



A PHARMACY CONTINUING EDUCATION PROGRAM

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July 2006 "HIV/AIDS Update Part 2" 707-000-06-007-H02



THIS MONTH
"HIV/AIDS 2006
UPDATE PART 2"

**IN THIS LESSON WE DISCUSS ANTIRETROVIRAL THERAPY,
COMBINATION THERAPIES & THERAPIES IN PREGNANCY
THAT PREVENT PERINATAL TRANSMISSION.**

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This is Part 2 of our Special Program on HIV/AIDS. This is an up to date review that concentrates on drug therapy. Our goal is to present the most current information on this subject. This lesson provides 1.5 hours of credit (0.15 CEUs), and is intended for pharmacists in all practice settings.

The ACPE program ID # for this lesson is 707-000-06-007-H02. Our CE Provider Registered # with CE Broker.com is 50-3170-1.

Pharmacists completing this lesson by July 31, 2009 may receive full credit.

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz via conventional mail, fax (847-945-5037), or send us a conventional email with your answers (info@wfprofessional.com). Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

Upcoming topics for continuous participants: Skin Exposure to Sunlight; and more.

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The objectives of this lesson are such that upon completion the participant will be able to:

1. Describe the indications for initiating antiretroviral therapy.
2. Differentiate between the classes of antiretroviral agents that are currently approved for treatment of HIV infection in the U.S.
3. List currently approved antiretroviral agents, describe pharmacology, recognize major adverse effects or toxicities, & identify significant drug-drug interactions associated with each.
4. List preferred first-line & alternative combination therapies for HIV.
5. Discuss antiretroviral therapy in pregnancy to prevent perinatal transmission.

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HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

Antiretroviral therapy has been one of the major advances in the fight against Human Immunodeficiency Virus (HIV), the virus that leads to acquired immunodeficiency syndrome (AIDS). The field of antiretroviral therapy has seen more dramatic changes than any other antimicrobial development in the past decade. Complete viral eradication is unlikely in chronically infected patients resulting in lifelong treatment. Clinical evidence shows that viral replication continues in the face of undetectable viral load. In other words, the infection may remain hidden but virulent. Therefore, **two primary goals of antiretroviral therapy remain to be virologic control** (measured as in reduced HIV RNA level) **and immune restoration** (measured as in increased CD4 count). Once these are achieved, clinicians are able to delay the progression of the disease, minimize opportunistic infections & malignancies, prolong survival, and improve quality of life. HAART has significantly improved morbidity and mortality by decreasing the risk of disease progression and prolonging life in HIV-infected patients. Despite these advances, long-term side effects and the need for nearly perfect adherence makes the management of these patients difficult.^{1,2}

ADHERENCE

Adherence is an important factor that determines degree and duration of virologic response. The ability of the patient to adhere to the prescribed regimen is critical for success of HAART and prevention of resistance. At least 90%-95% adherence is required to achieve undetectable viral load in 80% of patients. If adherence drops to 70-80%, only 25% of patients will likely achieve undetectable viral load. In short, less than perfect adherence leads to the development of drug resistance, limiting the effectiveness of therapy.^{1,2} Poor adherence has been shown to increase the likelihood of virologic failure and has been associated with increased morbidity and mortality. Due to increasing success of HAART, HIV/AIDS has become a chronic disease. It has become very difficult for patients to show perfect adherence to the regimens chronically. Reasons for lack of adherence include medication toxicities, complexity of the regimen such as multiple daily doses, increased pill burden, food and hydration requirements.^{1,2} For more predictable success of HAART, the pharmacist can prepare the patient for potential adverse effects, simplify regimens, avoid multiple drug-drug & drug-food interactions, reduce pill burden, explain goals of therapy and the importance of adherence, and most importantly, establish readiness to take medication before initiation of HAART.

ANTIRETROVIRAL AGENTS

Currently, five different classes of antiretroviral agents are available for the management of HIV disease: **nucleoside reverse transcriptase inhibitors (NRTIs)**, **non-nucleoside reverse transcriptase inhibitors (NNRTIs)**, **protease inhibitors (PIs)**, **nucleotide reverse transcriptase inhibitors (Nucleotide RTIs)** and **Fusion inhibitors (FIs)**. This lesson reviews the current treatment options for HIV infection.²

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

These were the first antiretroviral agents to be used for the treatment of HIV. These agents chemically mimic naturally occurring nucleosides used for viral DNA proliferation. Their mechanism of action involves inhibition of the viral enzyme, reverse transcriptase, which is responsible for the transcription of viral RNA to DNA within the host cell.³ Thus, these agents inhibit viral replication in early stages of the viral life cycle. The currently approved NRTIs for HIV treatment in the U.S. are: zidovudine (AZT, Retrovir®), didanosine (ddI, Videx®), zalcitabine (ddC, Hivid®), stavudine (d4T, Zerit®), lamivudine (3TC, Epivir®), abacavir (ABC, Ziagen®), and most recently emtricitabine (FTC, Emtriva®).^{1,2} Emtricitabine is a cytidine analogue; therefore, it cannot be used with lamivudine.⁴ All of these agents require intracellular metabolism to their triphosphate form before activation. Once activated, NRTIs competitively inhibit HIV reverse transcriptase, insert themselves into the growing viral DNA as a false nucleotide, block DNA synthesis, lead to chain termination, and subsequently inhibit viral replication.³

Three NRTI combination products are available to help improve adherence to HIV therapy by decreasing overall pill burden. Zidovudine and lamivudine are formulated together under the brand name Combivir®, and Trizivir® is a combination

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product containing zidovudine, lamivudine, and abacavir of which both are given twice daily. In addition, Epzicom® is a combination of abacavir and lamivudine which is one tablet daily.² These formulations are based on clinical data demonstrating the efficacy of these NRTIs in combination. Most of these agents are primarily excreted through the kidneys; therefore, dosage adjustments may be necessary for patients with renal impairment. In the near future, a combination pill of tenofovir 300mg, emtricitabine 200mg, and efavirenz 600mg will be available as one tablet daily.⁵ **Table 1** below summarizes the dosing and food effects for the NRTIs, while **Table 4** elaborates on adverse drug reactions with these agents.²

