



**A Pharmacist's
Guide to Antiretroviral
Medications
for HIV-infected Adults
and Adolescents
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**Free
Continuing
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ADDITIONAL RESOURCES

Mountain Plains AIDS Education and Training Center

School of Medicine, Division of Infectious
Diseases

University of Colorado Denver

303-724-0867 or www.mpaetc.org

AIDS Drug Assistance Program (ADAP)

Numbers:

Colorado	303-692-2716
Kansas	785-368-8218
Nebraska	402-559-4673
New Mexico	505-827-2363
North Dakota	701-328-2378
South Dakota	605-773-3737
Utah	801-538-6197
Wyoming	307-777-5800

HIV/AIDS Treatment Information Service (ATIS)

www.aidsinfo.nih.gov

Provides information on federally approved treatment guidelines for HIV/AIDS. Also provides updated medication and drug interaction information.

National Clinicians Consultation Center

For questions regarding:

Treatment/Pharmacologic Issues –
1-800-933-3413

Post-exposure Prophylaxis – 1-888-448-4911

Perinatal Transmission – 1-888-448-8765

<http://www.ucsf.edu/hiventr> for further training/educational tools and links to more sites with specific information regarding drug interactions and ART.

HIV InSite

<http://hivinsite.ucsf.edu>

Contains an extensive drug database and ART side effects tables.

AIDS Infonet

www.aidsinfonet.org

Provides one-page fact sheets on treatments, prevention, social service, and Web resources.

Available in English and Spanish and appropriate for patient and clinician education.

A Pharmacist's Guide to Antiretroviral Medications for HIV-infected Adults and Adolescents

Pharmacological treatment of HIV disease has advanced rapidly since 1995. This is primarily due to the development of new antiretroviral agents and the recognition that combination antiretroviral therapy (ART) is required to effectively inhibit viral replication, prevent drug resistance, and prevent immune dysfunction. These advances have improved the quality of life and increased the life span for HIV-infected patients; they have also increased the complexity of prescribing treatment and providing care. The pharmacist plays a key role in helping patients and clinicians meet the challenges of ART. These challenges include:

- Continuous changes in treatment options as new antiretroviral medications are approved and as data from longitudinal studies provide new information about established therapeutic agents;
- Known and emerging toxicities, side effects, and complications of ART as patients live longer and as antiretroviral medications are used in new combinations;
- Development of resistance to ART medications and the need for a high level of adherence to medications to prevent ART resistance;
- Potential interactions with other antiretroviral medications and medications used to prevent or treat opportunistic infections and/or co-morbid conditions;
- Ongoing revisions of publicly released treatment guidelines based on new information; and
- Psychosocial barriers patients may encounter to taking medications as prescribed.

Pharmacists can work with HIV-infected patients and clinicians to promote positive health outcomes in a number of ways. Effective treatment is facilitated when pharmacists take an active role in:

- Providing drug information to clinicians and patients,
- Counseling patients about treatment and side effects,
- Encouraging adherence and monitoring patients for difficulties with treatment adherence, and
- Screening prescriptions for appropriate dosages and potential drug interactions.

Learning Objectives

Upon completion of this activity participants will be able to:

- Describe how each class of antiretroviral agent works to impede viral replication.
- Identify the various stages of HIV infection at which the guidelines recommend initiation of ART.
- Discuss practical ways pharmacists can help improve patient adherence to ART.
- Identify common drug-drug interactions with ART and resources containing information on drug-drug interactions and toxicities associated with antiretroviral agents.

Currently Available Antiretroviral Drugs

Twenty-three antiretroviral agents are now approved for use in the United States with more in development. Antiretroviral drugs fall into five classes: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), entry inhibitors, and integrase inhibitors.

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) work at an early stage in viral replication. They block reverse transcriptase, an enzyme required for the virus to multiply, by mimicking nucleosides in the growing DNA chain. Once the DNA chain is terminated, the individual virus can no longer replicate. NRTIs are the cornerstone of combination therapy. Some of these agents are combined into fixed-dose formulations to help reduce the number of capsules/tablets patients take daily.

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) block reverse transcriptase through a more direct inhibition of the enzyme. Resistance develops quickly to NNRTIs when used alone, making it extremely important that they be used in maximally suppressive combination therapies. NNRTIs are often used in combination with NRTIs.

Protease Inhibitors (PIs) work against HIV in a late stage of viral replication by interfering with the protease enzyme's role in making new copies of HIV, thus producing viruses that are incapable of infecting new cells. The PIs, when used in combination with other antiretroviral agents, offer potent anti-HIV activity.

Entry Inhibitors prevent entry of HIV into the target cell through a variety of mechanisms. Enfuvirtide, a fusion inhibitor, interferes with the process of viral binding (fusion) to the cell membrane by binding to proteins on the surface of the cell, which then prevents the virus from binding to the target cell. Maraviroc prevents entry by blocking CCR5, a co-receptor on the cell, necessary for viral attachment. As some viral strains may use an alternate co-receptor CXCR4 for entry, a tropism assay is necessary to confirm that the patient's virus only uses CCR5 for entry.

Integrase Inhibitors block viral replication by preventing the incorporation of viral DNA into the host genome by inhibiting the HIV integrase enzyme.

Other Antiretroviral Therapies. The list of antiretroviral therapies continues to grow as clinical trials provide new options for treatment. Occasionally patients may be enrolled in clinical trials of these experimental drugs.

ART Recommendations

With the advent of combination treatment regimens, ART has become quite complex. A panel of experts periodically publishes revised principles and recommendations for HIV treatment. These guidelines provide recommendations on when to start therapy and which medication combinations have the best evidence of efficacy in the treatment of HIV. Please refer to the guidelines for concerns and specific issues regarding the use of ART in patients with drug resistance or in specific populations including adolescents; intravenous drug users; patients who are co-infected with hepatitis B, C, or with tuberculosis; and women of child-bearing age. They can be easily accessed at <http://www.aidsinfo.nih.gov/guidelines/>

Specific guidelines are also available for ART treatment in pregnant women and for prevention of perinatal transmission as well as for treatment of pediatric patients. Guidelines also exist for the use of antiretroviral agents for post-exposure prophylaxis for occupational and non-occupational exposures. The most recently updated versions of each of these guidelines are available at <http://www.aidsinfo.nih.gov/guidelines/>

Starting ART

Starting or changing therapy for the chronically HIV-infected adult or adolescent is based on clinical status, CD4 + T cell counts, HIV viral load as well as individual patient issues. ART is recommended for all patients with an AIDS-defining diagnosis or with CD4+ T cell count < 350 cells/mm³. Treatment is indicated for pregnant women, patients with HIV-associated nephropathy and for patients co-infected with Hepatitis B when treatment is indicated. Table 1 reviews current recommendations on when to initiate therapy. On occasion, earlier treatment may be considered based on the patient's individual risk for immunologic decline, disease progression, and motivation to begin therapy. Decisions regarding the initiation of ART must be individualized to the patient after appropriate patient education regarding disease

Table 1. Indications for Initiating Antiretroviral Therapy for the Chronically HIV-1 Infected Patient

This table provides general guidance rather than absolute recommendations for an individual patient. All decisions regarding initiating therapy should be made on the basis of prognosis as determined by the CD4+ T cell count, the potential benefits and risks of therapy, and the willingness of the patient. Before initiating therapy patient counseling and education should be provided with a focus on the benefits and risk of therapy, adverse effects, and adherence.

