing aluminum, magnesium hydroxide, or calcium carbonate)	Take antacids at least 2 hours before or 4 hours after rilpivirine.
H2-receptor antagonists (cimetidine [TAGAMENT], famotidine [PEPCID], nizatidine [AXID], ranitidine [ZANTAC])	Take H2-receptor antagonists at least 12 hours before or 4 hours after rilpivirine.
PPIs (esomeprazole [NEXIUM], lansoprazole [PREVACID], omeprazole [PRILOSEC], pantoprazole sodium [PROTONIX]*, rabeprazole [AXID]*)	Contraindicated, do not co-administer.

*Not available OTC

Table 11. Polyvalent Interactions with Integrase Strand Transfer Inhibitors (INSTIs)[11]				
	Bictegravir	**Dolutegravir**	**Elvitegravir**	**Raltegravir**
Polyvalent cation antacids or supplements (aluminum, calcium, iron, magnesium, zinc, and multivitamins with minerals) * Many oral multivitamins contain varying amounts of polyvalent cations; refer to packaging labels for specific ingredients	• Administer 6 hours before or 2 hours after aluminum- or magnesium-containing antacid • Give simultaneously with food if antacid contains calcium • Do not co-administer with a calcium-containing antacid on an empty stomach	• Give at least 2 hours before or at least 6 hours after antacid • May be taken at the same time as calcium or iron supplement if taken with food	• Separate elvitegravir and antacid administration by at least 2 hours	• Do not co-administer with aluminum- or magnesium-hydroxide antacids • Raltegravir HD (1200 mg once daily dose) is not recommended with calcium-containing acids • Raltegravir 400 mg twice daily can be given with calcium-containing antacids without any dose adjustment or separation needed

Protease Inhibitors (PIs)

Despite PIs having numerous drug interactions, the most notable OTC interaction occurs between atazanavir and acid suppressants. Similar to the NNRTI rilpivirine, atazanavir requires an acidic environment (low pH); the solubility of atazanavir decreases when gastric pH increases. Therefore, appropriate spacing or avoidance of these agents is recommended with antacids, H2-receptor antagonists, and PPI use, which increase gastric pH, in the presence of atazanavir. Furthermore, the use of PPIs is not recommended in treatment-experienced patients (**Table 12**).

Although the efficacy of darunavir is not affected by the use of PPIs, the efficacy of PPIs can be reduced with the use of ritonavir-boosted darunavir. The same interaction is expected with cobicistat-boosted darunavir. Therefore, the omeprazole dose or its equivalent may be increased up to 40 mg daily.

BARRIERS TO ART INITIATION

Prior to starting or restarting ART, it is essential to understand the patient's goals and motivation to take ART. If a patient is hesitant or their living situation is unstable to take or adhere to medication for the management of HIV, it may be wise to wait until the patient is ready to start ART. During this time, it is still important to engage in routine follow-up and discuss readiness to start ART at each visit.

Insurance and Provider

Various barriers to the starting and continuing of ART exist.[11] Unfortunately, each insurance company has its own formulary, co-payments, and requirements for prior authorization. In many instances, the patient's prescriber may be unaware of these issues. One best practice would be to inform the prescriber and/or their office of issues with a patient's medication such as lack of formulary coverage, high co-pays, and/or need of prior authorization. This is one way to reduce issues with ART non-adherence. If a patient is on more than one FDC, it is important that the patient understand they should take all their medications for HIV each day and not just one of the FDCs. For instance, if only one ARV is in stock, they should not start or continue taking their regimen until ALL agents are available to be taken together. If a patient does not take their regimen as prescribed, is missing a medication, or perhaps a medication is on backorder with an unknown date of release, this can cause their viral load to increase and potentially promote the development of resistance. It is also important for the patient to understand food requirements of taking ARVs as this can impact medication adherence (**Table 13 on page 16**).