Nucleotide Reverse Transcriptase Inhibitors (Nucleotide RTIs)

Tenofovir is an acyclic nucleoside phosphonate (nucleotide) with antiviral activity against HIV. It also has activity against Hepatitis B, but it is not currently approved to treat this infection.⁶ Tenofovir disoproxil fumarate is the first nucleotide analogue reverse transcriptase inhibitor approved in the U.S.⁶ Nucleotide analogues are monophosphorylated nucleoside analogues, and they block HIV replication in the same manner as NRTIs. Therefore, tenofovir is classified in several sources under NRTIs. Tenofovir is formulated with emtricitabine under the trade name Truvada®.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Like NRTIs, these drugs inhibit viral enzyme reverse transcriptase. However, they structurally bind to reverse transcriptase through a noncompetitive mechanism, making conformational change, rendering the reverse transcriptase enzyme less available for making proviral DNA.⁷ Unlike NRTIs, these drugs do not require intracellular metabolism for activation. Theoretically, drug resistance towards NRTIs would not affect NNRTIs or vice versa due to different site of action on reverse transcriptase. However, significant cross-resistance exists among NNRTIs within their class. There are three NNRTIs available: nevirapine (NVP, Viramune®), delavirdine (DLV, Rescriptor®), and efavirenz (EFV, Sustiva®). Usual adult doses and food effects for these agents are summarized in **Table 1**, while adverse effect data are listed in **Table 5**. **All available NNRTIs can cause a rash ranging from mild reactions to serious life threatening Steven's Johnson syndrome**^{1,2,7}

Protease Inhibitors

The third class of antiretrovirals, HIV protease inhibitors (PIs), was designed to inhibit viral replication during late stage in the life cycle of HIV. Protease is a viral enzyme responsible for cleaving complex viral polypeptide precursors into functional proteins that are essential for the maturation and assembly of virions. Activity of this enzyme is critical for the completion of HIV viral replication.⁸ PIs resemble the amino acid sequence where HIV protease binds or cleaves. Thus, PIs competitively inhibit HIV protease by binding to the active site of the enzyme. In other words, they inhibit production of new virions from chronically infected cells. There are currently nine PIs approved by the FDA for HIV treatment in the U.S.: saquinavir (SQV, Invirase®); ritonavir (RTV, Norvir®); indinavir (IDV, Crixivan®); nelfinavir (NFV, Viracept®); amprenavir (APV, Agenerase®); lopinavir/ritonavir (LPV/RTV, Kaletra®), atazanavir (ATZ, Reyataz®), fosamprenavir (Lexiva®) and most recently Tipranavir (TPV, Aptivus®).² See **Table #1** for dosing, food effects and storage requirements, and **Table #4** for adverse effects.²

Low dose ritonavir is clinically used in combination with multiple other PIs to help boost the pharmacokinetic levels of these agents to attain better viral suppression. The ritonavir increases the concentrations of the second PI via CYP 450 inhibition, allowing for less frequent administration. The ritonavir dose used to boost the second PI concentration ranges from 100-400 mg daily, which is subtherapeutic when used alone. The combinations of ritonavir with saquinavir, indinavir, amprenavir, fosamprenavir, atazanavir and lopinavir have been successfully used in both treatment-naïve and experienced patients.^{1,2} Tipranavir is the first non-peptidic protease inhibitor (NPPI) and has been approved for highly treatment experienced patients or HIV strains resistant to multiple protease inhibitors.⁹

Fusion Inhibitors (FIs)

Enfuvirtide (Fuzeon®) is the first in a new class of drugs called fusion inhibitors. These agents block fusion of HIV with the host cell before the virus enters the cell and begins the replication process.¹⁰ Enfuvirtide is indicated in combination with other antiretroviral agents in treatment experienced patients who continue to have evidence of HIV-1 replication despite current antiretroviral therapy. Unlike other antiretrovirals, enfuvirtide is administered by subcutaneous injection. The dose is 90mg (1 mL) twice daily subcutaneously injected into the upper arm, anterior thigh or abdomen. Enfuvirtide is supplied as a lyophilized powder to be reconstituted with sterile water. The powder can be stored at room temperature but once reconstituted the solution should be stored under refrigeration (2°C to 8°C) and used within 24 hours. The most common side effects in clinical trials were local injection site reactions that were described as painful, indurated, erythematous, or nodular cysts.¹⁰ It is important to educate patients on correct injection technique and site rotation to minimize site reactions.

NEW DRUGS IN THE RESEARCH

Numerous agents from the above five classes (NRTIs, NNRTIs, PIs, nucleotide RTIs and FIs) and from several new classes are being investigated and are in Phase I, II, or III of development.¹¹ As our understanding of the HIV life cycle increases, the

development of new targets for the inhibition of HIV replication also increases. For example, HIV integrase incorporates HIV DNA into host chromosomal DNA and is a novel target in drug development. For HIV cell entry, the binding of either coreceptor CCR5 or CXCR4 on host cells is required. Antagonists to these coreceptors are under development in Phase III trials. In addition to novel classes, antiretroviral in the current classes (i.e. NNRTI and PIs) are being developed for more treatment experienced patients.¹¹

Table 1. The Dosing /Administration and Storage Requirements for Antiretroviral Agents²