Clinical Conditions and/or CD4 + T cell Count	Recommendations
<ul style="list-style-type: none"> • History of AIDS-defining illness* • CD4+ T cell count < 200 cells/mm³ • CD4+ T cell count 200-350 cells/mm³ • Pregnant women** • Persons with HIV-associated nephropathy • Persons co-infected with hepatitis B virus (HBV), when HBV treatment is indicated (Treatment with fully suppressive antiviral drugs active against both HIV and HBV is recommended.) 	<p>Antiretroviral therapy should be initiated.</p>
<ul style="list-style-type: none"> • Patients with CD4 + T cell counts > 350 cells/mm³ who do not meet any of the specific conditions listed above 	<p>The optimal time to initiate therapy in asymptomatic patents with CD4 + T cell count > 350 cells/mm³ is not well defined. Patient scenarios and comorbidities should be taken into consideration.</p>

* AIDS-defining illness per CDC, 1993.
 ** For women who do not require ART for their own health, consideration can be given to discontinuing antiretroviral drugs postpartum. For more information, please refer to the *Recommendations for use of antiretroviral drugs in pregnant HIV-1-Infected women and interventions to reduce perinatal HIV-1 transmission in the United States*. These guidelines are available at <http://aidsinfo.nih.gov/guidelines/>

Table adapted from *Guidelines for the Use of antiretroviral agents in HIV-1-infected adults and adolescents*; DHHS, January 29, 2008, available at <http://aidsinfo.nih.gov/guidelines/>

stage, drug side effects, long-term toxicities, co-morbidities, and adherence issues. ART may also be recommended during acute infection, however, the benefits of treatment of acute HIV infection observed in clinical trials are inconclusive at this time. Acute HIV infection is a symptomatic illness occurring in 40%-90% of HIV-infected people during the initial weeks of infection. Acute HIV infection presents with fairly nonspecific symptoms including but not limited to: fever, lymphadenopathy, pharyngitis, rash, myalgias, diarrhea, nausea, vomiting, and neurologic symptoms. The potential benefits to treatment at this stage of infection include a reduction in viral replication, symptoms of acute HIV infection, disease progression, and the risk of viral transmission. Potential risks are drug toxicities, the development of drug resistance, the need for continuous therapy, an adverse effect on quality of life, and exposure to ART without known clinical benefit.

Laboratory Tests

Pharmacists may not be responsible for monitoring these tests, but may find it helpful in patient interactions to have a general knowledge of routine tests. Of the many laboratory tests used to support diagnosis and therapy in HIV infection, several are critical and used to determine the need to initiate or change a therapy regimen: HIV viral load assays, CD4+ T cell counts, and resistance testing. The combination of HIV viral load and CD4+ T cell testing provides the best information for initiating, monitoring, and changing ART. The HIV viral load indicates the current level of virus circulating in the blood and the ability of the virus to multiply. The CD4+ T cell count measures the ability of the immune system to protect the body. For patients stable on ART, the CD4+ T cell count and HIV viral load are repeated every 3-4 months.

HIV Viral Load Testing (HIV RNA Assay). HIV viral load is a quantitative measure of HIV viral RNA in the plasma. Viral replication in HIV infection is rapid and continuous. From the time of infection, billions of new viral copies are produced daily. During acute HIV infection the HIV viral load is high (10^6 to 10^7 copies/mL), then drops to a stable level or “set point” which remains relatively constant in the absence of disease progression, therapeutic effect, or disease exacerbations. Plasma HIV RNA quantification is the best determinant of treatment efficacy. After starting ART, the viral load is expected to decrease by $1.5-2 \log^{10}$ copies/mL at 4 weeks and to < 50 copies/mL at 16-24 weeks. If the viral load does not decrease by $1 \log^{10}$ copies/mL at 8 weeks, drug resistance, adverse drug reactions, and nonadherence are the major concerns.

CD4+ T Cell Count. The CD4+ T cell count is the best marker for immunodeficiency associated with HIV infection. The CD4+ T lymphocyte count reflects the number of CD4+ T cells/mm³ circulating in the blood. The laboratory will sometimes report a list of several types of lymphocytes, with relative percentages, along with the absolute count. The important values are the absolute number of CD4+ T cells/mm³ and the proportion of CD4+ T cells as a subset of all lymphocytes (CD4%). Depending on the laboratory, the normal range for an adult CD4+ T count will be about 800-1200 cells/mm³. The normal range for the CD4% (of total lymphocytes) will vary depending on the lab, but $> 29\%$ corresponds with a CD4+ T cell count $> 500/\text{mm}^3$ and $< 14\%$ corresponds with CD4+ T cell count $< 200/\text{mm}^3$ (which both qualify as an AIDS diagnosis). The absolute CD4+ T cell count can vary in the same individual depending on the time of day the blood is drawn, the laboratory used, or the presence of acute illness. The CD4% is a

more stable representation of the immune system, and is sometimes used in preference to the absolute number.

HIV Resistance Testing. Resistance testing is frequently performed in a number of situations for both treatment naïve and treatment experienced patients. Genotypes identify specific mutations associated with resistance in the genetic code of HIV. Phenotypes measure how well HIV replicates in the presence of specific antiretroviral medications. Approximately 6-16% of treatment naïve patients have baseline resistance to antiretroviral drugs. As a result, a genotype is recommended for every patient before initiating ART. Resistance testing is done during ART therapy if a regimen is not fully suppressive (VL > 1000 copies/mL). At this point, both a genotype and phenotype may be useful in assisting the clinician in the selection of a new ART regimen.

Additional Tests. A HLA-B*5701 genetic screening test should be ordered for all patients before they start a regimen that includes abacavir, as this medication may cause a hypersensitivity reaction in some patients. Signs and symptoms of a hypersensitivity reaction may include rash, fever, nausea, vomiting, malaise, fatigue and respiratory symptoms. If the patient is negative for HLA-B*5701, the chance of a hypersensitivity reaction to abacavir is extremely low and they may safely start this medication. Patients who are positive for HLA-B*5701 are at risk for developing hypersensitivity reaction and should never take abacavir. Abacavir should then be listed in the patient's chart under drug allergies.

ART Regimens

Combination therapy with at least three active antiretroviral drugs from two separate drug classes is currently recommended for patients starting treatment. Treatment with less than three drugs provides only partial suppression and is not recommended. For treatment naïve patients, the three drug regimen should consist of 1 NNRTI with 2 NRTIs or a PI boosted with ritonavir with 2 NRTIs. Boosting PIs with low dose ritonavir increases drug levels, prolongs the protease inhibitor half-life, and can reduce pill burden. For most patients on a PI-based regimen, boosting with ritonavir is recommended. Table 2 lists the recommended combinations of ART in ART naïve patients. Patients need to be aware that multi-drug regimens function as a whole, and that missing or stopping any of the medications can seriously jeopardize treatment effectiveness and future options.

Co-formulations of existing medications have improved dosing, reduced pill burdens and allowed most patients to have once or twice daily regimens with some patients taking a single pill once daily. Despite these developments, not all patients can tolerate, adhere to, or achieve an undetectable viral load (when the virus is too low to be detected by available viral load assays) with combination therapy. Partial viral suppression, i.e. more than a one-half log reduction in viral load, has been shown to provide clinical benefit. However, partial suppression supports the development of drug resistance that can ultimately lead to treatment failure, disease progression, and the risk of transmitting resistant strains of HIV. Additional factors that contribute to resistance include inappropriate prescribing by providers, unanticipated drug interactions,

Table 2. Antiretroviral Regimens Recommended for Treatment of HIV-1 Infection in Antiretroviral Naïve Patients.

