Management of HIV

Federal Bureau of Prisons

Clinical Practice Guidelines

June 2011

What's New in This Document?

The following changes have been made since the June 2006 version of these guidelines. Where appropriate, they are highlighted in yellow in the document.

General

- Tables of antiretroviral drugs are no longer included in these guidelines because they rapidly become outdated. Clinicians should routinely review updated Department of Health and Human Services (DHHS) guidelines at http://www.aidsinfo.nih.gov/guidelines/.
- Guidelines for post-exposure prophylaxis are compiled in a separate BOP clinical practice guideline. See *Medical Management of Exposures: HIV, HBV, HCV, Human Bites and Sexual Assaults* at http://www.bop.gov/news/medresources.jsp.

Nomenclature

- *Pneumocystis jiroveci* (pronounced "yee row vet zee") is the correct name for what was previously *Pneumocystis carinii.* PCP remains an appropriate abbreviation for pneumocystis pneumonia.

Treatment

- Treatment information was updated to be in line with the January 10, 2011 DHHS *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.*
- A section was added on Management of the Treatment-Experienced Patient.
- The immunization recommendations have been updated.

New Appendices

- A new appendix has been inserted: *Appendix 7, DHHS Antiretroviral Guidelines: Rating Scheme and Acronyms.*
- The procedure to follow when doing Pap smears is now outlined in *Appendix 11* for easy access.

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Tables

Appendices

1. Purpose and Overview

The BOP *Clinical Practice Guidelines for the Management of HIV Infection* provide guidance on the screening, evaluation, and treatment of federal inmates with HIV infection, with a focus on primary care. The BOP clinical practice guidelines are not intended to replace the more extensive guidelines published by the United States Public Health Services (USPHS), the Department of Health and Human Services (DHHS), the Centers for Disease Control and Prevention (CDC), the Infectious Disease Society of America (IDSA), and the International AIDS Society (IAS). See *Appendix 1*, *Guidelines Regarding Medical Care of HIV-Infected Persons*, for a list of these guidelines and the links for internet access. The *DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents* are updated regularly and should be consulted at: http://www.aidsinfo.nih.gov/guidelines/.

2. Diagnosis and Reporting

Indications for Testing for HIV

- **Voluntary testing** is done when the inmate requests testing via an Inmate Request to Staff Member (BP-S148) form, which will be turned into Health Services.
- **Mandatory testing** is performed when there are indications/risk factors and the test is clinically indicated and/or surveillance testing is required. Inmates must participate in mandatory HIV testing programs.
- **Involuntary testing** is performed following an exposure incident. Written consent of the inmate *is not* required. If an inmate refuses testing, testing will be conducted in accordance with the Program Statement on Use of Force.

Indications for HIV testing are described in detail in *Appendix 2*, *Criteria for Testing for HIV Infection*, and summarized in Table 1 below.

Table 1. Summary of Criteria for HIV testing

Criteria for HIV testing regardless of sentencing or duration of stay:

- Signs or symptoms of acute HIV infection
- Signs or symptoms of HIV-related condition
- Pregnancy
- Recent HIV exposure
- Active tuberculosis
- Or when otherwise clinically indicated

(Table 1 continues on next page.)

Table 1. Summary of Criteria for HIV testing *(continued)*

Criteria for mandatory HIV testing for sentenced (6 months or greater) inmates with the following risk factors:

- Injected illegal drugs and shared equipment
- (For males) sex with another man
- Unprotected intercourse with more than one sex partner
- History of gonorrhea or syphilis
- From a high-risk country (sub-Saharan Africa or West Africa)
- Received blood products between 1977 and 1985
- Hemophilia
- Percutaneuous exposure to blood
- Positive tuberculin skin test

Voluntary HIV testing for all sentenced inmates:

Many persons with HIV infection are asymptomatic and are unaware of their infection; therefore, consistent with guidelines from the Centers for Disease Control and Prevention and the issued memorandum from the BOP Medical Director, all sentenced inmates should universally be offered HIV testing at the time of incarceration.

Indications for Testing for HIV-2

Any asymptomatic, sentenced inmates who meet the criteria listed below in Table 2 should *also* be tested for HIV-2 infection through BOP reference laboratories.

Table 2. Criteria for Testing for HIV-2

- All inmates from West Africa where HIV-2 is endemic such as the countries of Benin, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone, Togo, Ghana, Burkina Faso, Gambia, and Côte d'Ivoire.
- Inmates who are or have been sex partners or needle-sharing partners of persons from West Africa or any person known to have HIV-2 infection.
- Inmates who have received transfusions in West Africa.

HIV Prevention Counseling

All inmates tested for HIV infection should receive counseling from qualified health care personnel in accordance with BOP policy, using the appropriate forms for HIV counseling and documentation. Counseling should provide information on HIV transmission, methods for preventing the spread of the virus while in prison and upon release to the community, the importance of obtaining test results, how to get the test results, and the meaning of the HIV test results. HIV prevention counseling should incorporate effective elements recommended by the CDC that include, but are not limited to: using open-ended questioning; carefully assessing

personal risk, based on self-reported behaviors and the inmate's medical evaluation; clarifying critical misconceptions; emphasizing risk reduction behaviors; and using clear and direct language when providing test results.

Antibody Testing and Interpretation of Results

Only FDA-approved HIV tests should be used for diagnostic purposes. The diagnosis of HIV infection is ordinarily determined by a screening immunoassay (EIA) or rapid HIV test followed by a confirmatory Western Blot (WB). Results of HIV WB are generally interpreted as outlined in Table 3 below. WB testing should always be coupled with EIA screening due to a 2% rate of false positives.

Table 3. Interpretation of Western Blot Results	
Negative	Nonreactive (no bands on Western blot)
Positive	Reactivity to: gp120/160 + either gp41 or p24
Indeterminate	Presence of any band patterns not meeting criteria for a positive result

False negative, false positive, and indeterminate results are uncommon. Reasons for such results are outlined in Table 4 below.

Table 4. Reasons for False Negative, False Positive, and Indeterminate HIV Test Results	
Reasons for False Negative Results	
Recent acute HIV infection	During the "window" period (i.e., the time between new infection and the development of HIV antibodies), HIV EIA tests may be negative. Some do not convert for 3 to 4 weeks. Nearly all infected persons develop HIV antibodies within 6 months of infection.
Seroreversion	Persons with documented HIV infection can lose HIV antibodies with late-stage disease (AIDS) or with immune reconstitution by effective antiretroviral therapy.
Agammaglobulinemia	Low antibodies (confirm with HIV viral load).
HIV O and HIV N	Standard EIA may be falsely negative in persons infected with HIV O subtype or HIV N subtype. O and N subtypes are extremely rare variants of HIV-1.
HIV-2	HIV-2 infection occurs primarily in West Africa. Standard HIV EIA tests are falsely negative in 20–30% of persons infected with HIV-2. Specific antibody tests for HIV-2 are available through the CDC via BOP reference laboratories.
(Table 4 continues on next page.)	

Table 4. Reasons for False Negative, False Positive, and Indeterminate HIV Test Results *(continued)*

Reasons for False Positive Results	
• **Autoantibodies** (extremely rare) • **Investigational HIV vaccines** • **Clerical error**	
Reasons for Indeterminate Results (see also discussion that follows table)	
Recent HIV infection	HIV antibodies differentially become detectable within weeks after infection. Anti-p24 is usually the first antibody to appear.
Atypical HIV strains	Infection with unusual strains of HIV such as HIV-2 infection, or HIV-1 subtypes O or N, may not produce typical diagnostic bands on Western blot analysis.
Cross reactive antibodies	Autoimmune diseases, certain malignancies, injection drug use, HIV vaccination, and recent immunization may yield antibodies that are detectable on HIV Western blot analysis.
Advanced HIV infection	Loss of HIV antibodies because of AIDS itself may affect Western blot analysis.

Adapted from: Bartlett JG, Gallant JE. *Medical Management of HIV infection*. 2009-2010 ed. Baltimore: Johns Hopkins University; 2009.

Inmates with indeterminate HIV test results should be referred to a physician for further evaluation as follows:

- **Physician interview** for HIV infection risk factors, symptoms of HIV infection and AIDS, and causes of indeterminate HIV test results.
- **Physician evaluation** of the inmate for conditions that may result in an indeterminate test result, when clinically indicated by the inmate's history and examination.
- **Repeat HIV testing:** Indeterminate results can usually be evaluated through risk assessment and viral load measurement. Patients evaluated as low-risk are seldom infected with HIV and may continue to show indeterminate results. These patients should be reassured that HIV infection is unlikely and should receive follow-up serology, to include viral load, at 3 months. Patients with risk factors, who are in the process of seroconversion, will usually have positive WBs within 1 month, as well as high viral loads. These patients should have repeat serology, to include viral load, in 1–2 months. Viral detection methods may be used as an adjunctive diagnostic tool, but should not supplant antibody testing.

Acute HIV Infection

Acute HIV Infection should be suspected in patients experiencing typical symptoms accompanied by high-risk exposure within the past 4 weeks. This diagnosis is supported by a high viral load (>10,000) accompanied by a negative or indeterminate serology. These patients should be counseled concerning the substantial risk of transmission during the acute phase of infection.

Reporting

All inmates diagnosed with HIV infection should be reported to state health authorities in accordance with state laws and regulations.