Generic Name, <i>Brand Name</i>	Class	Usual Adult Dose	Food Effect
Abacavir (ABC) <i>Ziagen</i> ® • 300mg tablets • 20 mg/mL oral solution	NRTI	300 mg po q12h 600mg po daily	Without regard to meals; alcohol increases ABC levels 41%; no effect on alcohol
Didanosine (ddI), <i>Videx EC delayed release capsules</i> ® • 125, 200, 250, 400mg	NRTI	>60kg • 200mg tablet q12h • 400mg capsule QHS • With Tenofovir: 250mg daily <60kg • 125mg tablet q12h • 250 mg capsule QHS	Take half hour before or 1 hour after meals Videx buffered tablet® distribution discontinued in 2006.
Lamivudine (3TC), <i>Epivir</i> ® • 150, 300mg tablets • 10mg/mL solution	NRTI	150 mg q12h 300mg QD	Without regard to meals
Stavudine (d4T), <i>Zerit</i> ® • 15, 20, 30, 40mg capsules • 1 mg/mL solution	NRTI	≥60kg = 40 mg q12h <60 kg = 30 mg q12h	Without regard to meals
Zalcitabine (ddC), <i>Hivid</i> ® • 0.375mg, 0.75mg tablets	NRTI	0.75 mg q8h	Without regard to meals
Zidovudine (AZT), <i>Retrovir</i> ® • 100mg capsules, 300mg tablets • 10mg/mL IV solution • 10mg/mL oral solution	NRTI	300 mg q12h	Without regard to meals
Emtricitabine (FTC) <i>Emtriva</i> ® • 200mg hard gelatin capsules	NRTI	200mg QD	Without regard to meals
Zidovudine/ Lamivudine: 300 mg / 150 mg, <i>Combivir</i> ®	NRTIs	1 Tablet q12h	Without regard to meals
Zidovudine/ Lamivudine/Abacavir 300mg/150mg/300mg, <i>Trizivir</i> ®	NRTIs	1 Tablet q12h	Without regard to meals
Lamivudine 300mg /Abacavir 600mg, <i>Epzicom</i> ®	NRTIs	1 tablet daily	Without regard to meals
Tenofovir, <i>Viread</i> ® 300mg tablet	Nucleotide RTI	300 mg QD	Without regard to meals
Tenofovir 300 mg/emtricitabine 200 mg, <i>Truvada</i> ®	Nucleotide RTI/NRTI	1 tablet daily	Without regard to meals
Delavirdine (DLV), <i>Rescriptor</i> ® • 100, 200mg tablets	NNRTI	400 mg q8h	Without regard to meals
Efavirenz (EFV), <i>Sustiva</i> ® • 50, 100, 200mg capsules • 600mg tablet	NNRTI	600 mg QHS	For tablets: avoid taking after high fat meals, levels increase 50%
Nevirapine (NVP) • 200mg tablet • 50mg/5mL oral suspension	NNRTI	200 mg QD x 14days then 200mg q12h	Without regard to meals

Amprenavir (APV), Agenerase® • 15 mg/mL oral solution (contains 42% alcohol)	PI	1400 mg q12h	High fat meal reduces AUC 21%; with or without food but avoid high fat meal. Capsules no longer available
Indinavir (IDV), <i>Crixivan</i> ® • 200, 333, 400mg capsules	PI	800 mg q8h (no longer recommended without ritonavir)	Levels decrease 77%, take 1 hour before or 2 hours after meals; drink plenty of fluids
Lopinavir/Ritonavir, <i>Kaletra</i> ® • 133.3mg/33.3 mg capsules • 200mg/50mg tablets • 80mg/20mg oral solution	PI	400mg/100mg q12 (either 3 capsules q12 or 2 tablets q12)	Take with food Distribution of capsules will end in 2006 Capsules should be refrigerated
Nelfinavir (NFV), <i>Viracept</i> ® • 250mg tablet • 625mg tablets	PI	750 mg q8h or 1250 mg q12h	Levels increase 2-3 fold, take with meal or snack
Saquinavir (SQV)-HGC, <i>Invirase</i> ® • 200mg capsules • 500mg tablets	PI	• not recommended without ritonavir • 1000mg q12h + ritonavir 100mg q12h	No food effect when taken with ritonavir Distribution of old SGC formulation (fortovase) discontinued in 2006
Fosamprenavir (fAPV) <i>Lexiva</i> ® • 700mg tablets	PI	Naïve pts: • 1400 mg q12h • 1400 mg QD + ritonavir 200mg QD • 700mg q12h + ritonavir 100mg q12h Experienced pts: • 700mg q12h + ritonavir 100mg q12h	Take without regard to meals
Atazanavir (ATZ) <i>Reyataz</i> ® • 100,150, 200mg capsules	PI	400mg QD 300mg + 100mg ritonavir	Food enhances bioavailability Take with food
Tipranavir Aptivus ® • 250mg capsules	PI	500mg + 200mg ritonavir po q12	Food enhances bioavailability. Take with food. Capsules should be refrigerated
Ritonavir (RTV) Norvir ® • 100mg capsules • 600mg/7.5mL solution	PI	Not generally used as a full dose but as a pharmacokinetic booster for other PIs from 100-400mg per day	Capsules should be refrigerated
Enfuvirtide, Fuzeon ® • 90mg vials	Fusion inhibitor	90mg SC q12	

INDICATIONS FOR ANTIRETROVIRAL AGENTS

Patients with established HIV infection are classified into one of the two clinical categories: asymptomatic infection or symptomatic disease (wasting, thrush, or unexplained fever > 2 weeks) including AIDS as defined according to 1993 CDC classification. The Department of Health and Human Services (DHHS) publishes guidelines for the use of antiretroviral agents in HIV-infected patients.² According to these guidelines, all patients with advanced HIV disease (AIDS) and symptomatic patients without AIDS should be treated with HAART, regardless of their plasma RNA levels or CD4 cell count.² Considerations for initiating antiretroviral therapy in asymptomatic patients are complex and depend upon virologic (viral load) and immunologic (CD4⁺ T cells count) factors. For asymptomatic patients with CD4⁺ T cell count 201-350 cell/mm³, treatment should usually be offered. The strength of the recommendation must be evaluated based on the readiness of the patient, consideration of the prognosis of disease-free survival (based on baseline CD4⁺ T cells count and viral load), and the benefits and risks of antiretroviral therapy. For patients with CD4⁺ T cell count exceeding 350 cells/mm³, viral load level helps predict the risk for AIDS defining complication within 3 years (see **Table #2**).² Advanced stage patients being maintained on an antiretroviral regimen should not have the HAART therapy discontinued during an acute opportunistic infection or other HIV complication, unless there are significant concerns regarding drug toxicity, intolerance, or drug interactions²