* A combination antiretroviral regimen in treatment-naïve patients generally contains 1 NNRTI with 2 NRTI or a single ritonavir-boosted PI with 2 NRTI. To construct a regimen choose one NNRTI or PI option from Column A and an NRTI option from Column B in the corresponding row. All medications are listed alphabetically.

	Column A	Column B	No. of tablets/capsules
Preferred Regimens	NNRTI option _ efavirenz ¹ OR PI Options _ atazanavir + ritonavir _ fosamprenavir + ritonavir (BID) _ lopinavir /ritonavir (BID)	WITH NRTI Options _ abacavir/lamivudine ² (co-formulated) ³ _ tenofovir/emtricitabine ² (co-formulated)	1-5
	NNRTI option _ efavirenz ¹	WITH NRTI Options _ didanosine + (emtricitabine or lamivudine) _ zidovudine/lamivudine ² (co-formulated), (preferred alternative NRTI combination)	3
Alternative Regimens	NNRTI option _ nevirapine ⁴	WITH NRTI Options _ abacavir/lamivudine ² (co-formulated) ³ _ didanosine + (emtricitabine or lamivudine) _ tenofovir/emtricitabine ² (co-formulated) _ zidovudine/lamivudine ² (co-formulated)	3-4
	PI Options _ atazanavir + ritonavir _ fosamprenavir + ritonavir (BID) _ lopinavir /ritonavir (BID)	WITH NRTI Options _ didanosine + (emtricitabine or lamivudine) _ zidovudine/lamivudine ² (co-formulated), (preferred alternative NRTI combination)	4-6
	PI Options _ atazanavir ⁵ _ fosamprenavir _ fosamprenavir + ritonavir (once daily) _ lopinavir /ritonavir (once daily) _ saquinavir + ritonavir	WITH NRTI Options _ abacavir/lamivudine ² (co-formulated) ³ _ didanosine + (emtricitabine or lamivudine) _ tenofovir/emtricitabine ² (co-formulated) _ zidovudine/lamivudine ² (co-formulated)	3-6

1. Efavirenz is not recommended for use in pregnancy or in women with high pregnancy potential. Pregnancy category D.
2. Lamivudine may be used in place of emtricitabine and vice versa.
3. Abacavir should only be used in patients who are HLAB*5701 negative.
4. Nevirapine should not be initiated in women with CD4 T cell counts > 250 cells/mm³ or in men with CD 4 T cell count > 400 cells/ mm³, due to increased risk for hepatic events.
5. Atazanavir must be boosted with ritonavir if used in combination with tenofovir.

Table adapted from *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents*; DHHS, January 29, 2008, available at <http://aidsinfo.nih.gov/guidelines/>

acquired drug resistance from HIV transmission, previous exposure to ART agents (especially in partially suppressive regimens), late stage disease with high viral loads and different viral strains, and patient non-adherence to treatment protocols.

These medications have side effects and complications that can affect quality of life, such as diarrhea, vomiting, vivid dreams, and peripheral neuralgias. Certain antiretroviral drugs have been shown to contribute to metabolic complications such as lipid abnormalities, insulin resistance, lactic acidosis, and bone abnormalities. Some side effects, such as hypersensitivity reactions or hepatotoxicity, can be very serious and sometimes fatal. Patients should be taught about potential side effects, toxicities and interactions, and given instructions on what to do to lessen the unfavorable symptoms, how to recognize serious symptoms, and what to do should they occur.

Drug interactions often occur between some of the antiretroviral agents, especially PIs and NNRTIs. Patients should also be advised to report all the medications they are taking (prescription, over-the-counter, supplements, and vitamins) at each visit. Some of the most common interactions occur between drugs metabolized by CYP450. Commonly used drugs that interact with ART include antifungals, anti-mycobacterials, hormonal contraceptives, lipid-lowering agents (particularly statins), anticonvulsants, and erectile dysfunction agents. These drug interactions can lead to toxicities or decrease in efficacy of either drug. More information on drug interactions is available at <http://aidsinfo.nih.gov/guidelines/>

Drug Resistance and Cross-Resistance

Antiretroviral drug resistance arises due to the rapid turnover of HIV (up to 10 billion virions per day in an untreated person) and the high error rate of HIV enzymes that generate mutational variants. Gene mutations can alter binding sites on these enzymes and result in an increase in the amount of drug necessary to inhibit enzyme activity. Some ART agents require only one mutation on the HIV genome to become ineffective (e.g., NNRTIs, lamivudine, nelfinavir, and emtricitabine) and others require multiple mutations in a single genome (e.g., PIs). Cross-resistance occurs when HIV strains develop resistance to one drug that confers insensitivity to other drugs in the same ART class, including drugs the patient has never taken.

Failure to suppress viral replication leads to the selection of drug-resistant strains. This can occur due to the following factors (please reference drug tables for more detailed information):

- Prescribing errors (e.g., incorrect doses; combinations that are antagonistic, such as zidovudine with stavudine; regimens with less than 3 active medications),
- Drug-drug interactions between ART and other drugs used concomitantly,
- Patient nonadherence to the prescribed ART regimen, and
- Pre-existing drug resistance with an absence of a fully suppressive treatment regimen.

The Vital Role of Pharmacists

What can pharmacists do to help decrease the incidence of drug resistance?

- Ensure that clinicians are prescribing ART agents correctly.
- Screen for drug-drug interactions.
- Monitor patients for medication adherence.

How can pharmacists improve adherence to ART?

Educate patients about antiretroviral medications and HIV therapy. Create a private environment for medication counseling where the patient feels comfortable discussing HIV and HIV treatment. The patient should be able to:

- Name/recognize all medications (trade name, generic name, initials)
- Explain how the medications work
- Describe how and when to take each one
- Discuss what happens when doses are missed
- List side effects that may occur
- State how side effects can be safely managed

Quiz patients to make sure they understand this information and help them develop a medication schedule. Use patient education tools such as the medication chart included with this booklet.

Encourage adherence. Follow up with patients who do not order refills on all ART drugs or who do not order refills on time. Do not be judgmental. Offer assistance and support and encourage patients to call their providers if they are missing doses. Recommend interventions to treat side effects such as diarrhea and nausea. Review the patient's medication schedule and offer advice on how to remember to take difficult doses. Offer adherence tools such as pillboxes and timers. Many ART drug companies have these tools available for free; just give them a call.

Assist the patients with timely refills of medications:

- Do not let a patient begin an incomplete regimen while waiting for other drugs in the regimen to come in.
- Avoid interruptions in therapy.
- Remember, partial ART (less than 3 drugs) encourages resistance. If a patient decides to stop therapy, all ART meds (not just one or two) should be stopped at once. (However, there are exceptions to this rule, such as efavirenz, etravirine and nevirapine which, due to a longer half-life, may need to be stopped approximately one week prior to other ART in the regimen with shorter half-lives. Tenofovir and emtricitabine or lamivudine may be concomitantly used in the treatment of hepatitis B and stopping them could cause a hepatitis B flare.) Patients should be advised to contact their medical provider prior to stopping any portion of an ART regimen.