A way to reduce confusion when a patient is changing ART is to request the prescriber's office to discontinue medication orders for previous regimens or to write in the special instructions area what medications have been discontinued so the dispensing pharmacy and patient are all aware of the medication changes. At any time when there is uncertainty, call or fax the prescriber's office to

Table 12. Acid Suppressant Interactions with Atazanavir[11]

Acid Suppressing Agent	Treatment-Naïve Dosing Recommendation	Treatment-Experienced Dosing Recommendation
Antacids	Give atazanavir-containing products at least 2 hours apart	
H2-receptor antagonists (H2RA)	• **Boosted atazanavir** with food should be given simultaneously with, and/or at least 10 hours after H2RA (comparable with famotidine 20 mg once daily up to a dose comparable with famotidine 40 mg twice daily) • **Unboosted atazanavir** 400 mg once daily with food should be administered at least 2 hours before and at least 10 hours after H2RA. (No single dose of the H2RA should exceed a dose comparable with famotidine 20 mg. The total daily dose should not exceed a dose comparable with famotidine 40 mg.)	H2RA dose should not exceed a dose comparable with famotidine 20 mg twice daily, atazanavir doses should be given simultaneously with, and/or at least 10 hours after the dose of the H2RA.
Proton pump inhibitors (PPIs)	Give atazanavir at least 12 hours after the PPI. (Dose of PPI should not exceed a dose comparable with omeprazole 20 mg daily)	Use is not recommended.

Table 13. Considerations with Food Requirements[11]

ARV-Class	Medications	Auxiliary Labels to Consider Adding
Non-nucleoside Reverse Transcriptase Inhibitor (NRTTI)	Fostemsavir	This medication may be taken with or without food.
Fusion Inhibitor	Enfuvirtide	This medication may be taken with or without food.
Entry Inhibitor	Maraviroc	
Nucleoside/-tide Reverse Transcriptase Inhibitor (NRTI)	Abacavir	
	Didanosine	
	Emtricitabine	
	Lamivudine	
	Tenofovir alafenamide	
	Tenofovir disoproxil fumarate	
	Zidovudine	
Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)	Doravirine	This medication may be taken with or without food.
	Efavirenz	May cause drowsiness or dizziness. Take on an empty stomach. Take at bedtime.
	Etravirine	Take with food.
	Nevirapine	This medication may be taken with or without food.
	Rilpivirine	Take with a full meal.
Integrase Strand Transfer Inhibitor (INSTI)	Bictegravir	This medication may be taken with or without food.
	Dolutegravir	
	Elvitegravir/cobicistat	Take with food.
	Raltegravir	This medication may be taken with or without food.
Protease Inhibitor (PI)	Atazanavir	Drink plenty of water. Take with food.
	Darunavir	Take with food.
	Fosamprenavir	
	Lopinavir	
	Nelfinavir	
	Ritonavir	
	Saquinavir	
	Tipranavir	
Post-attachment Inhibitor (PAI)	Ibalizumab-uiyk	This medication may be taken with or without food.
Single Tablet Regimens	EFV/TDF/FTC (ATRIPLA)	Take on an empty stomach at bedtime.
	EFV/TDF/3TC (SYMFI, SYMFI LO)	
	RPV/TDF/FTC (COMPLERA)	Take with a full meal.
	RPV/TAF/FTC (ODEFSEY)	
	DOR/TDF/3TC (DELSTRIGO)	Take with or without food.
	DRV/c/TAF/FTC (SYMTUZA)	Take with food.
	DTG/3TC (DOVATO)	Take with or without food.
	DTG/ABC/3TC (TRIUMEQ)	
	EVG/c/TDF/FTC (STRIBILD)	Take with food.
	EVG/c/TAF/FTC (GENVOYA)	
	BIC/TAF/FTC (BIKTARVY)	Take with or without food.

Key: 3TC = lamivudine; ABC = abacavir; BIC = bictegravir; c = cobicistat; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

make them aware of any issues or concerns. The prescriber may not be made aware of any issues by the patient until the next follow-up which may be months away.