Table 2. Initiation of Antiretroviral Agents²

Clinical Category	CD4 T-Cell Count	HIV RNA Level	Recommendation
Symptomatic (AIDS, thrush, weight loss, unexplained fever)	Any Value	Any value	Treat
Asymptomatic, AIDS	CD4 ⁺ T cell < 200/mm ³	Any value	Treat
Asymptomatic	CD4 ⁺ T cell >200/mm ³ but ≤ 350/mm ³	Any value	Offer treatment
Asymptomatic	CD4 ⁺ T cell >350/mm ³	≥100,000 (RT-PCR or bDNA)	Controversial, 3-year risk for developing AIDS in untreated patients >30%; some experts recommend deferring therapy and monitoring labs more frequently; clinical outcome data after initiating therapy are lacking
Asymptomatic	CD4 ⁺ T cell >350/mm ³	<100,000(RT-PCR or bDNA)	Defer therapy & observe 3-year risk for developing AIDS in untreated pts <15%

DEVELOPING THE REGIMEN

Combination of three or more antiretroviral agents has become the standard of care, when it comes to treatment of HIV infection. These therapies achieve goals more effectively than previous one or two drug combinations. The first antiretroviral regimen used has the greatest chance of success; subsequent regimens are often more complicated and have higher failure rate.² Recently, resistance testing has been recommended prior to initiating antiretroviral therapy in acute and chronically infected patients to assist with the selection of antiretroviral agents. **Table 3** provides a guide to the use of available treatment regimens for individuals with no prior, or with limited experience to HIV therapy.²

Table 3. Recommended Antiretroviral Agents for Initial Treatment²

NNRTI-based regimen	
Preferred regimen	Efavirenz +(lamivudine or emtricitabine) +(zidovudine or tenofovir DF) – except pregnant women or women with pregnancy potential
alternatives	Efavirenz +(emtricitabine) +(abacavir or didanosine or stavudine) - except pregnant women or women with pregnancy potential Nevirapine ***+ (emtricitabine or lamivudine) + (zidovudine or stavudine* or didanosine or abacavir)
PI-based regimen	
Preferred regimen	Lopinavir/ritonavir + (lamivudine or emtricitabine) + (zidovudine or tenofovir DF)
alternatives	Fosamprenavir** + (emtricitabine or lamivudine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine) Fosamprenavir/ritonavir** + (emtricitabine or lamivudine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine) Atazanavir + (emtricitabine or lamivudine) + (zidovudine or stavudine* or abacavir) or (tenofovir + 100 mg ritonavir) Indinavir/ritonavir** + (emtricitabine or lamivudine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine) Lopinavir/ritonavir + (emtricitabine or lamivudine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine) Nelfinavir + (emtricitabine or lamivudine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine) Saquinavir (soft-gel or hard-gel) /ritonavir** + (emtricitabine or lamivudine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine)
Triple NRTI Regimen – only when the above regimens cannot or should not be used as first line therapy	
	Abacavir + lamivudine + zidovudine – Only preferred when other regimens cannot or should not be used.
	*Higher incidence of lipoatrophy, hyperlipidemia, and mitochondrial toxicities reported with stavudine than with other NRTI
	**low dose ritonavir 100-400mg
	***High incidence of hepatic events were observed in women with CD4 >250 and men with CD4 >400, so caution should not started in these patients unless risk outweighs benefit

Regimens should be individualized based on the advantages and disadvantages of each combination such as number of pills, dosing frequency, adverse effects and drug-drug interactions. Also, considerations to patient specific variables such as co-morbid conditions, pregnancy and viral load should be made prior to selecting the regimen. The preferred regimens are in bold-type and suggest optimal and durable efficacy with acceptable tolerability and ease of use. The alternative regimens are second-line due to disadvantages compared to preferred regimens in terms of antiviral activity, durability, tolerability or ease of use. In some cases, the alternative regimens may be a preferred regimen based on patient specific variables. The designation of "preferred" and "alternative" regimens may change as more data emerges on the safety and efficacy. For the most current guidelines, refer to www.aidsinfo.nih.gov/guidelines/.² It is not advised to deviate from the above regimens in treatment naïve patients such as triple class regimens (i.e. NRTI + NNRTI +PI) or NRTI-sparing regimens because there is not sufficient data. (DHHS, GRIM) There are some combinations that should be avoided due to antagonism (i.e. zidovudine and stavudine). See Table 4.

TABLE 4: Antiretroviral regimens and components that should be avoided

Monotherapy or 2 NRTIs only	<ul style="list-style-type: none"> • high risk of development of resistance • inferior to combination therapy
Abacavir + Tenofovir + lamivudine (or emtricitabine) OR Tenofovir + didanosine + lamivudine (or emtricitabine) , as a triple NRTI regimen	<ul style="list-style-type: none"> • High rate of virologic failure
Amprenavir oral solution should not be used in: <ul style="list-style-type: none"> • Pregnant women, children < 4 years old, patients with renal or hepatic failure or patients on metronidazole or disulfuram 	Oral liquid contains large amounts of the excipient propylene glycol
Amprenavir oral solution + ritonavir solution	The vehicle of amprenavir solution (propylene glycol) may compete for elimination with the vehicle of ritonavir solution (ethanol)
Atazanavir + indinavir	Additive hyperbilirunemia
Didanosine + stavudine	High incidence of toxicities (peripheral neuropathy, pancreatitis, etc)
Didanosine + zalcitabine	Additive peripheral neuropathy
Efavirenz in first trimester of pregnancy	Teratogenic in nonhuman primates
Emitricabine + lamivudine Fosamprenavir + Amprenavir oral solution	Duplication of therapy
Lamivudine + Zalcitabine	In vitro antagonism
Nevirapine initiation in women with CD4 >250 or men CD4 >400	Higher incidence of hepatic events (and death)
Saquinavir hard gel capsule	<ul style="list-style-type: none"> • Poor bioavailability • Inferior antiviral activity
Stavudine + zalcitabine	Additive peripheral neuropathy
Stavudine + zidovudine	Antagonistic effect on HIV-1

Some potential advantages to NNRTI regimens include less fat maldistribution and dyslipidemia than PI-based regimens, and reserving the PI options for future use. The disadvantages of the NNRTI class include: low genetic barrier to resistance, cross-resistance among the NNRTI class, the adverse effect of skin rash and the potential for drug-drug interactions.^{1,2}