Generic Name (abbreviation) Trade Name®	Available Dosage Forms	Usual Dose*	Special Dosing Considerations	Common Adverse Effects
				Serious Adverse Effects
raltegravir (RAL) Isentress®	400 mg tablets	400 mg twice daily	Take with or without food	nausea, headache, diarrhea, fever, CPK elevation
Metabolism: UGT1a1-mediated glucuronidation				

Generic Name (abbreviation) Trade Name®	Available Dosage Forms	Usual Dose*	Special Dosing Considerations	Common Adverse Effects
				Serious Adverse Effects
Fusion Inhibitor: enfuvirtide (T-20) Fuzeon®	108 mg vials - reconstitute with 1.1 mL sterile water (90 mg/mL)	90 mg SQ every 12 hours	Patients must be willing and able to prepare and administer injections. Requires thorough education about storage, preparation, SQ injection, and prevention of injection site reactions. Reconstituted drug, may be refrigerated up to 12 hours prior to use.	local injection site reactions, diarrhea, nausea, fatigue hypersensitivity reaction, bacterial pneumonia
CCR5 Antagonist: maraviroc (MVC) Selzentry®	150 and 300 mg tablets	150 mg twice daily when given with strong CYP3A inhibitors (with or without CYP3A inducers) including PIs (except tipranavir/ritonavir) 300 mg twice daily when give with NRTIs, enfuvirtide, tipranavir/ritonavir, nevirapine, and other drugs that are not strong CYP3A inhibitors 600 mg twice daily when given with CYP3A inducers, including efavirenz, etravirine, rifampin, etc. (without a CYP3A inhibitor)	Take with or without food. Must reduce dose if patient has renal dysfunction.	abdominal pain, cough, fever, dizziness, headache, orthostatic hypotension, rash, musculoskeletal symptoms, upper respiratory infections, hepatotoxicity

Metabolism of Entry Inhibitors
enfuvirtide: catabolism to its constituent amino acids with recycling of amino acids in the body pool
maraviroc: cytochrome P450 (CYP3A substrate). Care should be used with administering maraviroc with a CYP3A inducer, as this could lower maraviroc concentrations.
Coadministration with a CYP3A inhibitor may raise maraviroc levels. In both cases dose adjustments may be necessary.

Medications that have clinically significant drug interactions with maraviroc*: clarithromycin, carbamazepine, delavirdine, efavirenz, intraconazole, ketoconazole, rifampin, phenobarbital, phenytoin, protease inhibitors (except tipranavir/ritonavir), St. John's wort
*This list is not all inclusive

Integrase Inhibitors

Entry Inhibitors

Trade Name® (Drug Name)	Available Dosage Forms	Usual Dose*	Special Dosing Considerations	Common Adverse Effects Serious Adverse Effects
atazanavir (ATV) Reyataz®	100, 150, 200, 300 mg capsules	400 mg daily If taken with efavirenz, etravirine, or tenofovir, RTV boosting required: RTV 100 mg + ATV 300 mg daily	Take with a meal or snack. Use with caution with any acid-reducing agents. Contraindicated with proton-pump inhibitors. Dose atazanavir 10 hours apart from H2 blocker dosing. Use caution in patients on medications that may cause PR interval prolongation or if underlying conduction defect.	prolonged PR interval, hyperglycemia, body fat changes, [†] hyperbilirubinemia, possible increased bleeding in patients with hemophilia
darunavir (DRV) Prezista®	400, 600 mg tablets	600mg bid twice daily + RTV 100mg twice daily or 800mg once daily + RTV 100mg once daily. (ART-naïve patients only) RTV Boosting required	Take with food. Use caution if known sulfa allergy.	skin rash, diarrhea, nausea, headache, cold-like symptoms elevated transaminases, hyperlipidemia, body fat changes, [†] hyperglycemia, erythema multiforme, possible increased bleeding in patients with hemophilia.
fosamprenavir (FPV) Lexiva®	700 mg tablet Oral suspension:50 mg/mL	ART-naïve patients: - 1400 mg twice daily or - 1400 mg + RTV 200 mg daily or - 700 mg + RTV 100 mg twice daily or - 1400 mg + 100 RTV daily	Use with caution with any acid-reducing agents.	hyperlipidemia, body fat changes, [†] transaminase elevation, hyperglycemia, possible increased bleeding in patients with hemophilia
indinavir (IDV) Crixivan®	200, 333, 400 mg capsules	800 mg every 8 hours With RTV: 800 mg + RTV 100 or 200 mg every 12 hours	Take on empty stomach or with a light meal or a low fat snack. May be taken with food if given with ritonavir. Drink 1.5 liters of water each day.	nausea, diarrhea, increased indirect bilirubin, headaches, blurred vision, dizziness, rash, hyperglycemia, body fat changes, [†] hyperlipidemia, nephrolithiasis, thrombocytopenia, hemolytic anemia, possible increased bleeding in patients with hemophilia
lopinavir + ritonavir (LPV/r) Kaletra™	LPV 200 mg + RTV 50 mg and LPV 100 mg + RTV 25 mg mg tablets	2 tablets or 5 mL of oral solution twice daily 4 tablets once daily (once daily dosing only recommended for treatment naïve patients)	Take with or without food. Does not need to be refrigerated.	nausea, diarrhea, taste perversion, perioral and circumoral paresthesia
nelfinavir (NFV) Viracept®	250, 625 mg tablets 50 mg/g oral powder	With EFV or NVP: Treatment experienced patients, 3 tablets or 6.7 mL of oral solution twice daily 1,250 mg twice daily or 750 mg three times daily	Take with food.	diarrhea, flatulence, nausea, rash hyperglycemia, hyperlipidemia, body fat changes, [†] elevated transaminases, possible increased bleeding in patients with hemophilia
ritonavir (RTV) Norvir®	100 mg capsules	Used primarily as a booster for other PIs – see specific PI	Take with food. Capsules must be refrigerated but may be stored at controlled room temperature for 30 days. Do not refrigerate oral solution.	nausea, vomiting, diarrhea, taste perversion, extremity and circumoral paresthesias, elevated transaminases, hyperglycemia, hyperlipidemia, body fat changes, [†] possible increased bleeding in patients with hemophilia
saquinavir hard gel capsule (SQV) Invirase®	200 mg hard gel capsules, 500 mg tablets	Unboosted use not recommended 1,000 mg + RTV 100 mg twice daily	Take within 2 hours of a meal.	nausea, diarrhea, headaches hyperlipidemia, elevated transaminases, hyperglycemia, body fat changes, [†] possible increased bleeding in patients with hemophilia
tipranavir (TPV) Aptivus®	250 mg capsules	500 mg + RTV 200 mg twice daily Risk-benefit not yet established in treatment naïve patients RTV boosting required	Take with food. Use with caution if known sulfa allergy. Administer 2 hours apart from ddl-EC and liquid antacids. Review complex drug-drug interactions before using this agent. Use with caution in setting of hepatic impairment. Refrigerate capsules, may be stored at controlled room temperature (77°F or below) for 60 days.	Black box warning: tipranavir has been associated with fatal and nonfatal intracranial hemorrhages.

†The association of PIs with changes in body fat varies from agent to agent.

*Usual doses are provided. Doses may vary based on weight, the presence of renal or hepatic failure, or when using combinations that have pharmacokinetic interactions.

Metabolism of Protease Inhibitors

All of the protease inhibitors are metabolized by the cytochrome P450 enzyme, primarily by the isoenzyme CYP3A4. All protease inhibitors inhibit the isoenzyme CYP3A4. The degree of inhibition is dependent on the particular protease inhibitor being used with ritonavir producing the greatest inhibition of the isoenzyme. Ritonavir induces the isoenzyme CYP1A2 and also inhibits CYP2A6, 2C9, 1A2, 2C19, 2D6, and 2E1.

Lopinavir/ritonavir inhibits CYP2D6.