3. Natural History of HIV Infection

Acute HIV infection leads to marked HIV viremia, with a rapid decline in CD4+ T cells that is usually associated with significant symptomatology—most commonly fever, rash, lymphadenopathy, and fatigue. Acute HIV infection is frequently unsuspected by the evaluating clinician, since signs and symptoms are relatively nonspecific and may not be reported by the patient. Less common manifestations of acute HIV infection include thrush, mucocutaneous ulcerations of the mouth and esophagus, diarrhea, aseptic meningitis, facial palsy, Guillain-Barre syndrome, and cognitive impairment.

The avid immune response following acute HIV infection is associated with HIV antibody development, an increase in CD4+ T cells, and a reduction in HIV viremia with the establishment of a viral load set point. Over time, the CD4+ T cell count gradually declines in persons chronically infected with HIV, whereas HIV RNA levels gradually increase.

In the absence of antiretroviral therapy, the average time from acute HIV infection to symptomatic HIV infection or AIDS is 8 years. AIDS is associated with marked immuno-suppression with a CD4+ T cell count <200 cells/mm^3, the development of opportunistic infections, neurologic complications, certain malignancies, and wasting syndrome. *Appendix 3* lists complications associated with declining CD4+ T cell counts.

Antiretroviral therapy markedly prolongs life and prevents the development of AIDS. Although antiretroviral therapy can suppress plasma HIV RNA to undetectable levels for years, treatment is not curative since reservoirs of HIV persist, particularly in latent CD4+ T cells. HIV-2 infection causes a cell-mediated immunodeficiency similar to HIV-1 infection; however, CD4+ T cells decline more slowly.

4. Baseline Medical Evaluation

The baseline medical evaluation that is indicated for inmates diagnosed with HIV infection ordinarily includes the following components, which are summarized in *Appendix 4*.

History and Physical Examination

Medical history: Obtain a comprehensive medical history, along with an assessment and documentation of HIV risk factors. The history should include the date when HIV infection was diagnosed and, when possible, the estimated date of infection (based on the history of prior negative results, the history of symptoms of acute retroviral infection, or the inmate's recollection of high-risk activities). History of prior HIV-related complications should be ascertained,

including opportunistic infections, malignancies, and HIV-related symptoms. If possible, prior medical records should be obtained.

Medication history: A thorough medication history is critical for patients with prior history of antiretroviral therapy; it should include regimens prescribed, response to each regimen, drug toxicities, adherence, and prior resistance test results.

Complete physical examination: The examination should include a fundoscopic examination for retinopathy, an oropharyngeal exam for thrush, a careful skin exam for dermatologic conditions, an abdominal exam for hepatosplenomegaly, an assessment of neurologic deficits, and a pelvic examination and Pap smear for women. The incidence of cervical pathology is 10 to 11-fold greater in HIV-infected women than in HIV-uninfected women.

Pap smears: Obtain Pap smears in accordance with the procedure outlined in *Appendix 11*. Pap smear results should be interpreted in accordance with established guidelines[1] as follows:

- Inmates with evidence of severe inflammation should be evaluated for infection and receive a repeat Pap smear in 3 months.
- Inmates with Pap smears with cellular atypia or atypical squamous cells of uncertain significance (ASCUS) should have follow-up Pap smears without colposcopy every 6 months for 2 years, until three Pap smears in a row are negative. If atypia is noted a second time, the inmate should be referred for colposcopy. HPV testing can also be performed in patients with ASCUS to identify HPV types 16, 18, 31, 33, or 35 that predispose to cervical cancer and warrant colposcopy.
- Inmates with Pap smears with low-grade cervical intraepithelial neoplasia (CIN I) require careful follow-up with repeat Pap smears every 6 months and referral for colposcopy if any repeat Pap smear is abnormal.
- Inmates with high-grade cervical intraepithelial neoplasia (CIN II or III), also termed carcinoma in situ, require colposcopy for potential biopsy and follow-up monitoring.
- Inmates with invasive carcinoma require immediate referral to a specialist for evaluation and treatment.

Laboratory Tests

The following laboratory tests, performed during the initial patient visit, are used to stage HIV disease and assist in the selection of antiretroviral drug regimens:

- HIV antibody testing (if prior documentation is not available or if HIV RNA is below the assay's limit of detection).
- CD4 T-cell count.
- Plasma HIV RNA (viral load).

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[1] CDC. Sexually Transmitted Diseases Treatment Guidelines, 2010. *MMWR* 2010;59(RR-12):74–76). Available at: http://www.cdc.gov/std/treatment/

- Complete blood count, chemistry profile, transaminase levels, blood urea nitrogen (BUN) and creatinine, urinalysis, and serologies for hepatitis A, B, and C viruses.
- Fasting blood glucose and serum lipids.
- Genotypic resistance testing at entry into care, regardless of whether antiretroviral therapy (ART) will be initiated immediately. For patients who have HIV RNA levels <500–1,000 copies/mL, amplification of virus for resistance testing may not always be successful.

Additional tests, including, screening tests for sexually transmitted infections and tests for determining risk for opportunistic infections and need for prophylaxis, should also be performed. Complete lists of recommended laboratories studies are included in Table 5 below. See also *Appendix 4, Baseline and Periodic Medical/Laboratory Evaluations for Inmates with HIV Infection*.

Table 5. Recommended Laboratory Studies for Patients Presenting with HIV Infection

Test	Comment(s)
HIV-disease tests • Serologic testing for HIV • CD4 cell count and percentage • Plasma HIV RNA level (viral load) • Coreceptor tropism assay . . . . . . • HIV resistance testing . . . . . . • HLA B*5701	 Recommended prior to prescribing a CCR5 entry inhibitor Genotype determination is preferred in antiretroviral-naïve patients Recommend prior to prescribing abacavir
Safety laboratory tests • Complete blood cell count with differential • Fasting lipid profile • Glucose-6-phosphate dehydrogenase . . . . . • Serum chemistry • Alanine aminotransferase, aspartate aminotransferase, bilirubin levels • Albumin level • Alkaline phosphatase level • Electrolytes, blood urea nitrogen, creatinine levels • Fasting blood glucose level • Urinalysis: RBC, WBC, proteinuria, sediment levels	 Screen for deficiency in appropriate racial or ethnic groups
Co-infection and co-morbidity laboratory tests (tuberculosis)	All HIV-infected patients should be tested for *M. tuberculosis* infection by TST upon initiation of care. For an HIV-infected person, induration of >5 mm is considered to be a positive result and should prompt chest radiography and other evaluation, as warranted, to rule out active tuberculosis.
Chest radiography	For patients with positive tuberculosis test result; consider in patients with underlying lung disease for use as comparison in evaluation of future respiratory illness.

(Table 5 continues on next page.)

Table 5. Recommended Laboratory Studies for Patients Presenting with HIV Infection *(continued)*	
Cytology: Pap test	Cytology: Pap test cervical.
Screening for syphilis (VDRL, RPR)	Confirm positives with FTA-ABS, MHA-TP, TPPA.
Screening for other STDs	Gonorrhea/*C. trachomatis* in sexually active patients.
Serologic testing for *Toxoplasma gondii*	All HIV-infected patients should be tested for prior exposure *to T. gondii* by measuring anti-*Toxoplasma* immunoglobulin (Ig) G upon initiation of care.
Viral hepatitis screening	Hepatitis B surface antigen, antibody to hepatitis B surface antigen or to hepatitis B core antigen, antibody to hepatitis C virus, total hepatitis A antibody.
Note: *RBC = red blood cell; STD = sexually transmitted disease; WBC = white blood cell.*	

Immunization Status

Recommended for All HIV Positive Adults

- **Hepatitis B vaccine:** Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low.
- **Influenza vaccine:** Must be given every year. Only injectable flu vaccine should be given to those who are HIV positive. *The nasal spray vaccine (FluMist/LAIV) should not be used in this population.*
- **Pneumococcal vaccine:** Should be given soon after HIV diagnosis, unless vaccinated within the previous 5 years. If CD4 count is <200 cells/mm^3 when the vaccine is given, immunization should be repeated when CD4 count is >200 cells/mm^3. Repeat one time after 5 years.
- **Tetanus and Diphtheria Toxoid (Td):** Repeat every 10 years.
- **Tetanus, Diphtheria, and Pertussis (Tdap):** Recommended for adults 64 years of age or younger and should be given in place of next Td booster.

Recommended for Some HIV Positive Adults

- **Refer to AIDSinfo:** http://www.aidsinfo.nih.gov/contentfiles/Recommended_Immunizations_FS_en.pdf.

Referrals and Treatment Plan

All inmates receiving a baseline evaluation for HIV infection should have a treatment plan that is developed by the evaluating clinician and approved by a physician. Subspecialty referrals should be initiated as medically necessary and should include:

- **Referral for examination by a dentist** for all HIV-infected inmates.
- **Psychology referral, if clinically indicated** (in addition to the mandatory referral made as part of post-test counseling, in accordance with BOP policy).

5. Classification of HIV Infection

All inmates diagnosed with HIV infection should be classified in accordance with the CDC classification system as outlined in *Appendix 5*. HIV risk factors and classification should be documented appropriately. An inmate's reclassification, and updated documentation of the reclassification, are indicated only when the inmate progresses to a more advanced stage of HIV infection, not during each evaluation or with clinical improvement.

6. Periodic Medical Evaluations

Periodic medical evaluations of inmates with HIV infection should include patient history, a physical examination, immunological monitoring, and laboratory and diagnostic studies—all briefly described below.