For the PI-based regimens, the advantages include: saving the NNRTI-class for future use and the longest prospective study data, including data on survival benefit. The disadvantages include metabolic complications such as fat maldistribution, dyslipidemia and insulin resistance, and the potential for multiple drug-drug interactions. The Triple-NRTI regimen has the advantages of low pill burden (i.e. zidovudine+lamivudine+abacavir are co formulated into Trizivir®), minimal drug-drug interactions, and reserving the PI and NNRTI for future use. The disadvantages include: inferior virologic response when compared to efavirenz-based and indinavir-based regimens, and the risk of abacavir hypersensitivity (approximately 5%).²

INDICATIONS FOR CHANGING THERAPY

Therapeutic goals of HAART include maximum viral suppression, optimum immunologic response, minimum adverse effects of antiretroviral medications, and the highest adherence. Change in therapy is warranted when any of these goals are not achieved.² Common reasons for altering therapy include drug intolerance, non-adherence, emergence of resistance, or failure to achieve sustained viral suppression. Changes based on inadequate virologic response should be confirmed using at least two measurements of viral loads. Such changes should be prompted by one of the following: virologic failure (defined as a confirmed HIV RNA level >400 copies/mL after 24 weeks, >50 copies/mL after 48 weeks, or a confirmed HIV RNA level >400 after suppression of viremia), or immunologic failure (defined as a failure to increase 25-50 cells/mm³ above the baseline during the first year).² Testing for antiretroviral resistance is recommended for virologic failure during combination antiretroviral therapy, or when suboptimal suppression of viral load after antiretroviral therapy initiation, or during acute HIV infection if therapy is initiated. Changing between drugs/classes with documented cross-resistance is not recommended. Single agent substitution is only recommended in case of drug toxicity. Based on the above recommendations, the decision to change therapy must be carefully evaluated, as delaying a switch in therapy may severely limit future therapeutic options due to

selection of resistance mutations.²

ADVERSE DRUG REACTIONS

With successful viral control and immune repair in patients taking HAART, complications due to therapy have become more prevalent than opportunistic infections and malignancies.¹ Most frequent adverse effects reported with all antiretrovirals remain to be GI related including nausea, vomiting, and flatulence. Several class-related adverse events have been recognized with antiretroviral drugs during the post-marketing period. Lactic acidosis, with hepatomegaly and hepatic steatosis including fatal cases, has been reported with the use of NRTIs alone or in combination with other antiretroviral agents. Hyperglycemia/diabetes mellitus, insulin resistance, increased bleeding episodes in patients with hemophilia, and lipodystrophy with and without serum lipid abnormalities have been associated with PI use with variable frequency.² Rash and skin reactions are relatively common events encountered during use of NNRTIs. A minority of these rashes is severe; potentially fatal cases of Stevens-Johnson's syndrome have been reported. Average time of onset is 1-3 weeks. In clinical studies, severity sufficient to require discontinuation is 7% with nevirapine and 2% with efavirenz.² Abacavir can cause a hypersensitivity reaction which can be characterized by several of the following symptoms: 1. fever 2. rash 3. gastrointestinal (nausea, vomiting, diarrhea or abdominal pain) 4. constitutional (malaise, fatigue, or achiness) 5. respiratory symptoms. Abacavir should be discontinued if a hypersensitivity reaction is suspected.¹² Fosamprenavir should be used cautiously in patients with known sulfonamide allergy because it contains a sulfonamide moiety.¹³ **Tables 5-9** review the incidence of common adverse drug reactions (ADRs) with different classes of antiretroviral agents.²

Table 5. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)²

Name of Drug	Adverse Effects
Abacavir Ziagen ®	Hypersensitivity reaction: <ul style="list-style-type: none"> • symptoms: fever, rash, nausea, vomiting, malaise or fatigue, loss of appetite, or respiratory symptoms (sore throat, cough, shortness of breath)
Didanosine Videx ®	<ul style="list-style-type: none"> • Pancreatitis (cases of fatal and nonfatal cases have occurred alone or in combination with stavudine, stavudine + hydroxyurea or ribavirin) • Peripheral neuropathy • Nausea • Diarrhea • Lactic acidosis with hepatic steatosis is rare but this is a potentially life-threatening toxicity associated with NRTIs
Emtricitabine Emtriva™	<ul style="list-style-type: none"> • Minimal toxicity • Lactic acidosis with hepatic steatosis is rare but this is a potentially life-threatening toxicity associated with NRTIs
Lamivudine Epivir®	<ul style="list-style-type: none"> • Minimal toxicity • Lactic acidosis with hepatic steatosis is rare but this is a potentially life-threatening toxicity associated with NRTIs
Stavudine Zerit ®	<ul style="list-style-type: none"> • Peripheral neuropathy • Lipodystrophy • Rapidly progressive ascending neuromuscular weakness (rare) • Pancreatitis (cases of fatal and nonfatal cases have occurred alone with didanosine or in combination with stavudine, stavudine + hydroxyurea or ribavirin) • Lactic acidosis with hepatic steatosis but this is a potentially life-threatening toxicity associated with NRTIs • Hyperlipidemia
Zalcitabine Hivid ®	<ul style="list-style-type: none"> • Peripheral neuropathy • Stomatitis • Lactic acidosis with hepatic steatosis is rare but this is a potentially life-threatening toxicity associated with NRTIs • Pancreatitis
Zidovudine Retrovir ®	<ul style="list-style-type: none"> • Bone marrow suppression: anemia or neutropenia • Subjective complaints: GI intolerance, headache, insomnia, asthenia • Lactic acidosis with hepatic steatosis is rare but this is a potentially life-threatening toxicity associated with NRTIs

Table #6: Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)²

Name of Drug	Adverse Effects
Nevirapine Viramune ®	<ul style="list-style-type: none"> • Rash • Hepatitis (including hepatitis necrosis have been reported)
Delavirdine Rescriptor ®	<ul style="list-style-type: none"> • Rash • Increased transaminases • Headaches
Efavirenz Sustiva ®	<ul style="list-style-type: none"> • Rash • CNS symptoms (dizziness, somnolence, abnormal dreams, confusion, etc – subside after 2-4 weeks of therapy) • False-positive cannabinoid test • Teratogenicity in monkeys (do not use in pregnancy)