Medications that should NOT be administered with Protease

Inhibitors amiodarone, asemizole, bepridil, cispripide, ergotamine derivatives, fexofenadine, lovastatin, midazolam, piroxicam, propafenone, quinidine, rilampin, rifampin, simvastatin, St. John's Wort, terfenadine, triazolam

Medications that have Clinically Significant Drug Interactions with Protease Inhibitors - Avoid Use Or Modify Dosages*

Azoxystatin, bupropion, carbamazepine, cerivastatin, clarithromycin, clonazepam, cyclosporine, delavirdine, dexamethasone, diltiazem, diltiazem, disopyramide, dronabinol, efavirenz, ethinyl estradiol, ethosuximide, fluticasone, itraconazole, lisdexine, meperidine, methadone, metoprolol, mexilitine, nefazodone, nevirapine, perphenazine, phenobarbital, phenytoin, prednisone, propoxyphene, quinine, rapamycin, rifabutin, risperidone, sedative/hypnotics, selective serotonin reuptake inhibitors, sildenafil, stimulants, tacrolimus, theophylline, thioridazine, timolol, tramadol, trazodone, tricyclic antidepressants, vardenafil, verapamil, voriconazole, warfarin *This list is not all inclusive. The presence and the degree of interaction are dependent on the particular protease inhibitor being used.

Protease Inhibitors

Generic Name (abbreviation) Trade Name®	Available Dosage Forms	Usual Dose*	Special Dosing Considerations	Common Adverse Effects Serious Adverse Effects
delavirdine (DLV) Rescriptor®	100, 200 mg tablets	400 mg 3 times a day; four 100 mg tablets can be dispersed in at least 3 oz. of water	Space doses one hour apart from antacids and didanosine chewable tablets, suspension, and oral solution.	rash, elevated liver enzymes, headaches, fatigue, GI upset, neutropenia
etravirine (ETV) Intelence™	100 mg	200 mg twice daily	Take following a meal.	erythema multiforme
efavirenz (EFV) Sustiva®	50, 100, 200 mg capsules or 600 mg tablets	600 mg daily at or before bedtime	Recommend taking on an empty stomach as high-fat/high caloric meals increase peak plasma concentrations. Should not be administered during pregnancy or in women with pregnancy potential, unless negative pregnancy test prior to initiation and patient is using 2 effective contraceptive methods, including 1 barrier method. Pregnancy category D.	rash, drowsiness, diarrhea, dizziness, anxiety, depression, trouble concentrating, unusual dreams (effects usually transient lasting 2-4 weeks), elevated liver enzymes
nevirapine (NVP) Viramune®	200 mg tablets 50 mg/5 mL oral suspension	200 mg daily for 14 days (lead-in dosing), 200 mg two times daily thereafter Not recommended for use if baseline CD4 + T cell count > 250 cells/mm ³ in females or > 400 cells/mm ³ in males	Baseline LFTs and monitor at 2 weeks, 4 weeks then frequently until 18 weeks of therapy. LFTs should continue to be monitored frequently after the initial 18 week period. Lead-in dosing should be repeated if the drug is interrupted for any reason for more than 7 days.	confusion, encephalopathy rash, GI upset, headaches, elevated liver enzymes erythema multiforme, hepatotoxicity (> risk if baseline CD4 + T cell count > 250 cells/mm ³ in females or > 400 cells/mm ³ in males)

* Usual doses are provided. Doses may vary based on weight, the presence of renal or hepatic failure, or when using combinations that have pharmacokinetic interactions.

Metabolism of NNRRTIs

Nevirapine:	cytochrome P450 metabolism primarily by CYP2B6 and CYP3A family; causes induction of CYP3A isoenzymes	Medications that should NOT be administered with NNRRTIs Nevirapine: rifampin, rifapentine, St. John's Wort Delavirdine: apرازolam, amiodarone, astemizole, bepridil, carbamazepine, cisapride, ergotamine derivatives, flecainide, fosamprenavir, H2 blockers, lovastatin, midazolam, phenytoin, phenobarbital, pimoziide, propafenone, proton pump inhibitors, rifabutin, rifampin, rifapentine, St. John's Wort, simvastatin, terfenadine, triazolam	Avoid Use or Modify Doses:* Nevirapine: ketoconazole, methadone, clarithromycin, oral contraceptives, protease inhibitors, rifabutin, voriconazole Delavirdine: amphetamine, amphotericin, antacids, atorvastatin, bupropion, calcium channel blockers, erivastatin, clarithromycin, clonazepam, dapsone, didanosine, dilydroxyridines, ethosuximide, ketoconazole, methadone, nefazodone, protease inhibitors, quinidine, sedative/hypnotics, selective serotonin reuptake inhibitors, sildenafil, tadalafil, vardenafil, voriconazole, warfarin Efavirenz: carbamazepine, clarithromycin, oral contraceptives, methadone, phenobarbital, phenytoin, pimoziide, protease inhibitors, rifabutin, rifampin, voriconazole, warfarin	Common Adverse Effects Serious Adverse Effects
Delavirdine:	cytochrome P450 metabolism primarily by isoenzymes from the CYP3A family although CYP2D6 may play a minor role; causes inhibition of CYP3A and CYP2D6 isoenzymes primarily by isoenzymes CYP3A4 and CYP2B6; causes induction of CYP3A4 isoenzyme; causes inhibition of CYP3A4	Medications that should NOT be administered with NNRRTIs Nevirapine: rifampin, rifapentine, St. John's Wort Delavirdine: apرازolam, amiodarone, astemizole, bepridil, carbamazepine, cisapride, ergotamine derivatives, flecainide, fosamprenavir, H2 blockers, lovastatin, midazolam, phenytoin, phenobarbital, pimoziide, propafenone, proton pump inhibitors, rifabutin, rifampin, rifapentine, St. John's Wort, simvastatin, terfenadine, triazolam	Avoid Use or Modify Doses:* Nevirapine: ketoconazole, methadone, clarithromycin, oral contraceptives, protease inhibitors, rifabutin, voriconazole Delavirdine: amphetamine, amphotericin, antacids, atorvastatin, bupropion, calcium channel blockers, erivastatin, clarithromycin, clonazepam, dapsone, didanosine, dilydroxyridines, ethosuximide, ketoconazole, methadone, nefazodone, protease inhibitors, quinidine, sedative/hypnotics, selective serotonin reuptake inhibitors, sildenafil, tadalafil, vardenafil, voriconazole, warfarin Efavirenz: carbamazepine, clarithromycin, oral contraceptives, methadone, phenobarbital, phenytoin, pimoziide, protease inhibitors, rifabutin, rifampin, voriconazole, warfarin	Common Adverse Effects Serious Adverse Effects
Efavirenz:	cytochrome P450 metabolism primarily by isoenzymes CYP3A4 and CYP2B6; causes induction of CYP3A4 isoenzyme; causes inhibition of CYP3A4	Medications that should NOT be administered with NNRRTIs Nevirapine: rifampin, rifapentine, St. John's Wort Delavirdine: apرازolam, amiodarone, astemizole, bepridil, carbamazepine, cisapride, ergotamine derivatives, flecainide, fosamprenavir, H2 blockers, lovastatin, midazolam, phenytoin, phenobarbital, pimoziide, propafenone, proton pump inhibitors, rifabutin, rifampin, rifapentine, St. John's Wort, simvastatin, terfenadine, triazolam	Avoid Use or Modify Doses:* Nevirapine: ketoconazole, methadone, clarithromycin, oral contraceptives, protease inhibitors, rifabutin, voriconazole Delavirdine: amphetamine, amphotericin, antacids, atorvastatin, bupropion, calcium channel blockers, erivastatin, clarithromycin, clonazepam, dapsone, didanosine, dilydroxyridines, ethosuximide, ketoconazole, methadone, nefazodone, protease inhibitors, quinidine, sedative/hypnotics, selective serotonin reuptake inhibitors, sildenafil, tadalafil, vardenafil, voriconazole, warfarin Efavirenz: carbamazepine, clarithromycin, oral contraceptives, methadone, phenobarbital, phenytoin, pimoziide, protease inhibitors, rifabutin, rifampin, voriconazole, warfarin	Common Adverse Effects Serious Adverse Effects
Etravirine:	cytochrome P450 metabolism. Causes induction of CYP3A4 isoenzyme; causes inhibition of CYP2C9 and CYP2C19.	Medications that should NOT be administered with NNRRTIs Nevirapine: rifampin, rifapentine, St. John's Wort Delavirdine: apرازolam, amiodarone, astemizole, bepridil, carbamazepine, cisapride, ergotamine derivatives, flecainide, fosamprenavir, H2 blockers, lovastatin, midazolam, phenytoin, phenobarbital, pimoziide, propafenone, proton pump inhibitors, rifabutin, rifampin, rifapentine, St. John's Wort, simvastatin, terfenadine, triazolam	Avoid Use or Modify Doses:* Nevirapine: ketoconazole, methadone, clarithromycin, oral contraceptives, protease inhibitors, rifabutin, voriconazole Delavirdine: amphetamine, amphotericin, antacids, atorvastatin, bupropion, calcium channel blockers, erivastatin, clarithromycin, clonazepam, dapsone, didanosine, dilydroxyridines, ethosuximide, ketoconazole, methadone, nefazodone, protease inhibitors, quinidine, sedative/hypnotics, selective serotonin reuptake inhibitors, sildenafil, tadalafil, vardenafil, voriconazole, warfarin Efavirenz: carbamazepine, clarithromycin, oral contraceptives, methadone, phenobarbital, phenytoin, pimoziide, protease inhibitors, rifabutin, rifampin, voriconazole, warfarin	Common Adverse Effects Serious Adverse Effects