History and Physical Examination/Laboratory Monitoring

The frequency of the clinician's physical examinations of an inmate with HIV infection should be based on the inmate's immune status and other relevant clinical factors, as determined by the inmate's physician. Medically complex inmates and inmates with AIDS should be followed closely by a physician. General guidelines regarding periodic medical evaluations are provided in *Appendix 4*. Patient interviews and physical examinations should target the diagnosis of complications of HIV infection, consistent with the inmate's stage of disease (see *Appendix 3*).

Immunologic/Virologic Monitoring

The inmate's immunologic/virologic status should be monitored by the measurement of CD4+ T cell counts and plasma HIV RNA levels respectively, using FDA-approved testing methods. General guidelines for routine CD4+ T cell counts and HIV plasma RNA testing are provided in *Appendix 4*; frequency of testing should be determined on an individual basis. The indications and frequency of other laboratory monitoring depend on the inmate's antiretroviral treatment regimen and prophylactic regimen for opportunistic infections.

Laboratory and Diagnostic Studies

The following additional studies should be considered during periodic evaluations of inmates with HIV infection:

- **Tuberculin skin tests (TST):** Annual TSTs are indicated for *all inmates with prior TST measurements of <5 millimeters in duration*. Inmates with HIV infection and a tuberculin skin test of 5 millimeters or greater are candidates for treatment of latent TB infection, presuming the evaluation for active TB disease is negative.
- **Periodic chest radiographs:** Periodic CXRs are required *only for inmates with both HIV and latent TB coinfection who do not complete treatment of latent TB infection*. In these cases, CXRs should be obtained semiannually for two years, and then continued semiannually only if the CD4+ T-cell count remains below 200/mm^3.

- **Glucose-6-phosphate dehydrogenase (G-6-PD) testing:** Baseline G-6-PD testing is not routinely recommended for inmates with HIV infection. Prior to initiating a potentially offending agent, G-6-PD testing should be initiated on a case-by-case basis (considering both the patient's risk for hemolytic anemia and the potential for serious complications from anemia). G-6-PD deficient inmates are susceptible to hemolytic anemia when exposed to oxidant drugs such as dapsone, primaquine, and, less commonly, sulfonamides. African Americans and persons from Mediterranean countries, India, and Southeast Asia are most susceptible. Hemolysis is usually self-limited, involving only the older red blood cells. A small subset of Mediterraneans have a genetic variant that causes severe hemolysis when exposed to oxidant drugs. Affected patients present with severe fatigue, dyspnea, anemia, high bilirubin and LDH, reticulocytosis, methemoglobinemia, and bite cells on peripheral smear. During hemolysis, G-6-PD levels may be normal, despite an inherent deficiency, as susceptible cells are destroyed. Testing may not detect G-6-PD deficiency until 30 days after cessation of the offending drug.
- **Serum lipid analysis:** Inmates with cardiovascular risk factors or elevated baseline fasting triglyceride levels or LDL cholesterol levels should have lipid parameters monitored periodically while on antiretroviral therapy. The frequency of monitoring and the decision to medically intervene should be made on an individual basis, depending on the inmate's medical history and the severity of any lipid abnormalities. More aggressive monitoring and treatment is indicated for inmates with multiple cardiovascular risk factors, pre-existing heart disease, diabetes, and other relevant complicating conditions.
- **Pap smears:** *Young women with HIV infection are at higher risk of cervical cancer than women without HIV infection.* A pelvic examination and Pap smear should be repeated at 6 months if normal at baseline—then, repeated annually thereafter— in accordance with the guidelines outlined above in *Appendix 11*, *Procedure for Pap Smears*, and the information on interpreting Pap smear results in *Section 4*, *Baseline Medical Evaluation*.

7. Prophylaxis for Opportunistic Infections (OIs)

Indications and Prophylaxis Regimens

Primary prophylaxis for opportunistic infections is indicated for inmates with HIV infection and significant immunosuppression (reduction in CD4+ T cells) to prevent acute illnesses that may require hospitalization. Prophylaxis should be prescribed in accordance with the most recent USPHS recommendations. Specific recommendations for prophylaxis for *Pneumocystis jiroveci*[2] pneumonia (PCP), *Toxoplasma gondii*-associated encephalitis, and disseminated infection with *Mycobacterium avium* complex (MAC) are outlined in *Appendix 6*. Primary prophylaxis for other opportunistic infections should be initiated in accordance with the following:

[2] *Pneumocystis jiroveci* (pronounced "yee row vet zee") is the correct name for what was previously *Pneumocystis carinii*. PCP remains an appropriate abbreviation for pneumocystis pneumonia.

Latent tuberculosis infection: Persons with HIV infection who are exposed to *M. tuberculosis* have a high risk of developing active TB disease. Treatment of latent TB infection is indicated for inmates with HIV infection who have tuberculin skin test results of 5 millimeters or greater. In addition, inmates who are close contacts of a contagious TB case require treatment for latent TB, regardless of their tuberculin skin test measurement.

The preferred treatment regimen is as follows:

- Isoniazid (900 mg) twice weekly by mouth (separated by at least 2 days), administered under direct observation for 9 months (a total of 78 doses);
- Pyridoxine (usually 50 mg per dose of isoniazid); and
- Baseline liver transaminases tests with monthly assessments for clinical signs and symptoms of hepatotoxicity. Regular monitoring is only required if inmate is at high risk for hepatotoxicity (see the BOP *Clinical Practice Guidelines for Management of Tuberculosis* at http://www.bop.gov/news/medresources.jsp).

Cytomegalovirus (CMV): Primary prophylaxis for CMV infection with oral gancyclovir is not routinely indicated, despite severe immunosuppression (CD4+ T cell counts <50 cells/mm^3) and positive CMV IgG titers. Although gancyclovir has efficacy as a prophylactic agent, gancyclovir treatment does not increase survival, may promote CMV resistance, and requires a significant pill burden for the patient.

Fungal infections: Primary prophylaxis for fungal infections is not routinely indicated for patients with AIDS. Although primary prophylaxis with fluconazole for oral candidiasis is effective, long-term fluconazole use may promote candidal resistance, is not cost effective, and is less clinically important, since oral candidiasis is usually readily treatable with short-term fluconazole therapy. Primary itraconazole prophylaxis for histoplasmosis (CD4+ T cell count <100 cells/mm^3) may be considered for inmates with unique indications.

Discontinuation of OI Prophylaxis

Discontinuation of primary and secondary prophylaxis of OIs should be considered on an individual basis, using the following USPHS guidelines:

***Pneumocystis jiroveci* (PCP):** Primary and secondary prophylaxis for PCP can be discontinued for inmates whose CD4+ T cell count increases to >200 cells/mm^3 for at least 3 months in response to antiretroviral therapy (ART). Primary or secondary prophylaxis should be reintroduced if the CD4+ T cell count decreases to <200 cells/mm^3 or if PCP reoccurs at a higher CD4+ T cell count.

***Toxoplasma gondii*:** Primary prophylaxis for toxoplasmosis encephalitis can be discontinued for inmates whose CD4+ T cell count increases to >200 cells/mm^3 for at least 3 months in response to ART. Secondary prophylaxis (chronic maintenance) for toxoplasmosis can be discontinued on an individual basis for asymptomatic inmates whose CD4+ T cell count has increased to >200 cells/mm^3 for at least 6 months in response to ART. Primary or secondary prophylaxis should be reinitiated if the CD4+ T cell count decreases to <200 cells/mm^3.

***Mycobacterium avium* complex (MAC):** Primary prophylaxis for disseminated MAC disease can be discontinued for inmates whose CD4+ T cell count increases to >100 cells/mm^3 for at least 3 months. Secondary prophylaxis (chronic maintenance) for disseminated MAC disease can be discontinued on a case-by-case basis for asymptomatic inmates who have successfully completed a 12-month course of MAC treatment, and have a sustained increase in their CD4+ T cell count, i.e., >100 cells/mm^3 for at least 6 months on an ART regimen.

Cytomegalovirus (CMV): Secondary prophylaxis (chronic maintenance) for CMV can be discontinued for inmates with a history of CMV retinitis on an individual basis, in consultation with the treating ophthalmologist, if the CD4+ T cell count increases to >100 cells/mm^3 for 3-6 months in response to ART. Factors to consider before discontinuing secondary prophylaxis include inmate adherence to ART, the location and extent of retinal disease, and the vision in the contralateral eye. Close follow-up with an ophthalmologist is indicated. Prophylaxis should be reinitiated if the CD4+ T cell count decreases to <100 cells/mm^3.

Fungal infections: Guidelines for discontinuation of prophylaxis for fungal infections are outlined below:

- **Cryptococcal meningitis:** Secondary fluconazole prophylaxis (chronic maintenance) for cryptococcal meningitis can be discontinued on an individual basis for asymptomatic inmates whose CD4+ T cell count increases to ≥200 cells/mm^3 for at least 6 months in response to ART. Reinitiate fluconazole if the CD4+ T cell count declines to <200 cells/mm^3.
- **Histoplasmosis:** Inmates with prior histoplasmosis ordinarily require prolonged secondary prophylaxis with oral itraconazole (200 mg twice daily). Secondary prophylaxis/chronic maintenance therapy can be discontinued if the following criteria are fulfilled: (1) itraconazole for ≥1 yr, (2) negative blood cultures, (3) CD4+ count >150 cells/mm^3 for > 6 months in response to ART, and (4) Serum histoplasma antigen <2 units.
- **Coccidioidomycosis:** Inmates with prior coccidioidomycosis ordinarily require lifelong secondary prophylaxis with either oral fluconazole (400 mg daily) or oral itraconazole (200mg twice daily).