Table #7: Nucleotide Reverse Transcriptase Inhibitors²

Name of Drug	Adverse Effects
Tenofovir Viread®	<ul style="list-style-type: none"> • Asthenia, headache, diarrhea, nausea, vomiting and flatulence • Potentially, Lactic acidosis with hepatic steatosis (not reported with tenofovir) • Renal insufficiency

Table #8: Protease Inhibitors²

Name of Drug	Adverse Effects
Amprenavir Agenerase®	<ul style="list-style-type: none"> • GI intolerance: nausea, vomiting, diarrhea • Rash • Oral paresthesias • Transaminase elevation • Hyperglycemia • Fat maldistribution and lipid abnormalities • Possible increased bleeding episodes in patients with hemophilia
Atazanavir Reyataz®	<ul style="list-style-type: none"> • Increased indirect bilirubinemia (which can result in jaundice) • Prolong PR interval – some patients experienced asymptomatic 1st degree AV block • Use caution in patients with underlying defects • Hyperglycemia • Fat maldistribution • Possible increased bleeding in patients with hemophilia
Fosamprenavir Lexiva®	<ul style="list-style-type: none"> • Skin rash (19%) • Diarrhea, nausea, vomiting • Headache • Transaminase elevation • Hyperglycemia • Fat maldistribution and lipid abnormalities • Possible increased bleeding episodes in patients with hemophilia
Indinavir Crixivan®	<ul style="list-style-type: none"> • Nephrolithiasis • Collagen related • Dry skin • GI intolerance: nausea • Increased indirect bilirubinemia • Misc: headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia and hemolytic anemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding in patients with hemophilia
Lopinavir / Ritonavir Kaletra ®	<ul style="list-style-type: none"> • GI intolerance: nausea, vomiting, diarrhea • Asthenia • Elevated transaminases • Hyperglycemia • Fat maldistribution • Possible increased bleeding in patients with hemophilia • Oral solution contains 42% alcohol
Nelfinavir Viracept®	<ul style="list-style-type: none"> • Diarrhea • Hyperglycemia • Fat maldistribution and lipid abnormalities • Possible increased bleeding in patients with hemophilia • Elevated transaminases
Ritonavir Norvir ® (full dose)	<ul style="list-style-type: none"> • GI intolerance: nausea, vomiting, diarrhea • Paresthesias • Hepatitis • Pancreatitis • Asthenia • Taste perversion • Hyperglycemia • Fat maldistribution • Possible increased bleeding in patients with hemophilia • Hypertriglyceridemia
Saquinavir HGC Invirase ®	<ul style="list-style-type: none"> • GI intolerance: nausea and diarrhea • Headache • Elevated transaminases • Hyperglycemia • Fat maldistribution and lipid abnormalities • Possible increased bleeding in patients with hemophilia
Tipranavir Aptivus ®	<ul style="list-style-type: none"> • Hepatotoxicity • Skin rash • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Increased bleeding in patients with hemophilia

Table 9. Fusion Inhibitor²

Name of Drug	Adverse Effects
Enfuvirtide Fuzeon ®	<ul style="list-style-type: none"> Local injection site reactions (pain, erythema, induration, nodules and cysts, pruritis, ecchymosis) Increased rate of bacterial pneumonia Hypersensitivity reaction (<1%)

DRUG INTERACTIONS

Antiretroviral therapy has become increasingly more complex due to the propensity for drug-drug interactions with these medications. Drug(s) affecting plasma concentrations of concurrent medication(s) may result in reduced efficacy or increased toxicity. Most interactions with antiretroviral agents revolve around the hepatic enzyme system, cytochrome P450 (CYP450). NRTIs, including nucleotide RTIs, do not undergo extensive CYP450 metabolism. They are eliminated predominantly through renal mechanisms. Therefore, drug interactions are less common with these two classes. Nonetheless, there are a few clinically significant drug interactions involving the NRTIs.^{1,2} Zidovudine and stavudine appear to compete for phosphorylation; therefore, they are not recommended in combination with each other.² Tenofovir has multiple drug-drug interactions in which the mechanism is unknown. When tenofovir is combined with didanosine, there is an increased risk of pancreatitis, due to increase in the AUC of didanosine. Therefore, the dose of didanosine should be decreased to 250mg (in a patient >60kg).⁶ When atazanavir and tenofovir are combined, atazanavir levels are decreased so atazanavir must be combined with low dose ritonavir to boost the levels of atazanavir.^{6,14} Unlike NRTIs, protease inhibitors are extensively metabolized by CYP450. All protease inhibitors are competitive inhibitors of cytochrome P-450, predominantly the CYP3A4 isoform. PIs increase plasma drug levels of concurrent medications metabolized by this enzyme system.^{1,2} Of the protease inhibitors, ritonavir is the most potent enzyme inhibitor; saquinavir is the least potent inhibitor; while indinavir, nelfinavir, atazanavir, amprenavir (fosamprenavir) and lopinavir fall in between those two.¹ In fact, ritonavir has been utilized extensively with other PIs to increase blood levels of the concurrent agent.^{1,2} Tipranavir can induce and inhibit CYP450 resulting in a complex drug-drug interaction profile.⁹ Drugs that should not be used in combination with PIs include simvastatin, lovastatin, cisapride, rifampin, midazolam, triazolam, astemizole, terfenadine, dihydroergotamine (DHE) & other ergotamines, and St. John's wort. Furthermore, concurrent use of amiodarone, flecainide, propafenone, quinidine, bepridil, meperidine, rifabutin, diazepam, and bupropion should be avoided with ritonavir.²

Like protease inhibitors, NNRTIs are associated with several significant drug interactions.^{1,2} The NNRTIs have complex metabolic pathways. Delavirdine inhibits, while nevirapine induces, CYP450 (3A4 and 2D6 isoforms). Efavirenz both induces and inhibits CYP450 (3A4 and 2D6 isoforms) lending to multiple drug-drug interactions. Nevirapine and efavirenz both induce their own metabolism, while delavirdine may inhibit its own metabolism.² Due to their effects on CYP450, NNRTIs have potential to alter plasma concentrations of concurrent drugs metabolized by some isoforms of CYP450. Drugs that should not be used with efavirenz include astemizole, terfenadine, cisapride, midazolam, triazolam, DHE & other ergotamine derivatives.² **Tables #10 a-b** review contraindicated drug-drug interactions with specific antiretrovirals.² In addition to the drugs to avoid with these agents, there are many other clinically significant drug-drug interactions that require careful evaluation and monitoring by the pharmacist to avoid adverse drug reactions or inadequate drug concentrations. Some examples include: methadone, oral contraceptives, erectile dysfunction agents like sildenafil, and antifungals like fluconazole and itraconazole. In addition, several over the counter acid suppressant agents (such as ranitidine, omeprazole, etc) can decrease concentrations of atazanavir resulting in subtherapeutic concentrations.¹³ In short, with the knowledge of current nomenclature of drug interactions with the CYP450 system, clinicians should be able to predict most of these interactions. For specific details regarding other potentially significant drug-drug interactions, consult www.aidsinfo.nih.gov/guidelines or other pertinent references.