* This list is not all inclusive.

Generic Name (abbreviation) Trade Name®	Available Dosage Forms	Usual Dose*	Special Dosing Considerations	Common Adverse Effects Serious Adverse Effects
Combivir® (AZT/3TC)	AZT 300 mg + 3TC 150 mg	1 tablet every 12 hours	Take with or without food.	see individual components
Epzicom® (ABC/3TC)	ABC 600 mg + 3TC 300 mg	1 tablet daily	Take with or without food.	risk of hypersensitivity reaction see individual components
Trizivir® (AZT/3TC/ABC)	ABC 300 mg + AZT 300 mg + 3TC 150 mg	1 tablet twice daily	Take with or without food.	risk of hypersensitivity reaction see individual components
Truvada® (FTC/TDF)	FTC 200 mg + TDF 300 mg	1 tablet daily	Take with or without food.	see individual components
Atripla® (FTC/TDF/EFV)	FTC 200 mg + TDF 300 mg + EFV 600 mg at or before bedtime	1 tablet daily	Recommend taking on an empty stomach as high-fat/high-caloric meals increase peak plasma concentrations. Should not be administered during pregnancy or in women with pregnancy potential, unless negative pregnancy test prior to initiation and patient is using 2 effective contraceptive methods, including 1 barrier method. Pregnancy category D.	see individual components

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)

Fixed Dose Combinations

Generic Name (Abbreviation) Trade Name®	Available Dosage Forms	Usual Dose*	Special Dosing Considerations	Common Adverse Effects Serious Adverse Effects
abacavir (ABC) Ziagen®	300 mg tablets 20 mg/mL oral solution	300 mg twice daily or 600 mg once daily	Take with or without food. Alcohol increases abacavir levels 41%; abacavir has no effect on alcohol. Hypersensitivity Reaction , which may be fatal: signs/symptoms may include rash, fever, nausea, vomiting, malaise, fatigue, loss of appetite, respiratory symptoms such as sore throat, cough, or shortness of breath. Screening with a genetic test, HLA-B*57:01, greatly reduces the risk of this reaction.	nausea, body fat changes† If signs/symptoms of the reaction occur: seek medical evaluation immediately to determine need to discontinue and DO NOT restart. Abacavir rechallenge has been associated with fatal hypersensitivity reaction
didanosine (ddI) Videx EC®	125, 200, 250 or 400 mg	Body weight \geq 60 kg: 400 mg once daily (EC capsule) With TDF: 250 mg daily < 60 kg: 250 mg daily EC capsule With TDF: 200 mg daily	All ddl preparations must be taken on an empty stomach, at least 30 minutes before or 2 hours after eating. With tenofovir, dose may be reduced to 250 mg per day and may be taken with a light meal or snack. Monitor for ddl toxicity. Concomitant use with d4T not recommended. Separating some medication administration from ddl dose may be necessary. Must reduce dose if patient has renal dysfunction.	nausea, vomiting, diarrhea, peripheral neuropathy, headaches, rash pancreatitis, hepatitis, lactic acidosis with hepatic steatosis, body fat changes†
emtricitabine (FTC) Emtriva™	200 mg capsule 10 mg/mL oral solution	200 mg daily or 240 mg (24 mL) oral solution daily	Take with or without food. Must reduce dose if patient has renal dysfunction.	headache, diarrhea, nausea, rash, skin discoloration lactic acidosis with hepatic steatosis, body fat changes†
lamivudine (3TC) EpiVIR®	150 mg tablets 300 mg tablets	> 50 kg: 300 mg daily or 150 mg twice daily < 50 kg: 2 mg/kg twice daily	Take with or without food. Must reduce dose if patient has renal dysfunction.	nausea lactic acidosis with hepatic steatosis, body fat changes†
stavudine (d4T) Zertiv®	15, 20, 30, and 40 mg capsules 1 mg/mL oral solution	> 60 kg: 40 mg twice daily < 60 kg: 30 mg twice daily	Take with or without food. Dosage reduction may be effective for peripheral neuropathy and is necessary if renal dysfunction. Concomitant use with ddl or AZT not recommended.	peripheral neuropathy, nausea pancreatitis, lactic acidosis with hepatic steatosis (higher incidence than with other NRTIs), hyperlipidemia, body fat changes†
tenofovir (TDF) Viread®	300 mg tablet	1 tablet daily	Take with or without food. Must reduce dose if patient has renal dysfunction.	nausea, diarrhea vomiting, flatulence, asthenia, renal insufficiency, lactic acidosis with hepatic steatosis
zidovudine (AZT) Retrovir®	100 mg capsules, 300 mg tablets 10 mg/mL IV solution, 10 mg/mL oral solution	300 mg twice daily or 200 mg three times a day	Take with or without food. Must reduce dose if patient has renal dysfunction. Concomitant use with d4T not recommended.	nausea, vomiting, headaches, insomnia anemia, neutropenia, pancreatitis, lactic acidosis with hepatic steatosis, body fat changes†

*Usual doses are provided. Doses may vary based on weight, the presence of renal or hepatic failure, or when using combinations that have pharmacokinetic interactions. Dosage reduction may be required.