Treatment of Opportunistic Infections

Inmates diagnosed with OIs related to HIV infection should be treated and maintained on secondary prophylaxis, based upon the current DHHS guidelines (available at http://www.aidsinfo.nih.gov/guidelines/).

8. Treatment: Antiretroviral Therapy (ART)

Treatment Goals

Eradication of HIV infection cannot be achieved with available ART regimens because of the pool of latently infected CD4 T-cells that persist despite prolonged suppression of plasma viremia. Maximal and durable suppression of plasma viremia delays or prevents the selection of

drug-resistance mutations, preserves CD4 T-cell numbers, and confers substantial clinical benefits. Therefore the primary goals for initiating ART are to:

- Reduce HIV-associated morbidity and prolong the duration and quality of survival.
- Restore and preserve immunologic function.
- Maximally and durably suppress plasma HIV viral load,
- Prevent HIV transmission.

HIV suppression with ART may also decrease the inflammation and immune activation thought to contribute to higher rates of cardiovascular disease and other end-organ damage that are reported in HIV-infected cohorts.

Achieving viral suppression requires the use of antiretroviral (ARV) regimens with at least two, and preferably three, active drugs from two or more drug classes. Baseline resistance testing and patient characteristics should guide the specific regimen design. When viral suppression is not achieved or is lost, rapidly changing to a new regimen with at least two, and preferably three, active drugs is required.

Viral load reduction to below detection limits in ART-naïve patients usually occurs within the first 12–24 weeks of therapy. *Virologic success* can be predicted, based on: excellent adherence to highly potent ARV regimens, low baseline viremia, higher baseline CD4 counts, and rapid reduction of viremia in response to treatment.

Initiating Antiretroviral Therapy in Treatment-Naïve Patients

Use of CD4 Counts for Initial Assessment

The CD4 count is one of the most important factors in the decision to initiate ART and/or prophylaxis for opportunistic infections, and it is the strongest predictor of subsequent disease progression and survival. A significant change between two tests is approximately a 30% change in absolute count, or an increase or decrease in CD4 percentage by 3 percentage points.

Viral Load Testing

Viral load testing serves as a surrogate marker for treatment response and can be useful in predicting clinical progression. The minimal change in viral load considered to be statistically significant is a 3-fold change. Optimal viral suppression is generally defined as a viral load consistently below the level of detection. Isolated "blips" (viral loads transiently detectable at <400 copies/ml) and low-level positive viral load results (<200 copies/ml) are not thought to predict virologic failure. *Virologic failure* is defined as confirmed viral load >200 copies/ml, which may also be useful in clinical practice.

HIV Drug-Resistance Testing

HIV drug-resistance testing is recommended for persons with HIV infection when they enter into care, and genotypic testing is the preferred resistance testing to guide therapy in ARV-naïve patients.

Recommendations for Initiating Therapy

Note: *The rating scheme for the DHHS recommendations is described in Appendix 7.*

Decisions about initiating antiretroviral therapy should be made as recommended below. These BOP guidelines are based on the current DHHS Guidelines presented in *Appendix 8*.

- ART should be initiated in all patients with a history of an AIDS-defining illness or with a CD4 count of <350 cells/mm^3 **(AI)**.
- ART is also recommended for patients with CD4 counts between 350 and 500 cells/mm^3 **(A/B-II)**
- ART should also be initiated, regardless of CD4 count, in patients with the following conditions: HIV- associated nephropathy **(AII)** and HBV coinfection when treatment of HBV is indicated **(AIII)**.
- A combination ARV drug regimen is also recommended for pregnant women who do not meet criteria for treatment with the goal to prevent perinatal transmission **(AI)**
- Patients with CD4 counts >500 cells/mm^3 should be considered only on a case-by-case basis, as data on the clinical benefits of starting treatment at such levels are not conclusive.
- Patients initiating ART should be willing and able to commit to lifelong treatment, and should understand the benefits and risks of therapy and the importance of adherence (**AIII**).
- Patients may choose to postpone therapy, and providers, on a case-by-case basis, may elect to defer therapy based on clinical and/or psychosocial factors.

Conditions favoring more rapid initiation of therapy:

- Pregnancy **(AI).** (Clinicians should refer to the DHHS *Perinatal Guidelines* for more detailed recommendations for the management of HIV-infected pregnant women.)
- AIDS-defining conditions **(AI)**.
- Acute opportunistic infections.
- Lower CD4 counts (e.g., <200 cells/mm^3) **(AI)**.
- Rapidly declining CD4 counts (e.g., >100 cells/mm^3 decrease per year) **(AIII)**.
- Higher viral loads (e.g., >100,000 copies/ml) **(BII)**.
- HIV-associated nephropathy **(AII)**.
- HBV coinfection when treatment for HBV is indicated **(AIII)**.

Conditions where temporary deferral of therapy might be considered:

- Deferring treatment for patients with higher CD4 counts who are at risk of poor adherence may be prudent while the barriers to adherence are being addressed
- Deferral of ART may be considered when either the treatment or manifestations of other medical conditions could complicate the treatment of HIV infection, or vice versa
- There are some less common situations in which ART may not be indicated at any time while CD4 counts remain high.
- Consideration should be given to situations, within the BOP system, in which the patient may be better served by delaying treatment (e.g., short length of stay, hold-over/transfer status).

Adherence considerations:

Strict adherence to antiretroviral therapy is necessary for drug effectiveness and prevention of drug resistance. Patient adherence should be assessed individually. Known predictors of poor adherence to HIV treatment regimens include low levels of literacy, age-related challenges, psychosocial issues, substance abuse, difficulty taking medication, complex regimens, adverse drug effects, and treatment fatigue. It is critical that inmate education by clinicians, pharmacists, and the nursing staff take place *before* initiating complicated antiretroviral drug treatment regimens. Counseling should include a discussion of the risks and benefits of ART, potential drug side effects, methods for managing side effects, instructions for taking scheduled medications by dose and time, and the need to report missed doses. *Mental health conditions should be evaluated, treated, and stabilized prior to initiating antiretroviral therapy.*

Table 6. Strategies to Improve Adherence to Antiretroviral Therapy

- Use a multidisciplinary team approach (i.e., medical, nursing, pharmacy, dental, etc.). Provide an accessible, trusting health care team. Provide education on medication dosing.
- Establish a trusting relationship with the patient.
- Establish readiness to start ART.
- Identify potential barriers to adherence prior to starting ART.
- Provide resources for the patient.
- Involve the patient in antiretroviral (ARV) regimen selection.
- Assess adherence at every clinic visit.
- Identify the type of non-adherence.
- Identify reasons for non-adherence.
- Assess and simplify regimen, if possible.

Adapted from: Table 12 in Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services*. January 10, 2011; 1–166. Available at: http://www.aidsinfo.nih.gov/guidelines/

Antiretroviral medications should initially be administered by direct observation on a dose-by-dose or daily basis. Directly observed medication delivery should be maintained or gradually changed to inmate self-administration at the discretion of the treating physician, based on patient adherence and the virologic response to therapy. Soon-to-be-released inmates on directly observed antiretroviral medications should be gradually transitioned to a self-administration regimen prior to release.

Where to Start: Initial Combination Regimens for the Antiretroviral-Naïve Patient

The selection of an initial antiretroviral treatment regimen should ordinarily be consistent with the DHHS preferred regimens as described in *Appendix 9*. See the DHHS guidelines, referenced in *Appendix 9*, for a discussion of the advantages and disadvantages of different initial regimens.

Preferred Regimens

The following regimens are preferred because they have optimal and durable efficacy, a favorable tolerability and toxicity profile, and ease of use.

(1) Non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen:

- Efavirenz 600mg/emtricitabine 200mg/tenofovir 300mg ***once daily***.

  Note: *Efavirenz should not be used during the first trimester of pregnancy or in women trying to conceive or not using effective and consistent contraception.*

(2) Protease inhibitor (PI)-based regimens:

- Atazanavir 300mg/ritonavir 100mg + emtricitabine 200mg/tenofovir 300mg ***once daily***.

  Note: *Atazanavir/ritonavir should not be used in patients who require >20mg of omeprazole equivalent per day.*

- Davunavir 800mg/ritonavir 100mg + emtricitabine 200mg/tenofovir 300mg ***once daily***.

(3) Integrase strand transfer inhibitor (INSTI)-based regimen:

- Raltegravir 400mg ***twice daily*** + emtricitabine 200mg/tenofovir 300mg ***once daily***.

  Note: *Raltegravir should only be considered on an individual basis because of its relatively low barrier to resistance and the lack of experience with raltegravir verses other recommended regimens. The BOP formulary does not include raltegravir, and it should normally be reserved as part of a 2nd or 3rd line ART regimen for patients with resistant viral strains.*

(4) Preferred Regimen for Pregnant Women

- Lopinavir 200mg/ritonavir 50mg (***2 tablets twice daily***)/zidovudine 300mg/lamivudine 150mg ***twice daily***.