Table 10a: Drugs that should NOT be used with Protease Inhibitors²

Indinavir	<ul style="list-style-type: none"> simvastatin, lovastatin rifampin, rifapentine astemizole terfenadine cisapride pimozide midazolam triazolam dihydroergotamine, ergotamines (and other forms), ergonovine, methylergonovine, St. John's wort (herbal) Atazanavir
Ritonavir	<ul style="list-style-type: none"> bepridil amiodarone, flecainide propafenone, quinidine simvastatin, lovastatin

	<ul style="list-style-type: none"> • rifapentine • astemizole , terfenadine • cisapride • pimozide • midazolam, triazolam • dihydroergotamine (D.H.E. 45) ergotamine† (various forms) ergonovine methylergonovine • St. John's wort • Fluticasone (inhaled and nasal formulations) • Voriconazole (with ritonavir > 400 mg bid)
Saquinavir	<ul style="list-style-type: none"> • simvastatin, lovastatin • rifampin, rifabutin, rifapentine (not contraindicated if saquinavir is combined with ritonavir) • astemizole , terfenadine • cisapride • pimozide • midazolam (single use okay), triazolam • dihydroergotamine (D.H.E. 45) ergotamine (various forms) ergonovine methylergonovine • St. John's wort • Garlic supplements
Nelfinavir	<ul style="list-style-type: none"> • simvastatin, lovastatin • rifampin, rifapentine
	<ul style="list-style-type: none"> • astemizole , terfenadine • cisapride • pimozide • midazolam, triazolam • dihydroergotamine (D.H.E. 45) ergotamine (various forms) ergonovine methylergonovine • St. John's wort
Amprenavir/Fosamprenavir	<ul style="list-style-type: none"> • Bepridil • simvastatin ,lovastatin • rifampin, rifapentine • astemizole , terfenadine • cisapride • pimozide • midazolam, triazolam • dihydroergotamine (D.H.E. 45) ergotamine (various forms) ergonovine methylergonovine • St. John's wort • Delavirdine
Lopinavir/ritonavir	<ul style="list-style-type: none"> • Flecainide, propafenone • simvastatin ,lovastatin • rifapentine, rifampin • astemizole , terfenadine • cisapride • pimozide • midazolam, triazolam • dihydroergotamine (D.H.E. 45) ergotamine (various forms) ergonovine methylergonovine • St. John's wort • Fluticasone (inhaled and nasal formulations)
Atazanavir	<ul style="list-style-type: none"> • Bepridil • simvastatin ,lovastatin • rifampin, rifapentine • astemizole , terfenadine • cisapride, proton pump inhibitors • pimozide • midazolam, triazolam • dihydroergotamine (D.H.E. 45) ergotamine (various forms) ergonovine methylergonovine • St. John's wort • Indinavir • Ironotecan
Tipranavir	<ul style="list-style-type: none"> • Bepridil • Flecainide, propafenone, amiodarone, quinidine • simvastatin ,lovastatin • rifapentine, rifampin • astemizole , terfenadine • cisapride • pimozide • midazolam, triazolam • dihydroergotamine (D.H.E. 45) ergotamine (various forms) ergonovine methylergonovine • St. John's wort • Fluticasone

Table 10b: Drugs that should NOT be used with NNRTI²

Nevirapine	<ul style="list-style-type: none"> • Rifampin, rifapentine • St. John's wort
Delavirdine	<ul style="list-style-type: none"> • simvastatin, lovastatin • rifampin, rifabutin, rifapentine • astemizole , terfenadine • cisapride, H2 blockers, proton pump inhibitors • midazolam, triazolam, alprazolam • dihydroergotamine (D.H.E. 45) ergotamine† (various forms) ergonovine methylergonovine • St. John's wort • fosamprenavir/amprenavir • carbamazepine, Phenobarbital, phenytoin
Efavirenz	<ul style="list-style-type: none"> • rifapentine • astemizole , terfenadine • cisapride • midazolam, triazolam • dihydroergotamine (D.H.E. 45) ergotamine† (various forms) ergonovine methylergonovine • St. John's wort • Voriconazole

TREATMENT DURING PREGNANCY

Treatment guidelines during pregnancy have also been developed for HIV-infected pregnant women and prevention of vertical transmission.¹⁵ If these women satisfy criteria for therapy, DHHS guidelines should be followed for treatment like any other HIV infected patient. Pregnant women should be offered the standard combination antiretroviral therapy to prevent perinatal transmission. The most significant data on prevention for perinatal transmission comes from the Pediatric AIDS Clinical Trial Group Protocol 076 (PACTG 076). This pivotal trial demonstrated that AZT reduced the rate of perinatal transmission by 66%.¹⁵ As per AZT 076 protocol, zidovudine chemoprophylaxis is a three part regimen consisting of maternal AZT therapy from week 14 to delivery, followed by intrapartum IV AZT administration, which is then followed by 6 weeks of AZT for the newborn. When combination therapy is administered to pregnant women, zidovudine should be included in the regimen unless substantial zidovudine-related toxicities occur. Due to the risk of lactic acidosis, stavudine and didanosine should not be used in combination in pregnant women.^{2,15}