Patient Adherence (Compliance)

Patient adherence to treatment can depend on many factors including, but not limited to, privacy concerns, ability to afford medication, understanding and education regarding the medication, substance use, psychiatric illness, insurance status, socioeconomic status, language or cultural barriers, and homelessness. It is essential to ask patients open-ended questions when discussing medication adherence to avoid a judging tone (e.g., how many doses of ART have you missed in the last month, two weeks, etc.). Some ways the pharmacist or pharmacy technician can promote ART adherence include:

- recommending weekly pill boxes.
- encouraging automatic refills.
- minimizing pill burden and use daily dosing, where appropriate.
- educating the patient to take medications at the same time every day to create a routine.
- recommending the patient set a reminder through an alarm or phone application.
- suggesting if a family member or friend is aware of the patient's HIV status, ask for a daily reminder.
- encouraging the patient to track daily medication usage with a phone application or paper medicine diary and record when medication is taken. Review this diary to identify periods of missed ART.
- educating the patient to keep medical appointments as missed appointments correlate to medication non-adherence.
- encouraging the patient to communicate with the pharmacy and/or prescribers' office if unable to access medication or have difficulty paying for the medication (e.g., patient assistance programs, co-pay cards, AIDS Drug Assistance Program [ADAP]).
- coordinating medication delivery services (e.g., confidential mail or pick-up services).
- combining pharmacy and clinical services to enhance self-management of HIV.
- using telemedicine to provide education and discuss adherence – allows pharmacists using this model to check the status of a patient's medication treatment and understand any barriers to medication taking behaviors.
- providing specialty pharmacy services to properly monitor for drug-drug interactions, side effects, and adherence while involving the patient in creating medication therapy reviews and creating medication action plans.
- integrating community pharmacies with primary medical prescribers who manage HIV and share patient clinical information, identify therapy-related problems, and develop therapy-related action plans.

Although the importance of medication adherence is stressed to a patient, one or two missed doses of ART will not likely cause resistance. Some patients call in a panic when they have missed a dose of their ART. It is important to reassure them that there will likely be no untoward effects but this should not become a habit. If a patient misses their medication, they should take it as soon as they remember and resume their next dose as prescribed. If the patient typically takes their ART in the evening to avoid side effects (e.g., efavirenz causing drowsiness), but they realize during the day that they missed their dose, they can skip the dose until the next one is due.

CONCLUSION

The role of the pharmacy technician in the management of HIV care is crucial. In many instances, the pharmacy technician is the first-line of communication between a prescriber's office and the patient. Therefore, it is essential to understand the role of ARVs in the management and prevention of HIV as well as ways to promote medication adherence.

Test Your Knowledge #1

Answers on page 22.

Match the definitions.

Matching			
	CD4 count	a.	Use within 72 hours of a known or unknown exposure to prevent HIV
	Viral load	b.	Taking a medication everyday as prescribed
	Transmitted drug resistance	c.	An unwanted effect of a medication
	Adherence	d.	People at risk for HIV take a daily medicine to prevent HIV
	Side effect	e.	Amount of virus in a patient's blood and body fluids
	Drug interaction	f.	Used to treat HIV
	Treatment-naïve	g.	Reaction between ≥2 drugs or supplements
	Preexposure prophylaxis (PrEP)	h.	Never received treatment or prevention for HIV
	Post-exposure prophylaxis (PEP)	i.	Infection-fighting cell
	Antiretroviral therapy (ART)	j.	Mutations that can be transmitted from person to person

Test Your Knowledge #2

Word Search

Single Tablet Regimens for HIV

I F E D Q F R H A M W D U N A

N I B I K T A R V Y Y C X C Y

G A W C Y X E T Q B R D U D X

J J D R B L Q R P V D L Z F K

J Q N W P G G I O B U I N O L

O N V M R E C U A J P B T T K

Q G O A N T B M X Z U I V A T

A C I V I H K E G L U R J V A

A T O R S I E Q N K T T O O W

C Y R Q T I Q Y Z U V S M D P

A L K I K S Y E S F E D O Y E

G R Q M P M L U D Q K E U R S

I G E V K L V E B K Z I I S X

J A N I W N A F D Q Y L B Q O

C S Z Y X W Z N M N M F H X A

ATRIPLA
BIKTARVY
COMPLERA
DELSTRIGO
DOVATO
GENVOYA
JULUCA
ODEFSEY
STRIBILD
SYMTUZA
TRIUMEQ

Answers on page 22.