  Note: *For more detailed recommendations, refer to the DHHS Perinatal Guidelines at: http://www.aidsinfo.nih.gov/guidelines/.*

Alternative Regimens

The following regimens are effective and tolerable, but have potential disadvantages compared to the preferred regimens

Note: *Alternative regimens that include abacavir require screening for HLA-B 5701 before starting patients on abacavir. HLA-B 5701-positive patients should not be prescribed abacavir.*

(1) NNRTI-based regimens:

- Efavirenz + (abacavir or zidovudine)/lamivudine
- Nevirapine + zidovudine/lamivudine

  Note: *Nevirapine should not be used in patients with moderate to severe hepatic impairment. Nevirapine should not be used in women with pre-ARV CD4 counts >250 or men with CD4 counts >400.*

(2) PI-based regimens:

- Atazanavir/ritonavir + (abacavir *or* zidovudine)/lamivudine
- Fosamprenavir/ritonavir + either (abacavir *or* zidovudine/lamivudine) *or* emtricitabine/tenofovir
- Lopinavir/Ritonavir + either (abacavir *or* zidovudine/lamivudine) *or* emtricitabine/tenofovir

Notes Regarding Initial Regimens:

➡ The following combinations listed above are available as fixed-dose combination formulations: ABC/3TC, EFV/TDF/FTC, LPV/r, TDF/FTC, and ZDV/3TC.

➡ ***Appendix 10*** **lists antiretroviral medications that should *never* be prescribed, and those that should *not* be prescribed as *initial therapy*.**

➡ FDA-approved antiretroviral medications and their dosing recommendations are enumerated in the DHHS guidelines. *Clinicians managing inmates with HIV infection should regularly review the DHHS guidelines* to keep abreast of new FDA-approved antiretroviral medications, changes in antiretroviral dosages, drug side effects and adverse reactions, monitoring parameters, and complex drug interactions.

➡ See Table 7 below for a comparison of NNRTI-based and PI-based regimens.

Comparison of Preferred Regimens

Table 7 compares the advantages and disadvantages of NNRTI-based and PI-based regimens:

Table 7. Comparison of Preferred Regimens

Advantages	Disadvantages
NNRTI-Based Regimen (Efavirenz + TDF/FTC)	
• NNRTI-based regimens have demonstrated virologic potency and durability. • A single tablet co-formulated with TDF, FTC, and EFV provides one-tablet, once-daily dosing and is currently the preferred NNRTI-based regimen.	• Prevalence of NNRTI-resistant viral strains in ART-naïve patients. • Low genetic barrier of NNRTIs for development of resistance. • Requires only a single mutation to confer resistance, and cross-resistance affecting DLV, EFV, and NVP. • EFV should not be used in pregnant women (especially during the first trimester), or in women of childbearing potential who are planning to conceive or who are sexually active with men and not using effective and consistent contraception. • Central nervous system adverse effects, which usually resolve over a few weeks.
PI-Based Regimen	
• PI-based regimens have demonstrated more virologic potency and durability and higher barriers to resistance than NNRTI- and INSTI-based regimens.	• A number of metabolic abnormalities have been associated with PI use, including dyslipidemia, insulin resistance, and hepatotoxicity. • Higher pill count. • Greater potential of drug-drug interactions. • The main adverse effect associated with ATV/RTV is indirect hyperbilirubinemia. • Gastrointestinal adverse effects.

Immune Reconstitution

Effective antiretroviral therapy may result in immune reconstitution with paradoxical inflammatory reactions to certain pathogens. These acute reactions can include inflammatory masses or adenitis related to *M. avium* infection, active tuberculosis, viritis associated with CMV infection, cryptococcal meningitis, active hepatitis B and C, and herpes zoster. Illnesses secondary to immune reconstitution ordinarily do not require discontinuation of antiretroviral therapy.

Management of the Treatment-Experienced Patient

Virologic and Immunologic Definitions

- **Virologic suppression:** A confirmed HIV RNA level below the limit of assay detection (e.g., <48 copies/ml).
- **Virologic failure:** The inability to achieve or maintain suppression of viral replication (to an HIV RNA level <200 copies/ml).
- **Incomplete virologic response:** Two consecutive plasma HIV RNA levels >200 copies/ml after 24 weeks on an ARV regimen. Baseline HIV RNA may affect the time course of response, and some regimens will take longer than others to suppress HIV RNA levels.
- **Virologic rebound:** Confirmed detectable HIV RNA (to >200 copies/ml) after virologic suppression.
- **Persistent low-level viremia:** Confirmed detectable HIV RNA levels that are <1,000 copies/ml.
- **Virologic blip:** After virologic suppression, an isolated detectable HIV RNA level that is followed by a return to virologic suppression.

Assessment of Virologic Failure

It is important to distinguish among the reasons for virologic failure because the approaches to subsequent therapy differ. The following potential causes of virologic failure should be explored in depth.

- **Adherence:** Assess the patient's adherence to the regimen and address the underlying causes. Simplify the regimen if possible
- **Medication intolerance:** Assess the patient's tolerance of the current regimen and consider the following management strategies:
  - Symptomatic treatment (e.g., antiemetics, antidiarrheals).
  - Changing one ARV to another within the same drug class.
  - Changing from one drug class to another.
- **Pharmacokinetic issues:** Assess/review the following underlying causes:
  - Food/fasting requirements for each medication.
  - Gastrointestinal symptoms (vomiting/diarrhea) causing short-term malabsorption.
  - Concomitant medications/dietary supplement resulting in drug interaction and make appropriate substitutions.
  - Consider therapeutic drug monitoring when pharmacokinetic issues are suspected.

- **Suspected drug resistance:**
  - Obtain resistance testing while the patient is taking the failing regimen, or within 4 weeks after regimen discontinuation if the plasma HIV RNA level is >500 copies/ml.
  - Evaluate the degree of drug resistance from the current resistance test, understanding that drug resistance tends to be cumulative for a given individual; thus, all prior treatment history and resistance test results should be taken into account.
  - Genotypic and phenotypic testing provides information relevant for selecting a new regimen with a better virologic response.

Changing ART

Consult with a physician who has HIV treatment expertise and/or a BOP HIV Clinical Pharmacist before initiating an alternative regimen**.** Consider the following guidance:

- The goal of ART is to suppress HIV replication to a level where drug-resistance mutations do not emerge.
- Selection of drug resistance does not appear to occur in patients with persistent HIV RNA levels suppressed to <48 copies/ml.
- Persistent HIV RNA levels >200 copies/ml often are associated with evidence of viral evolution and drug-resistance mutation accumulation. Persistent plasma HIV RNA levels in the 200–1,000 copies/ml range should therefore be considered as virologic failure.
- Viremia "blips" (e.g., viral suppression followed by a detectable HIV RNA level, and then subsequent return to undetectable levels) usually are not associated with subsequent virologic failure.

Management of Virologic Failure

Clinical scenarios can be reviewed in the DHHS guidelines, which include the following guidance:

- Once virologic failure is confirmed, generally the regimen should be changed as soon as possible to avoid progressive accumulation of resistance mutations.
- New ARV regimen should contain at least two, and preferably three, fully active drugs on the basis of drug treatment history, resistance testing, or new mechanistic class. *Adding a single, fully active ARV in a new regimen is* ***not*** *recommended because of the risk of rapid development of resistance.*
- Because of the potential for drug-class cross resistance that reduces drug activity, using a "new" drug that a patient has not yet taken may not mean that the drug is fully active.
- Factors associated with better virologic responses to subsequent regimens:
  - Lower HIV RNA level and/or higher CD4 cell count at the time of therapy change.
  - Using a new (i.e., not yet taken) class of ARV drugs.
  - Using ritonavir (RTV)-boosted PIs in PI-experienced patients.
- Higher genotypic and/or phenotypic susceptibility scores (quantitative measures of drug activity) are associated with better virologic responses.

- Patients who receive more active drugs have a better and more prolonged virologic response than those with fewer active drugs in the regimen.
- Discontinuing or briefly interrupting therapy in a patient with viremia may lead to a rapid increase in HIV RNA and a decrease in CD4 T-cell count, which increases the risk of clinical progression. Therefore, this strategy is not recommended.

Regimen Simplification

Regimen simplification can be defined broadly as a change in established effective therapy to reduce pill burden and dosing frequency, to enhance tolerability, or to decrease specific food and fluid requirements. Systematic reviews in the non-HIV literature have shown that adherence is inversely related to the number of daily doses. Review the DHHS Guidelines for suggested candidates for regimen simplification and the types of treatment simplification. ART simplification should normally be accomplished in consultation with a physician who has HIV treatment expertise and/or a BOP HIV Clinical Pharmacist.

Discontinuation or Interruption of ART

Discontinuing ART may result in viral rebound, immune decompensation, and clinical progression although an unplanned interruption of ART many become necessary because of severe drug toxicity, intervening illness, surgery that precludes oral therapy, or unavailable antiviral medication. Review the DHHS guidelines for guidance in discontinuing ART. Discontinuing ART should normally be accomplished in consultation with a physician who has HIV treatment expertise and/or a BOP HIV Clinical Pharmacist.

Guidance regarding interruptions of ART:

- **Unanticipated need for short-term interruption:** *When a patient experiences a severe or life-threatening toxicity or unexpected inability to take oral medications*—all components of the drug regimen should be stopped simultaneously, regardless of drug half-life.
- **Planned short-term interruption (1–2 days):** Stopping ARV drugs for a short time (i.e., 1 to 2 days) due to medical/surgical procedures can usually be done by holding all drugs in the regimen.
- **Planned short-term interruption (>2–3 days):**
  - **When all regimen components have similar half-lives and do not require food for proper absorption**—all drugs may be given with a sip of water, if allowed; otherwise, all drugs should be stopped simultaneously. All discontinued regimen components should be restarted simultaneously.
  - **When all regimen components have similar half-lives and require food for adequate absorption, and the patient cannot take anything by mouth for a sustained period of time**—temporary discontinuation of all drug components is indicated. The regimen should be restarted as soon as the patient can resume oral intake.