†The association of NRTIs with body fat changes varies from agent to agent. **Metabolism of NRTIs** AZT-hepatic via glucuronidation; renal excretion of metabolites; ddl - 55% renally eliminated as unchanged drug; d4T-renal excretion 50%; 3TC-renally eliminated; abacavir-hepatic via alcohol dehydrogenase and glucuronyl transferase; metabolites excreted renally 85%; FTC-renally eliminated; tenofovir-renally eliminated

Medications that may have Clinically Significant Drug Interactions with NRTIs
AZT aspirin, cimetidine, cytotoxic drugs, d4T, indomethacin, methadone, probenecid, ribavirin, drugs that interfere with RBC/WBC
ddl atazanavir, dapsone, indinavir (Separate doses by at least 2 hours with indinavir and ddl chewable tabs), pentamidine, drugs that cause pancreatitis/peripheral neuropathy; tenofovir, ribavirin
d4T zidovudine, drugs that cause peripheral neuropathy/pancreatitis
ABC ethanol
TDF atazanavir, ddl, lopinavir/ritonavir, cidofovir, valganciclovir

*This list is not all inclusive.

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI/NtRTI)

Encourage patients to discuss all treatment issues with their providers:

- Even something as simple as an over-the-counter treatment for diarrhea may be important in the overall approach to care.
- Stopping ART can be especially risky and scheduled treatment interruptions are not recommended. Patients need to have an in-depth discussion with their providers before stopping any medication.

Keep up with changes in ART medications and treatment guidelines. New drugs and new formulations of existing drugs are continually being developed and approved. In addition, guidelines change often. Make it a habit to get updated on a regular basis. For up-to-date information, visit <http://www.aidsinfo.nih.gov>

Case Study

1. A new patient, Melissa, presents to your pharmacy to pick up a prescription for abacavir/lamivudine (Epzicom®, ABC/3TC), one tablet once daily, atazanavir 300 mg (Reyataz®, ATV), one tablet daily, and ritonavir 100 mg (Norvir®, RTV), one tablet daily. She has no previous history of taking ART. You take Melissa aside to a private area where you can more easily discuss each of her medications, how they work, and when and how to take them. Which one of the following would also be important information to include in the conversation?
 - a. “It is important to take these medications on an empty stomach.”
 - b. “Be sure to take these 12 hours apart from each other.”
 - c. “It is important to take your medications every day to avoid viral resistance. Let us know before you run out of them, so you don’t miss any doses.”
 - d. “It is very important to take these medications every day, so if you run out of one of them, you should still keep taking the other two.”

2. Melissa returns a week later and says, “I have this horrible rash and fever; I feel so tired and my stomach is upset. What can you recommend?” What would be the best response?
 - a. “Since your HIV medications are probably making you feel this way, you should just take half of your normal dose for a couple of days until you feel better.”
 - b. “One of the medications you are on can sometimes cause a serious sensitivity reaction. Why don’t we call your provider and find out if she can see you today?”
 - c. “Some of the HIV medications can cause these side effects, but they usually go away within a couple of weeks.”
 - d. “In order to help you keep taking these medications, I would recommend these OTC options, to help you deal with the symptoms.”

3. After going to see her provider, Melissa returns to the pharmacy with a new prescription for tenofovir/emtricitabine (Truvada™, TDF/FTC) one tablet daily. She says her provider did think she was having a hypersensitivity reaction and gave her this new prescription. She asks what she should do with the rest of her abacavir/lamivudine (Epzicom®, ABC/3TC). What is your best reply?
- “These are such similar medications that you can keep taking the abacavir/lamivudine (Epzicom®, ABC/3TC) until you run out and then switch to the tenofovir/emtricitabine (Truvada™, TDF/FTC).”
 - “You should switch immediately to the tenofovir/emtricitabine (Truvada™, TDF/FTC), but save the rest of the abacavir/lamivudine (Epzicom®, ABC/3TC) in case you ever need it again.”
 - “You should switch immediately to tenofovir/emtricitabine (Truvada™, TDF/FTC) but keep the leftover abacavir/lamivudine (Epzicom®, ABC/3TC), as your provider will probably put you back on it once the reaction subsides.”
 - “You should stop the abacavir/lamivudine (Epzicom®, ABC/3TC) immediately and get rid of it. Once you’ve had a hypersensitivity reaction it can be more serious, even fatal, if you ever take it again. Be sure to always let your providers know that you can’t take this medication or any containing abacavir (Ziagen®, ABC).”
4. Melissa returns in a couple of weeks. Her symptoms from the hypersensitivity reaction have resolved. She requests a refill of simvastatin (Zocor®), which her PCP had prescribed for her prior to starting ART. What would be the best response?
- Advise Melissa of an interaction between simvastatin (Zocor®) and atazanavir (Reyataz®, ATV) and she must take these medications 12 hours apart.
 - Fill the prescription as written. There is no interaction between the medications and the prescription refill has not expired.
 - Notify Melissa of the interaction between simvastatin (Zocor®) and atazanavir (Reyataz®, ATV). Contact her HIV provider to find an alternative statin.
 - Tell Melissa, “Now that you are receiving HIV care, I can no longer fill any of the prescriptions from your PCP without an OK from your HIV provider.”

Case Study Answers

1. Advice regarding new ART regimen

- a. There are no food considerations for abacavir/lamivudine (Epzicom®, ABC/3TC). Atazanavir (Reyataz®, ATV) and ritonavir (Norvir®, RTV), should be taken with a meal or a snack.
- b. These medications can be taken at the same time, they do not need to be taken separately.
- c. **This is the correct answer. Adherence is critical in order to avoid viral resistance. It is important for patients to be aware of this issue. Evidence has shown that the most effective regimens involve three medications from two different classes. Thus, it is critical that the patient avoid taking one or two medications without the other.**
- d. This is incorrect. Although it is important not to miss doses, monotherapy or dual therapy can do more harm than good, as it does not allow for complete suppression of HIV and resistance is more likely to develop.

2. Side effects

- a. Most antiretrovirals have multiple side effects, however any regimen containing abacavir (Ziagen®, ABC) should cause you to be alert for a hypersensitivity reaction. It is not advisable for a patient to reduce her dose in order to diminish side effects as this puts her at risk for developing viral resistance to the ART regimen.
- b. **This is the best answer. Abacavir (Ziagen®, ABC) is known to cause a hypersensitivity reaction in some patients. This reaction can be fatal and signs and symptoms may include rash, fever, nausea, vomiting, malaise, fatigue, loss of appetite, and respiratory symptoms such as sore throat, cough, or shortness of breath. The patient should seek medical consultation immediately to rule out a hypersensitivity reaction. The risk of this reaction can be greatly reduced by a genetic screening test, HLA-B*5701. Patients who test positive for HLA-B*5701 should not be prescribed Abacavir.**
- c. As in answer a, with the use of this medication a hypersensitivity reaction should be ruled out. In any case, it is important to increase adherence by minimizing medication side effects through pharmacological and non-pharmacological methods.
- d. If you were not concerned about a hypersensitivity reaction this would be a good option, as long as the patient was also advised to seek medical care should symptoms persist or worsen. However, you should always consider a hypersensitivity reaction with abacavir.

3. Leftover abacavir/lamivudine (Epzicom®, ABC/3TC).

- a. One antiretroviral should never be substituted for another. However, the more serious issue is that the patient mentioned a history of hypersensitivity reaction to Abacavir (Ziagen®, ABC). The pharmacist should be aware of this reaction and help ensure that the patient does not continue taking this medication or receive it again in the future. A rechallenge to abacavir (Ziagen®, ABC) can cause a more serious and even fatal reaction.
- b. See answer a.
- c. See answer a.
- d. This is the correct answer. It ensures the patient is aware of the seriousness of continuing abacavir (Ziagen®, ABC) or ever taking it again. It is important to let the patient know that abacavir (Ziagen®, ABC) is also contained in various combination antiretrovirals.**

4. Statins.

- a. See answer c. Spacing these medications will not resolve the drug-drug interaction.
- b. See answer c.
- c. When taken with atazanavir (Reyataz®, ATV), simvastatin (Zocor®) levels can be dangerously increased. An alternative statin such as atorvastatin (Lipitor®) or pravastatin (Pravachol®) should be used. Always start with the lowest dose and monitor for toxicities.**
- d. This is not an appropriate answer. In many cases PCPs will continue to provide care to their patients. However, they need to be made aware of drug-drug interactions.