Appendix A. HIV Terminology Abbreviations

2DR	2-drug regimens
3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
ATV	Atazanavir
AZT	Zidovudine
BIC	Bictegravir
COBI	Cobicistat
d4T	Stavudine
ddC	Zalcitabine
ddI	Didanosine
DOR	Doravirine
DRV	Darunavir
DTG	Dolutegravir
EFV	Efavirenz
EVG/c	Elvitegravir/cobicistat
FDC	Fixed-dose combination
FTC	Emtricitabine
HBV	Hepatitis B Virus
HIV	Human immunodeficiency virus
HSR	Hypersensitivity reaction
INSTI	Integrase strand transfer inhibitor
IRIS	Immune reconstitution syndrome
LPV	Lopinavir
MVC	Maraviroc
nPEP	Non-occupational post exposure prophylaxis
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleos(t)ide reverse transcriptase inhibitor
NRTTI	Nucleoside reverse transcriptase translocation inhibitor
NVP	Nevirapine
PAI	Post-attachment inhibitor
PEP	Post-exposure prophylaxis
PI	Protease inhibitor
PLWH	People living with HIV
PrEP	Pre-exposure prophylaxis
RAL	Raltegravir
RAL HD	Raltegravir high dose
RPV	Rilpivirine
RTV	Ritonavir
STR	Single tablet regimen
T20	Enfuvirtide
TAF	Tenofovir alafenamide
TasP	Treatment as Prevention
TDF	Tenofovir disoproxil fumarate
U=U	Undetectable = Untransmittable

Appendix B. HIV Medications

Generic Name	Acronym	Single Agent Brand Name	Fixed Dose Combination Brand Name
Nucleoside Reverse Transcriptase Translocation Inhibitor (NRTTI)			
Fostemsavir	FTR	RUKOBIA	---
Entry Inhibitor			
Enfuvirtide	T20	FUZEON	---
Fusion Inhibitor			
Maraviroc	MVC	SELZENTRY	---
Post-Attachment Inhibitor			
Ibalizumab-uyik	IBA	TROGARZO	---
Nucleoside Reverse Transcriptase Inhibitor (NRTI)			
Abacavir	ABC	ZIAGEN	EPZICOM TRIUMEQ TRIZIVIR
Didanosine	ddI	VIDEX VIDEX EC	---
Emtricitabine	FTC	EMTRIVA	ATRIPLA BIKTARVY COMPLERA DELSTRIGO DESCOVY GENVOYA ODEFSEY STRIBILD SYMTUZA TRUVADA
Lamivudine	3TC	EPIVIR	CIMDUO COMBIVIR DOVATO SYMFI SYMFI LO TEMIXYS TRIUMEQ
Tenofovir Alafenamide	TAF	VEMLIDY (Note: only approved for HBV)	DESCOVY
Tenofovir Disoproxil Fumarate	TDF	VIREAD	ATRIPLA CIMDUO COMPLERA DELSTRIGO STRIBILD SYMFI SYMFI LO TEMIXYS TRUVADA
Zidovudine	AZT	RETROVIR	COMBIVIR TRIZIVIR

Generic Name	Acronym	Single Agent Brand Name	Fixed Dose Combination Brand Name
Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)			
Doravirine	DOR	PIFELTRO	DELSTRIGO
Efavirenz	EFV	SUSTIVA	ATRIPLA SYMFI SYMFI LO
Etravirine	ETR	INTELENCE	---
Nevirapine	NVP	VIRAMUNE VIRAMUNE XR	---
Rilpivirine	RPV	EDURANT	COMPLERA JULUCA ODEFSEY
Integrase Strand Transfer Inhibitors (INSTI)			
Bictegravir	BIC	---	BIKTARVY
Dolutegravir	DTG	TIVICAY	DOVATO JULUCA TRIUMEQ
Elvitegravir	EVG	---	GENVOYA STRIBILD
Raltegravir	RAL	ISENTRESS ISENTRESS HD	---
Protease Inhibitor (PI)			
Atazanavir	ATV	REYATAZ	EVOTAZ
Darunavir	DRV	PREZISTA	PREZCOBIX SYMTUZA
Fosamprenavir	FPV	LEXIVA	---
Lopinavir	LPV	---	KALETRA
Nelfinavir	NFV	VIRACEPT	---
Ritonavir	RTV	NORVIR (Note: only used for boosting properties)	KALETRA
Saquinavir	SQV	INVIRASE	---
Tipranavir	TPV	APTIVUS	---
Pharmacokinetic Enhancer (Booster)			
Cobicistat	COBI	TYBOST	EVOTAZ GENVOYA PREZCOBIX STRIBILD SYMTUZA