- **When the ARV regimen contains drugs with differing half-lives**—stopping all drugs simultaneously may result in functional monotherapy with the drug with the longest half-life (typically a non-nucleoside reverse transcriptase inhibitor—NNRTI).

Guidance regarding discontinuing therapy with NNRTIs:

NNRTIs (efavirenz and nevirapine) have a long half-life, remaining in the blood after other antiretroviral drugs have cleared. For this reason, patients taking regimens containing an NNRTI are at risk of developing resistance to the NNRTI following cessation of the regimen.

- **The optimal strategy for safely stopping an NNRTI-containing regimen is uncertain**, but potential options include: (1) discontinue the NNRTI and substitute a PI for 4 weeks, and then stop all drugs together; or (2) discontinue the NNRTI and continue other drugs for 1 additional week
- **Interruption of therapy after pregnancy:** ARV drugs for prevention of perinatal transmission of HIV are recommended for all pregnant women, regardless of whether they have indications for ART for their own health. Following delivery, considerations regarding continuation of the ARV regimen for maternal therapeutic indications are the same as for other nonpregnant individuals.

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B/HIV Coinfection

Review the DHHS Guidelines for additional information, which includes the following guidance:

- The progression of chronic HBV to cirrhosis, end-stage liver disease, and/or hepatocellular carcinoma is more rapid in HIV-infected persons than in persons with chronic HBV alone.
- ART may attenuate liver disease progression in persons coinfected with HBV by preserving or restoring immune function.
- ARV drugs active against both HIV and HBV may also prevent the development of significant liver disease by directly suppressing HBV replication. Such drugs include: tenofovir disoproxil fumarate (TDF), lamivudine (3TC), and emtricitabine (FTC).
- ART including drugs active against both HIV and HBV should be started in all patients coinfected with HBV who are also going to receive HBV treatment.
- **Preferred regimen:** The combination of TDF + FTC *or* TDF + 3TC should be used as the NRTI backbone of a fully suppressive ARV regimen and for the treatment of HBV infection.
- Persons with chronic HBV infection who are already receiving ART active against HBV should undergo quantitative HBV DNA testing every 6–12 months to determine the effectiveness of therapy in suppressing HBV replication. The goal of HBV therapy with NRTIs is to prevent liver disease complications by sustained suppression of HBV replication to the lowest achievable level.

Hepatitis C/HIV Co-infection

Review the DHHS Guidelines for additional information, which includes the following guidance.

- The rate of progression to cirrhosis for persons coinfected with HCV/HIV is about three times higher than the rate for HCV mono-infected patients.
- HCV infection does not significantly alter the virologic or immunologic response to effective ART.
- All patients with HCV/HIV coinfection should be evaluated for HCV therapy. HCV treatment is recommended according to standard guidelines with strong preference for treating patients who have higher CD4 counts. For patients with lower CD4 counts (<200 cells/mm^3), it may be preferable to initiate ART and delay HCV therapy until HIV treatment results in increased CD4 counts.
- ART should be started in HCV/HIV-coinfected persons in accordance with the DHHS Panel's recommendation for initiating ART in ART-naïve patients.
- Concurrent treatment of both HIV and HCV is feasible with the following notable considerations:
  - Didanosine (ddI) should not be given with ribavirin because of the potential for drug-drug interactions.
  - Zidovudine (ZDV) combined with ribavirin should be avoided when possible because of the higher rates of anemia.
  - Abacavir (ABC) has been associated with decreased response to peginterferon plus ribavirin in some, but not all, retrospective studies; current evidence is insufficient to recommend avoiding this combination.
  - Growth factors (e.g., filgrastim and erythropoietin) may be required to manage interferon-associated neutropenia and ribavirin-associated anemia.

Tuberculosis/HIV Co-Infection

Review the DHHS Guidelines for additional information, which includes the following guidance:

- The treatment of active tuberculosis (TB) disease in patients with HIV infection should follow the same principles for persons without HIV infection
- All HIV-infected patients with the diagnosis of active TB should be started on TB treatment immediately and should also continue ART. If the patient is not yet on ART, it should be initiated under the following guidelines:
  - For patients with CD4 count <200 cells/mm^3, ART should be initiated within 2–4 weeks of starting TB treatment.
  - For patients with CD4 count of 200–500 cells/mm^3, initiate ART within 2–4 weeks, or at least by 8 weeks after commencement of TB therapy.
  - For patients with CD4 count >500 cells/mm^3, start ART within 8 weeks of TB therapy on a case-by-case basis.

- Immune reconstitution inflammatory syndrome (IRIS) may occur after initiation of ART, and occurs more commonly in patients initiating ART earlier after starting TB treatment. Both ART and TB treatment should be continued while managing IRIS. (An augmented immune or inflammatory response in patients with some manifestations of TB, such as meningitis, pericarditis, or respiratory failure, might be life-threatening. In these circumstances, delaying initiation of ART briefly beyond recommended intervals may be appropriate.)
- ARV regimens should be assessed with particular attention to potential pharmacokinetic interactions with rifamycins. The patient's regimen may need to be modified to permit use of the optimal TB treatment regimen.

Pregnancy

Clinicians should refer to *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States for the Management of HIV-Infected Pregnant Women.* (Available at: http://www.aidsinfo.nih.gov/guidelines/.)

Wasting Syndrome

The CDC defines the HIV wasting syndrome as progressive, involuntary weight loss (10% reduction in baseline body weight) plus chronic diarrhea, chronic weakness, or documented fever in the absence of an explanatory concurrent illness or condition. Smaller reductions in weight (5–10%) without associated symptoms, however, may be clinically significant in persons with HIV infection, particularly when complicated by AIDS. Other potential causes of weight loss such as active TB, malignancies, drug side effects, depression, and opportunistic infections associated with AIDS should be actively identified and treated. Effective antiretroviral therapy should be initiated or improved in order to maximize HIV RNA suppression. Oral nutritional supplements ordinarily do not provide any additional benefit to a healthy diet.

Adverse Drug Reactions

Antiretroviral dosing, side effects, monitoring parameters, and potential drug interactions should be carefully reviewed. See the DHHS guidelines, prior to prescribing or changing antiretroviral therapy, and consider the following:

- Adverse effects have been reported with all ARV drugs and are among the most common reasons for switching or discontinuing therapy, as well as for medication nonadherence.
- Rates of treatment-limiting adverse events in ART-naïve patients enrolled in randomized trials appear to be declining with newer ARV regimens, and are generally now less than 10%.
- Factors may predispose individuals to adverse effects of ARV medications:
  - Women seem to have a higher propensity of developing Stevens-Johnson syndrome, rashes, and hepatotoxicity from nevirapine, as well as higher rates of lactic acidosis from nucleoside reverse transcriptase inhibitors (NRTIs).
  - Reactions can result from concomitant use of medications with overlapping and additive toxicities.

- Comorbid conditions that may increase the risk of or exacerbate adverse effects (e.g., alcoholism or coinfection with viral hepatitis, which may increase risk of hepatotoxicity).
- Drug-drug interactions that may lead to an increase in dose-related toxicities.
- Genetic factors predisposing patients to abacavir (ABC) hypersensitivity reaction.

9. Transition to the Community

Continuity of prescribed treatments, particularly antiretroviral medications, is medically critical for inmates who are released directly to the community or to community placement facilities such as halfway houses. Preparation for transitional medical needs should be initiated well in advance of anticipated release, in accordance with the following guidelines:

- Release planning should be coordinated with the inmate's case manager and community corrections staff, in accordance with BOP policy.
- The inmate's primary provider or other knowledgeable health care provider should meet with the inmate to finalize the treatment plan and ensure that the inmate understands the importance of adherence to prescribed treatments and specific follow-up instructions.
- Specific efforts should be made by BOP staff to coordinate access to federally funded drug assistance programs such as ADAP (AIDS Drug Assistance Program), as well as other recommended treatments such as mental health care and substance abuse programs. Consultation with BOP social workers should be pursued on a case-by-case basis to assist with release planning efforts.
- A consent for release of medical information should be obtained from the inmate, in accordance with BOP policy, so that the inmate's treatment plan can be discussed with the community health care provider.
- An adequate supply of medications should be provided to the inmate prior to release or during community placement, in accordance with BOP policy.

10. Infection Control

Transmission

HIV is spread primarily through percutaneuous blood exposures such as injection drug use, unprotected vaginal and anal intercourse, and transfusion of contaminated blood products (received prior to 1985). HIV is also transmitted from mother to child perinatally during pregnancy and through breastfeeding. HIV is not spread by sneezing, hugging, coughing, sharing eating utensils and drinking glasses, or casual contact; nor is it spread in food or water.

All inmates should be counseled during orientation to the institution, and when appropriate during clinical evaluations, of the importance of preventing blood exposures to others during activities of daily living.

These counseling messages should be reinforced for all inmates diagnosed with HIV infection:

- Do not have sex while in prison; do not have unprotected sex upon release to the community.
- Do not shoot drugs.
- Do not share tattooing or body piercing equipment.
- Do not share personal items that might have your blood on them such as toothbrushes, dental appliances, nail clippers or other nail-grooming equipment, or razors.
- Cover your cuts and skin sores to keep your blood from contacting other persons, and report to your health care provider should you have an open, draining wound.

Additionally, inmates with HIV infection should be given the following guidance:

- Do not donate blood, body organs or other tissue, or semen.
- Always wash hands before eating, after touching contaminated clothing/bedding, after attending to personal hygiene, after gardening or other outdoor activities, after touching animals, or after touching any other contaminated items.
- Wash fresh fruits and vegetables thoroughly before eating.
- Avoid eating undercooked or raw meats.
- Stop smoking, and do not begin smoking again upon release.
- Avoid touching stray animals.