Post-test for Pharmacy Module

1. **Sam works in a pharmacy in a rural setting. A client presents a prescription at the window for zidovudine (Retrovir®, ZDV). He says he was recently diagnosed with AIDS and given this prescription. He adds that he is terrified of dying and wants to start the medication as soon as possible so that he will feel better. What is your biggest concern in this situation?**
 - a. Does the pharmacy carry antiretrovirals such as zidovudine (Retrovir®, ZDV)? Filling his prescription urgently is a big concern (especially in rural areas) since HIV needs to be treated as soon as possible to avoid serious complications.
 - b. Will Sam be able to provide appropriate patient education? Zidovudine (Retrovir®, ZDV) has some problematic side effects that this patient will need to know about. It is important for the pharmacist to be sure that the patient is aware of these potential problems.
 - c. Monotherapy can compromise the efficacy of future antiretroviral therapy by leading to drug resistance. This is crucial to the long-term success of HIV treatment. Sam should call the prescriber to clarify the prescription.
 - d. Although you are concerned that the client may require other antiretrovirals, his current prescription should be filled as instructed by the medical provider. If there is an error in the prescription it can easily be remedied at a later point.

2. **Adam tells you he has HIV and was started on medications but has been experiencing a lot of diarrhea. He asks you to direct him to the best over-the-counter agent. What would be your best response?**
 - a. “Many over-the-counter agents could cause problems with your HIV medications. You need to get a prescription from your doctor to treat your diarrhea.”
 - b. “I can recommend something to help, but persistent diarrhea should be evaluated by your provider. Make sure your provider knows about any over-the-counter medications you take.”
 - c. “If you are having diarrhea from your HIV medications, they should be changed to alleviate side effects.”
 - d. “The HIV medications that you are taking commonly cause diarrhea. It should improve with time.”

3. **Adam returns a few weeks later and tells you he is still having diarrhea. He has a prescription for an antidiarrheal medication, but he says, “If this is what I can expect from HIV medications maybe I would be better off without them.” What would be the best response?**
 - a. “Hang in there; it’s better than the alternative.”
 - b. “It may just take time for you to adjust. You should try to stick with it no matter what.”
 - c. “You can stop the protease inhibitor portion of your regimen and give yourself a break. That’s the part that usually causes diarrhea.”
 - d. “The initial antiretroviral regimen is often the best hope for success. How about trying this prescription to see if it helps? If it persists, be sure to tell your medical provider.”

4. You are giving a patient, Linda, information about her new medication Atripla®, (tenofovir (TDF), emtricitabine (FTC), efavirenz (EFV)). What side effects are the most important to tell her about?
- Diarrhea, nausea, rash, headaches, and hot flashes
 - Abdominal pain, vomiting, and fatigue
 - Dizziness, unusual dreams, rash, and potential fetal defects
 - Trouble concentrating, rash, and paresthesias
5. A new client, Lee, is filling prescriptions for nevirapine (Viramune®, NVP) and zidovudine/lamivudine (Combivir®, AZT/3TC). Your instructions would include which of the following?
- “Start by taking one tablet of nevirapine (Viramune®, NVP) every day for 14 days and then increase that to one tablet twice a day.”
 - “Be sure to follow up with your doctor soon for a urinalysis.”
 - “Stop taking the medication immediately if you notice a rash.”
 - “Don’t start the nevirapine (Viramune®, NVP) until two weeks after you start the zidovudine/lamivudine (Combivir®, AZT/3TC).”
6. Several months later you see Lee as he fills his prescriptions. You ask how he is doing with the new regimen and he says, “It’s going well, but I’m out of one of my HIV medications.” When you pull up Lee’s information you notice that the medications he’s taking were last filled on the same day. What is the best course of action?
- Call the client’s provider immediately to report an adherence problem.
 - Ask Lee how he is taking the medications and offer strategies to avoid missed doses. Notify Lee’s provider of potentially missed doses.
 - Give Lee reassurance that he is doing well with his medications.
 - No action is necessary.
7. While assisting an established client, she tells you how glad she is that her gynecologist has put her back on birth control pills. You know that she has been taking zidovudine/lamivudine (Combivir®, AZT/3TC) and lopinavir/ritonavir (Kaletra®) for the past 8 months. What would be an appropriate comment?
- “You know you still have to use condoms.”
 - “Ethinyl estradiol cannot be used with antiretroviral medications.”
 - “The protease inhibitor that you are on can interact with birth control pills and make both medications less effective. Do you mind if I call and talk to your provider about this?”
 - “Great – I’ll get this filled as quickly as possible and get you on your way!”

8. **Kristina, a new client, presents with a prescription for Trizivir® (ABC/3TC/AZT) one tablet, twice a day. She has no other prescriptions with her and states this is the only medication she takes for her HIV. What is your best course of action?**
- Fill the prescription as prescribed, it does include three separate, potentially active, antiretroviral medications.
 - Contact Kristina's provider to verify the prescription since Trizivir® (ABC/3TC/AZT) should be dosed as two tablets twice a day.
 - Fill the prescription as prescribed, she must be resistant to most medications and on a salvage regimen.
 - Contact Kristina's provider to verify the prescription since Trizivir® (ABC/3TC/AZT) includes three medications all in the same class and guidelines recommend three medications from two different drug classes.
9. **A client is taking atazanavir (Reyataz®, ATV) and tenofovir/emtricitabine (Truvada®, TDF/FTC). What should you be aware of with this regimen?**
- NSAIDS should not be used with tenofovir.
 - Acetaminophen should not be used with most antiretroviral medications because of the risk to the liver.
 - There would be very few drug interactions with over-the-counter medications and this regimen.
 - When atazanavir (Reyataz®, ATV) and tenofovir/emtricitabine (Truvada®, TDF/FTC) are used together, boosting with ritonavir (Norvir®, RTV) is recommended.
10. **A client presents you with a prescription for stavudine (Zerit®, D4T), zidovudine (Retrovir®, AZT), and efavirenz (Sustiva®, EFV). What's wrong with this regimen?**
- Proper antiretroviral treatment requires at least 3 drugs from 3 separate classes.
 - Zidovudine, (Retrovir®, AZT) should not be combined with stavudine (Zerit®, D4T).
 - Proper antiretroviral therapy always includes a protease inhibitor (PI).
 - This is an appropriate regimen.
11. **After describing the side effects of Atripla®, Linda asks you if she can take Atripla® in the morning during breakfast. What is the best response to her question?**
- Yes, you can take this medication anytime throughout the day, as long as it's the same time everyday.
 - Yes, but she needs to take the medication with food and at the same time everyday.
 - No, this medication should be taken in the evening on an empty stomach or two hours after eating.
 - No, this medication should be taken in the evening with food to minimize side effects.

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Name	Affiliation	Organization
Steven Johnson	Consultant	GSK, Gilead, Abbott, Tibotec, Merck
Jennifer Kiser	Advisory Board Speaker's Bureau	Tibotec Abbott

All other faculty reported no commercial affiliation.

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