REFERENCES

1. HIV.gov. What Are HIV and AIDS? Available at: https://www.hiv.gov/hiv-basics/overview/about-hiv-and-aids/what-are-hiv-and-aids. Accessed May 14, 2020.
2. HIV.gov. U.S. Statistics. Available at: https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics. Accessed May 14, 2020.
3. Centers for Disease Control and Prevention (CDC). Screening in Clinical Settings. Available at: https://www.cdc.gov/hiv/clinicians/screening/clinical-settings.html. Accessed May 14, 2020.
4. CDC. HIV Risk Behaviors. Available at: https://www.cdc.gov/hiv/risk/estimates/riskbehaviors.html. Accessed May 14, 2020.
5. CDC. HIV Transmission. Available at: https://www.cdc.gov/hiv/basics/transmission.html. Accessed May 14, 2020.
6. CDC. Anal Sex. Available at: https://www.cdc.gov/hiv/risk/analsex.html. Accessed May 14, 2020.
7. CDC. Pre-Exposure Prophylaxis (PrEP). Available at: https://www.cdc.gov/hiv/risk/prep/index.html. Accessed May 14, 2020.
8. Descovy [package insert]. Foster City, CA: Gilead Sciences, Inc; 2020.
9. Truvada [package insert]. Foster City, CA: Gilead Sciences, Inc; 2020.
10. U.S. Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Accessed June 29, 2020.
11. Department of Health and Human Services. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed May 16, 2020.
12. CDC. PEP. Available at: https://www.cdc.gov/hiv/basics/pep.html. Accessed June 15, 2020.
13. Joyce MP, Kuhar D, Brooks JT. Notes from the Field: Occupationally Acquired HIV Infection Among Health Care Workers — United States, 1985–2013. *MMWR* 2015:63;1245-1246.
14. Kuhar DT, Henderson DK, Struble KA, et al. Updated US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis. *Infect Control Hosp Epidemiol.* 2013:34;875-892.
15. CDC. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016. Available at: https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf. Accessed June 16, 2020.
16. CDC. PEP 101. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-pep101.pdf. Accessed June 16, 2020
17. Department of Health and Human Services. AIDSinfo Glossary of HIV/AIDS-related terms. Available at: https://aidsinfo.nih.gov/contentfiles/glossaryhivrelatedterms_english.pdf. Accessed June 29, 2020.
18. Department of Health and Human Services. The HIV Life Cycle. Available at: https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/73/the-hiv-life-cycle. Accessed June 29, 2020.
19. Department of Health and Human Services. HIV Treatment: The Basics. Available at: https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/51/hiv-treatment--the-basics. Accessed June 18, 2020.
20. Department of Health and Human Services. Drug Resistance. Available at: https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/56/drug-resistance. Accessed June 29, 2020.
21. O'Brien ME, Clark RA, Besch CL, et al. Patterns and correlates of discontinuation of the initial HAART regimen in an urban outpatient cohort. *J Acquir Immune Defic Syndr.* 2003;34:407-414.
22. Department of Health and Human Services. HIV Medicines and Side Effects. Available at: https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/22/63/hiv-medicines-and-side-effects. Accessed June 29, 2020.
23. Department of Health and Human Services. What is a Drug Interaction? Available at: https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/95/what-is-a-drug-interaction-. Accessed June 29, 2020.