Protecting Correctional Workers

Staff should use the following infection control guidelines when managing inmates:

- Use *correctional standard precautions* (see *Definitions*) when in contact with any inmate's blood or other potentially infectious materials, whether or not the inmate is known to have HIV infection.
- Use infection control practices in which non-disposable patient-care items are appropriately cleaned, disinfected, or sterilized, based on the use. Take measures to prevent cross-contamination during patient care (e.g., dialysis, vascular access, cauterizing, or dental procedures), in accordance with the Centers for Disease Control *Guidelines on Hand Washing and Hospital Environmental Control*.
- Use the appropriate airborne, droplet, and/or contact transmission precautions when indicated for inmates with HIV infection who have or may have acute secondary infections that are transmissible by respiratory contact, or by direct hand or skin-to-skin contact.

Definitions

CD4+ T cell is a T-cell lymphocyte that is essential for human cellular immunity. HIV infection results in a decline of CD4+ T cells, immunosuppression, and susceptibility to opportunistic infections.

Clinician is a physician or mid-level provider.

Directly observed therapy (DOT) for HIV infection is the unit dose administration of antiretroviral medications to an inmate by a clinician, nurse, pharmacist, or specially trained staff person who directly observes ingestion.

EIA is Enzyme Immunoassay, a laboratory test for detecting antibodies.

ART is highly active, antiretroviral therapy that can achieve sustained, undetectable HIV RNA levels in infected persons.

HIV RNA test is a laboratory assay used to quantitatively measure the presence of HIV viral particles in serum, expressed as copies per milliliter (cps/mL) and referred to as viral load or viral burden. HIV RNA levels are measured for the staging of HIV infection and therapeutic monitoring. Standard and ultrasensitive assays are available.

Immune reconstitution is the regaining of functional CD4+ T cells (host cellular immunity) following treatment of a previously immunocompromised condition such as AIDS. Immune reconstitution in the context of HIV infection results from effective antiretroviral therapy and may paradoxically be associated with inflammatory reactions to certain pathogens such as *M. tuberculosis*, cytomegalovirus, and *M. avium* complex.

Infection control precautions include the following categories of precautions relevant to the correctional setting:

- **Standard precautions** apply to blood and all other body fluids, secretions, and excretions (except sweat), whether or not they contain visible blood; nonintact skin; and mucous membranes. Standard precautions include:
  - Adequate hand hygiene measures in accordance with CDC guidelines after touching blood, body fluids, secretions, excretions (including wound drainage), and contaminated items, whether or not gloves are worn.
  - Routine use of personal protective equipment such as gloves, masks, eye protection or face shields, and gowns whenever contact with blood, body fluids, secretions, excretions (including wound drainage) is anticipated.
  - Ensuring that environmental surfaces in the health care setting are routinely cleaned and disinfected.
  - Ensuring that linens are handled and cleaned in a manner that prevents staff exposure to contaminated laundry and that avoids the transfer of microorganisms from person to person, or from place to place.

- Safe disposal of needles and other sharp instruments and devices in appropriate leak-proof and puncture-resistant containers.
- Placing in a private room those patients who may contaminate the environment or cannot be expected to maintain adequate hygiene or a sanitary environment.

- **Hospital standard precautions** are infection control practices used in the hospital setting to reduce the risk of transmission of microorganisms from both recognized and unrecognized sources of infection.
- **Correctional standard precautions** are *hospital standard precautions* that have been adapted to the correctional setting by taking into account security issues, inmate housing factors, and infection control concerns inherent in jails and prisons.

  ➡ See the relevant appendices in the *BOP Clinical Practice Guidelines for the Management of Methicillin-Resistant Staphylococcus aureus (MRSA) Infections*, available at http://www.bop.gov/news/medresources.jsp.

- **Contact transmission precautions** are indicated for inmates with pediculosis, scabies, impetigo, and noncontained skin infections such as abscesses, cellulitis, and decubiti; viral conjunctivitis; certain highly contagious enteric infections such as *Clostridium difficile* or diarrhea combined with infection with hepatitis A virus, Shigella, or *Escherichia coli* O157:H7; and gastrointestinal, respiratory, skin, or wound infections or colonization with certain multi-drug resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA).

  Contact precautions include routine *standard precautions*, as well as the following additional measures:

  - The inmate should be placed in a private cell. Inmates with the same infection can be housed together if single-cell status is not feasible.
  - Clean, nonsterile gloves should be worn when entering the cell. Gloves should be changed when grossly contaminated with potentially infectious material such as fecal material and wound drainage. Gloves must be removed and hands cleaned immediately (by washing with an antimicrobial agent or by using a waterless antiseptic agent) *before* leaving the inmate's cell. Once hands have been cleaned, care must be taken not to touch potentially contaminated environmental surfaces or items.
  - A clean, nonsterile gown should be worn when entering the inmate's cell whenever direct contact with the inmate or with environmental surfaces or items in the cell is anticipated. The gown should be removed *before* leaving the inmate's cell, taking care not to have one's clothing contact potentially contaminated environmental surfaces.
  - The inmate should leave his or her cell for essential purposes only. If the inmate leaves the cell, precautions should be taken to minimize the risk of transmitting microorganisms to other persons and to avoid contamination of environmental surfaces or items.
  - Noncritical patient care equipment should be dedicated to a single inmate. Common medical equipment that must be shared between patients must be adequately cleaned and disinfected before use by another inmate.

- No special requirements are indicated for eating utensils. Disposable or reusable utensils may be used. The use of detergent and washing procedures for decontamination are sufficient.

- **Droplet transmission precautions** are indicated for inmates with illnesses such as influenza, mumps, rubella, streptococcal pharyngitis or pneumonia, invasive *Haemophilus influenzae* type b disease such as pneumonia and epiglottitis, or invasive *Neisseria meningitidis* disease such as meningitis and pneumonia, as well as MRSA pneumonia.

  Note: *Inmates with an unknown respiratory illness compatible with tuberculosis should be managed with airborne precautions.*

  Illnesses requiring droplet precautions are caused by infectious agents that are transmitted in large-particle droplets (>5 μm in size) when an infectious patient coughs, sneezes, talks, or has certain procedures performed such as suctioning and bronchoscopy. Transmission of infection occurs when droplets containing the microorganism are propelled a short distance in the air and then deposited on the host's mouth, nasal mucosa, or conjunctivae. Large-particle droplets do not remain suspended in the air. Droplet precautions include routine standard precautions, as well as the following measures:

  - The inmate should be placed in a private cell (it does not require negative pressure or a special air handling system). The door of the cell may be opened without concern that the infectious agent will be transmitted to others. Inmates with the same infection may be housed together if single-cell housing status is not feasible.
  - A mask, eye protection, or a face shield should be worn to protect mucous membranes of the eyes, nose, and mouth during procedures and patient care activities that are likely to generate splashes or sprays. Masks should be worn when entering the cell or when within three feet of the inmate. An N95 respirator is not required.
  - Isolated inmates must wear a surgical mask if they must leave their cell. Inmate movement outside the cell should be limited to essential purposes.

- **Airborne transmission precautions** are protective measures used to prevent the spread of infections such as tuberculosis, varicella (chicken pox), and rubeola (measles) that are transmitted by inhalation of microorganisms, 5 μm or smaller in size. These tiny germs can remain suspended in airborne nuclei in poorly circulated air and can be potentially transmitted over long distances from the source patient.

  Infection control airborne precautions include the isolation of contagious inmates in a cell with monitored, negative air pressure in accordance with CDC guidelines and BOP policy. Inmates infected with the same microorganism can be cohorted together in the same cell. If a negative pressure cell is not available, the optimal management of the inmate should be determined on a case-by-case basis in consultation with a knowledgeable infection control practitioner.

  Staff entering the cell of an inmate who has pulmonary tuberculosis should wear appropriate respiratory protection (i.e., HEPA or N-95 respirators). Susceptible staff should not enter the cell of an inmate who has varicella or measles unless it is absolutely essential, and then only with respiratory protection. Staff who are immune to varicella or measles do not

require respiratory protection when entering the cell of an isolated inmate who has varicella or measles. Contagious inmates infected with pathogens transmitted by airborne microorganisms should wear a surgical mask whenever medical or security measures require them to leave the negative-pressure isolation cell.

- **Correctional transmission-based precautions** are contact, droplet, and airborne precautions that have been adapted to the correctional setting, taking into account relevant security concerns, inmate housing factors, and infection control issues inherent in jails and prisons. See the relevant appendices in the *BOP Clinical Practice Guidelines for the Management of Methicillin-Resistant Staphylococcus aureus (MRSA) Infections*, available at http://www.bop.gov/news/medresources.jsp.

Resistance testing for HIV refers to genotypic and phenotypic assays that assess HIV resistance to specific antiretroviral drugs. *Genotypic assays* measure specific mutations to viral enzymes (reverse transcriptase/protease). *Phenotypic assays* measure the ability of HIV to grow in various concentrations of antiretroviral drugs.

Undetectable HIV is the measurement of HIV RNA at levels that are below the level of detectability of specific assays, <48 cps/mL.