Not much is known about the use of antiretroviral agent in pregnant women and their effect on the developing fetus. The data, to date, supports the safety of antiretroviral agents in pregnancy except for ddI + d4T, efavirenz, and hydroxyurea.¹⁵ The pregnant HIV-infected women should be extensively counseled on the risks and benefits of antiretroviral therapy for the mother and the newborn infant. Some authorities recommend HAART therapy be delayed or interrupted during the first trimester, as safety of these agents is sometimes questioned during this, the most vulnerable, part of the pregnancy. This involves a risk-benefit decision, and recommendations should be based on theoretical concerns as well as on clinical findings (CD4⁺ T cell count, viral load, symptoms, etc.).^{2,14} Nevirapine is another antiretroviral agent with proven efficacy in preventing vertical transmission, given as a single dose to the mother during labor and as a single dose to the infant 24-72 hours after delivery but high rates of resistance have been found in postpartum period and therefore is not currently recommended.¹⁴ Women with CD4⁺ T cell counts > 250 cells/mm³, including pregnant women receiving chronic nevirapine are at risk for fatal hepatotoxicity (i.e. cholestatic hepatitis, hepatic necrosis and hepatic failure.) Patients with signs or symptoms of hepatitis and associated symptoms (i.e rash) must discontinue nevirapine and seek medical attention.¹⁵

CONCLUSION

Treatment of HIV is complex requiring a full understanding of both the disease state and the medications associated. Pharmacists can play an important role in HIV treatment by assessing adherence to treatment regimens, educating patients about drug toxicity and educating clinicians to avoid interacting drugs.

REFERENCES

1. Jain R, Clark NM, Diaz-Linares M, Grim S. Limitations of Current Antiretroviral Agents and Opportunities for Development, *Curr Pharm Des* 2006, Volume 12: Issue 36
2. Department of Health and Human Services, Guidelines for Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents; May 4th, 2006.
3. Fischl M. Zidovudine. In *AIDS Therapy*. 2nd Edition. Dolin R, Masur H, Saag MS ed. Churchill Livingstone. 2003; 23-38
4. Emtriva® package insert. Gilead Sciences; 2003 Jul.
5. Press Release. Bristol-Myers Squibb And Gilead Sciences Submit New Drug Application To U.S. FDA For A Once-Daily Single Tablet Regimen Of Sustiva® (efavirenz) And Truvada® (emtricitabine and tenofovir disoproxil fumarate) For HIV Treatment. April 27th, 2006 Found at: <http://www.bms.com/news/data/index.html>
6. Viread® package insert. Gilead Sciences; 2006 Mar.
7. Montaner JSG, Lange JMA. Nevirapine. In *AIDS Therapy*. 2nd Edition. Dolin R, Masur H, Saag MS ed. Churchill Livingstone. 2003; 134-144.
8. Collier AC, Squires KE. Saquinavir. In *AIDS Therapy*. 2nd Edition. Dolin R, Masur H, Saag MS ed. Churchill Livingstone. 2003; 157-173.
9. Aptivus® package insert. Boeringher Ingleheim; 2006 Mar
10. Fuzeon® package insert. Roche Pharmaceuticals; 2003 Mar.
11. Hanson K, Hicks C. New antiretroviral drugs. *Current HIV/AIDS Rep*. May 2006; 3(2): 93-101.
12. Ziagen® package insert. GlaxoSmithKline; 2006 Mar.
13. Lexiva® package insert. GlaxoSmithKline; 2003 Oct.
14. Reyataz® package insert. Bristol-Myers Squibb Co; 2003 Jun.
15. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States; November 17th, 2005

THIS CONCLUDES THE 2 – PART DISCUSSION OF HIV/AIDS.

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Please fill-out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

Describe the indications for initiating antiretroviral therapy	Yes	No		
Differentiate between the classes of antiretroviral agents	Yes	No		
List currently approved antiretrovirals, describe pharmacology, recognize major adverse effects or toxicities, & identify drug interactions		Yes	No	
List preferred 1 st line & alternative combination therapies for HIV	Yes	No		
Discuss antiretroviral therapy in pregnancy to prevent transmission		Yes	No	

2. Was the program independent & non-commercial?

	Yes	No		
			Excellent	

3. Relevance of topic to your practice

	Poor		Average					
	1	2	3	4	5	6	7	

4. What did you like most about this lesson? _____

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(WATCH OUR WEBSITE FOR RESULTS OF PARTICIPANT EVALUATIONS)

Quiz—Please Select the Most Correct Answer

- | | |
|--|---|
| <ol style="list-style-type: none"> 1. Which of the following is a common reason for lack of adherence? <ol style="list-style-type: none"> A. Racial background B. Simplicity of the regimen C. Medication toxicities D. Drug resistance 2. Low dose ritonavir is clinically used to help boost the pharmacokinetic levels of: <ol style="list-style-type: none"> A. Enfuvirtide B. Protease inhibitors C. NRTIs D. Didanosine 3. Advantages of treatment initiation with a NNRTI-containing regimen, include: <ol style="list-style-type: none"> A. High genetic barrier to resistance B. Low incidence of cross resistance between NNRTIs C. Lower incidence of fat maldistribution D. High incidence of insulin resistance 4. Which of these should be administered on an empty stomach? <ol style="list-style-type: none"> A. Abacavir B. Ritonavir C. Atazanavir D. Didanosine 5. Treatment guidelines suggest that antiretroviral therapy should be offered to individuals with symptomatic diseases of CD4 & HIV RNA levels. <ol style="list-style-type: none"> A. True B. False | <ol style="list-style-type: none"> 6. Atazanavir should not be used in combination with: <ol style="list-style-type: none"> A. Indinavir B. Proton pump inhibitors C. Simvastatin D. All of these 7. The following is true for enfuvirtide. <ol style="list-style-type: none"> A. Administered subcutaneously B. Most common side effect is diarrhea C. Has a half-life requiring only weekly administration D. Should not be used in combination with rifampin 8. Therapeutic goals of HAART include: <ol style="list-style-type: none"> A. Maximum viral suppression B. Minimum adverse effects C. Highest degree of adherence D. All of these 9. Lactic acidosis with hepatic steatosis is an adverse event associated with the use of: <ol style="list-style-type: none"> A. Protease inhibitors B. NNRTIs C. Fusion inhibitors D. NRTIs 10. If combination therapy is administered to pregnant women, when possible, zidovudine should be included in the regimen. <ol style="list-style-type: none"> A. True B. False |
|--|---|

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