Test Your Knowledge
Answer Key

Test Your Knowledge #1

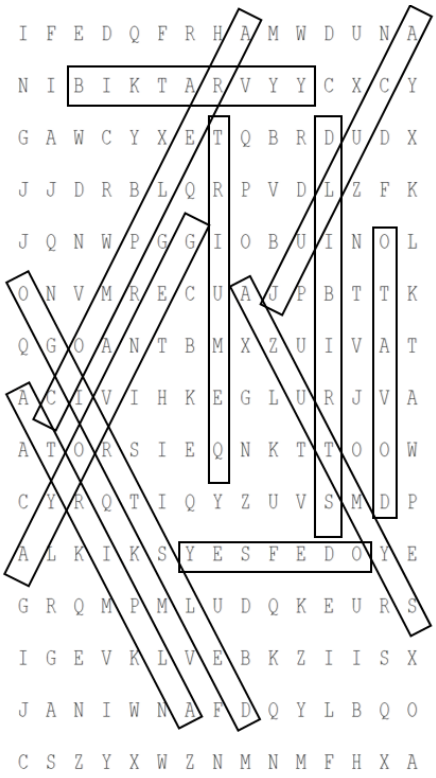
Match the definitions.

Matching			
i	CD4 count	a.	Use within 72 hours of a known or unknown exposure to prevent HIV
e	Viral load	b.	Taking a medication everyday as prescribed
j	Transmitted drug resistance	c.	An unwanted effect of a medication
b	Adherence	d.	People at risk for HIV take a daily medicine to prevent HIV
c	Side effect	e.	Amount of virus in a patient's blood and body fluids
g	Drug interaction	f.	Used to treat HIV
h	Treatment-naïve	g.	Reaction between ≥2 drugs or supplements
d	Preexposure prophylaxis (PrEP)	h.	Never received treatment or prevention for HIV
a	Post-exposure prophylaxis (PEP)	i.	Infection-fighting cell
f	Antiretroviral therapy (ART)	j.	Mutations that can be transmitted from person to person

Test Your Knowledge #2

Word Search

Single Tablet Regimens for HIV



ATRIPLA
DELSTRIGO
JULUCA
SYMTUZA
BIKTARVY
DOVATO
ODEFSEY
TRIUMEQ
COMPLERA
GENVOYA
STRIBILD

SELF ASSESSMENT QUESTIONS

Note:
If you purchase a paper subscription, but complete the Self-Assessment Test online at pharmacytechtopics.com, you will be required to take the Pre-Test first, then the final test and evaluation. This Pre-Test does not affect your final test results but will be used to evaluate the effectiveness of the continuing education program.

1. **In the US, what mode of transmission is the most common cause of HIV transmission?**
    a. Receptive anal intercourse
    b. Insertive anal intercourse
    c. Injection drug use with needle sharing
    d. Biting or spitting

2. **What practice is <u>least</u> likely to prevent the transmission of HIV?**
    a. Pre-exposure prophylaxis
    b. Treatment as prevention
    c.. Post-exposure prophylaxis
    d. Medication non-adherence

3. **What is the most appropriate PrEP regimen to start in a 26-year old woman?**
    a. Tenofovir alafenamide/emtricitabine (DESCOVY)
    b. Tenofovir disoproxil fumarate/emtricitabine (TRUVADA)
    c. Abacavir/lamivudine (EPZICOM)
    d. Darunavir/cobicistat (PREZCOBIX)

4. **In what scenario should PEP be initiated?**
    a. 60-hours after a condom broke during sexual intercourse with someone of unknown HIV status
    b. 79-hours after a health care worker was stuck with a needle
    c. 120-hours after a sexual assault
    d. 150-hours after sharing needles while injecting drugs

5. **By using Table 4, what is the most appropriate regimen to dispense in an otherwise healthy 37-year-old male starting PEP?**
    a. Tenofovir alafenamide 25 mg/emtricitabine 200 mg (DESCOVY) once daily plus dolutegravir (TIVICAY) 50 mg PO daily
    b. Tenofovir disoproxil fumarate 300 mg/emtricitabine (TRUVADA) once daily plus raltegravir (ISENTRESS) 400 mg PO BID
    c. Zidovudine 300 mg/lamivudine 150 mg (COMBIVIR) one tablet twice daily plus lopinavir 200 mg/ritonavir 50 mg (KALETRA) two tablets PO twice daily
    d. Tenofovir alafenamide 10 mg/emtricitabine 200 mg/cobicistat 150 mg/darunavir 800 mg (SYMTUZA) one tablet PO daily

6. **What should be considered when starting patients on ART?**
    a. Prescription insurance coverage
    b. What type of job the patient has
    c. Ability to comply with therapy
    d. A and C are correct

7. **What antiretroviral can commonly cause rash?**
    a. Darunavir
    b. Lamivudine
    c. Tenofovir
    d. Zidovudine

8. **What ARV is the preferred medication in pregnant women?**
    a. Fostemsavir
    b. Dolutegravir
    c. Rilpivirine
    d. Stavudine

9. **What two-drug regimen (2DR) is indicated for most naïve patients starting their first HIV regimen?**
    a. Darunavir (PREZISTA)/dolutegravir (TIVICAY)
    b. Dolutegravir/lamivudine (DOVATO)
    c. Dolutegravir/rilpivirine (JULUCA)
    d. Tenofovir disoproxil fumarate/emtricitabine (TRUVADA)

10. **What medication requires HLA-B*5701 testing prior to start of treatment?**
    a. Abacavir
    b. Bictegravir
    c. Darunavir
    d. Dolutegravir

11. **What class of antiretrovirals is most likely to be associated with weight gain?**
    a. Fusion inhibitor
    b. Integrase strand transfer inhibitor
    c. Entry inhibitor
    d. Post-attachment inhibitor

12. **Which herbal medication commonly interacts with ART?**
    a. Valerian root
    b. Ginseng
    c. St. John's wort
    d. Echinacea

13. **What antiretroviral is most likely to cause worsening of kidney function with use of ibuprofen?**
    a. Abacavir
    b. Emtricitabine
    c. Lamivudine
    d. Tenofovir disoproxil fumarate

14. **Which of the following antiretrovirals can cause severe flare up in hepatitis B virus liver disease with discontinuation?**
    a. Darunavir (DRV)
    b. Dolutegravir (DTG)
    c. Raltegravir (RAL)
    d. Tenofovir alafenamide (TAF)

15. **What antiretroviral is contraindicated with the use of proton pump inhibitors (e.g., omeprazole)?**
    a. Abacavir
    b. Darunavir
    c. Dolutegravir
    d. Rilpivirine

16. **A patient initiating bictegravir/ emtricitabine/ tenofovir alafenamide (BIKTARVY) reports taking over-the-counter supplements. Which of the following supplements should be separated from the patient's ART?**
    a. Calcium
    b. Folic Acid
    c. Vitamin D
    d. Ginkgo Biloba

17. **What is a potential barrier to re-starting a patient on antiretroviral therapy (ART)?**
    a. Hesitation to restart ART due to unstable living situation
    b. Stable living environment with supportive family members
    c. Clean and sober living for the last 10 years
    d. Employed with active medical and prescription insurance

18. **When asking a patient living with HIV about medication adherence, which of the following options would be most appropriate?**
    a. Did you miss any doses of antiretroviral therapy in the last week?
    b. You didn't miss any doses of your HIV medications in the last month, did you?
    c. Do you have any HIV medications left from your last refill?
    d. In the last month, how many doses of antiretrovirals would you say you missed?

19. **Which of the following interventions would promote medication adherence for a patient?**
    a. Expect the patient to call each month for refills on antiretroviral therapy
    b. Increase the number of antiretroviral tablets taken each day
    c. Recommend the patient switch from daily to twice daily medications
    d. Encourage the patient to set a daily alarm or phone application as a medication reminder

20. **Which of the following circumstances is associated with medication non-adherence?**
    a. $0 co-payment for antiretroviral therapy
    b. Missed clinic appointments
    c. Participation in a drug treatment program
    d. Enrollment in the AIDS Drug Assistance Program (ADAP)