Appendix 1. Guidelines Regarding Medical Care of HIV-Infected Persons

Topic	Title	Link	Agency
HIV Testing and Counseling	*Revised Guidelines for HIV Counseling, Testing, and Referral*	http://www.cdc.gov/hiv/topics/testing/guideline.htm *or* http://www.aidsinfo.nih.gov/guidelines/	CDC
Risk Assessment	*Incorporating HIV Prevention into the Medical Care of Persons Living with HIV*	http://www.cdc.gov/hiv/topics/prev_prog/ahp/resources/guidelines/pro_guidance/medical_care.htm *or* http://www.aidsinfo.nih.gov/guidelines/	CDC HRSA NIH IDSA
Antiretroviral Therapy	*Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents*	http://www.aidsinfo.nih.gov/guidelines/	DHHS
Antiretroviral Therapy for Pregnant Women	*Recommendations for the 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*	http://www.aidsinfo.nih.gov/guidelines/	DHHS
Resistance Testing	*Antiretroviral Drug Resistance Testing in Adults Infected with Human Immunodeficiency Virus Type 1*	http://www.iasusa.org/pub/2005.html	IAS-USA
Opportunistic Infections	*Guidelines for Preventing Opportunistic Infections among HIV-Infected Persons*	http://www.aidsinfo.nih.gov/guidelines/	DHHS
Sexually Transmitted Diseases	*Sexually Transmitted Diseases Treatment Guidelines, 2010*	http://www.cdc.gov/std/treatment/	CDC
Immunizations	*Adult Immunization Schedule*	http://www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm	CDC ACIP
Occupational Exposures	*Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis*	http://www.aidsinfo.nih.gov/guidelines/	CDC
Non-Occupational Exposures	*Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States*	http://www.aidsinfo.nih.gov/guidelines/	CDC

ACIP = Advisory Committee on Immunization Practices; **CDC** = Centers for Disease Control and Prevention; **DHHS** = Department of Health and Human Services; **IDSA** = Infectious Disease Society of America; **IAS-USA** = International AIDS Society-USA; **NIH** = National Institutes of Health; **USPHS** = U.S. Public Health Service

Appendix 2. Criteria for Testing for HIV Infection

Test all inmates with the following , regardless of sentencing or duration of stay:	
Condition	***Comments***
Unexplained signs/symptoms compatible with acute HIV infection	Including, but not limited to: fever, adenopathy, pharyngitis, rash, myalgias, diarrhea and headache.
Signs/symptoms of HIV-related condition	Including, but not limited to: thrush, herpes zoster, oral hairy leukoplakia, severe seborrhea, unexplained lymphadenopathy, and opportunistic infections.
Pregnancy	Testing is recommended for all pregnant women as early as possible during pregnancy. Current antiretroviral therapy and obstetrical interventions markedly reduce the risk of transmitting HIV from infected mothers to their infants.
Recent exposures to HIV	Follow-up HIV-antibody testing should be performed at the following intervals after the exposure date: 6 weeks, 12 weeks, and 6 months (and 12 months for those who become infected with HCV after exposure to a source coinfected with HIV and HCV).
Active tuberculosis	HIV infection is a potent risk factor for developing active tuberculosis.
Otherwise clinically indicated	On a case-by-case basis.
Mandatorily test sentenced (6 months or more) inmates with the following risk factors:	
• Injected illegal drugs and shared equipment • (For males) sex with another man • Had unprotected intercourse with a person with known or suspected HIV infection • History of gonorrhea or syphilis • Had unprotected intercourse with more than one sex partner • From a high-risk country (sub-Saharan Africa or West Africa). • Received blood products between 1977 and May 1985 • Hemophilia • Percutaneous exposure to blood • Positive tuberculin skin test	
Offer voluntary testing to all sentenced inmates at the time of incarceration:	
Many persons with HIV infection are asymptomatic and are unaware of their infection; therefore, consistent with guidelines from the Centers for Disease Control and Prevention and the issued memorandum from the BOP Medical Director, all sentenced inmates should universally be offered HIV testing at the time of incarceration.	

Appendix 3. Correlation of Complications with CD4+ T Cell Count*

CD4+ T cells/mm^3	Infectious Complications	Non-Infectious Complications**
>500	• Acute retroviral syndrome • Candidal vaginitis	• Persistent generalized lymphadenopathy (PGL) • Guillain-Barré syndrome • Myopathy • Aseptic meningitis
200–500	• Pneumococcal and other bacterial pneumonia • Pulmonary tuberculosis • Herpes zoster • Oropharyngeal candidiasis (thrush) • Cryptosporidiosis, self-limited • Kaposi's sarcoma • Oral hairy leukoplakia	• Cervical intraepithelial neoplasia • Cervical cancer • B-cell lymphoma • Anemia • Mononeuronal multiplex • Idiopathic thrombocytopenic purpura • Hodgkin=s lymphoma • Lymphocytic interstitial pneumonitis
<200	• Pneumocystis pneumonia • Disseminated histoplasmosis • Coccidioidomycosis • Miliary/extrapulmonary TB • Progressive multifocal leukoencephalopathy (PML)	• Wasting • Peripheral neuropathy • HIV-associated dementia • Cardiomyopathy • Vacuolar myelopathy • Progressive polyradiculopathy • Non-Hodgkin's lymphoma
<100	• Disseminated herpes simplex • Toxoplasmosis • Cryptococcosis • Cryptosporidiosis, chronic • Microsporidiosis • Candidal esophagitis	
<50	• Disseminated cytomegalovirus (CMV) • Disseminated *Mycobacterium avium* complex	• Central nervous system (CNS) lymphoma

* Most complications occur with increasing frequency at lower CD4+ T cell counts.

** Some conditions listed as *non-infectious* are probably associated with transmissible microbes. Examples include lymphoma (Epstein-Barr virus [EBV]) and cervical cancer (human papilloma virus [HPV]).

Source: Bartlett JG, Gallant JE. *Medical Management of HIV infection*. 2009-2010 ed. Baltimore: Johns Hopkins University; 2009.

Appendix 4. Baseline and Periodic Medical/Laboratory Evaluations for Inmates with HIV Infection

Baseline		Periodic
History/Physical: • Fundoscopic exam • Pap smear (women) • CD4+T cell count (absolute and %) • HIV RNA (viral load) • Resistance testing • CBC, platelets, differential • Serum chemistries, transaminase levels, BUN, creatinine, urinalysis	• RPR/FTA • TST/TB symptom review • Chest radiograph • Toxoplasma gondii IgG • Hepatitis A, B, & C serologies • Influenza vaccine • Pneumococcal vaccine • Hepatitis B vaccine (if at risk) • Fasting lipid profile & glucose	• CBC, platelets, differential (q 3 to 6 months while on antiretroviral therapy) • Periodic RPR (as clinically indicated) • Pap smear within 6 months; then annually (refer to gynecologist as indicated for colposcopy) • Influenza vaccine annually • Other laboratory tests as indicated

Laboratory Monitoring Schedule for Patients Prior to and After Initiation of Antiretroviral Therapy
(Based on January 10, 2011 DHHS Guidelines)

	Entry into care	Follow-up before ART	ART indication of modification	2-8 weeks post-ART initiation or modification	Every 3-6 months	Every 6 months	Every 12 months	Treatment failure
CD4 Count	X	q 3-6 mo.	X		X		X	X
Viral Load	X	q 3-6 mo.	X	X	X			X
Resistance Testing	X		X					X
HLA-B 5701			if considering ABC					
Tropism Testing			if considering CCR5 ant.					If considering CCR5 ant.
Hep B Serology	X		May repeat if neg. at baseline					
Basic Chemistry	X	q 6-12 mo.	X	X	X			
ALT, AST, T. bili	X	q 6-12 mo.	X	X	X			
CBC w/ Differential	X	q 3-6 mo.	X	if on zidovudine	X			
Lipid Profile	X	if normal, annually	X	consider 4-8 wk w/ new ART		if it was high	X	
Fasting Glucose	X		X		X	X		
UA	X		X			if TDF	X	
Pregnancy Test			if starting EFV					

Appendix 5. HIV Classification System

CD4+ T cells/ mm^3	A Asymptomatic	B Symptomatic Disease	C AIDS Indicator Conditions
≥500	A1	B1	C1*
200–499	A2	B2	C2*
<200	A3*	B3*	C3*

** 1993 CDC Classification System: Categories A3, B3, C1, C2, and C3 are AIDS reportable.*

A – Asymptomatic

- Acute (primary) HIV infection
- Persistent generalized lymphadenopathy (PGL)

B – Symptomatic Disease

Symptomatic conditions that are attributed to HIV infection, or conditions that have a clinical course complicated by HIV. Conditions include, but are not limited to:

- Bacillary angiomatosis
- Oral candidiasis
- Vulvovaginal candidiasis: persistent (>1 month or poorly responsive to therapy)
- Cervical dysplasia (moderate–severe or CIS)
- Idiopathic thrombocytic purpura (ITP)
- Oral hairy leukoplakia
- Listeriosis
- Herpes zoster (involving more than 1 dermatome or 2 separate episodes)

C – AIDS Indicator Conditions

- Candidiasis: esophagus, trachea, bronchi or lungs
- Cervical cancer (invasive)
- Coccidioidomycosis (extrapulmonary)
- Cryptococcosis (extrapulmonary)
- Cryptosporidiosis with diarrhea (>1 month)
- Cytomegalovirus of any organ other than liver, spleen, or lymph nodes; eye
- Herpes simplex with genital/oral ulcers >1 month, or bronchitis, pneumonitis, esophagitis
- Histoplasmosis (extrapulmonary)
- HIV-associated dementia
- HIV-associated wasting syndrome
- Isoporosis with diarrhea (>1 month)
- Kaposi's sarcoma in patient under 60 years
- Lymphoma (Burkitt's, immunoblastic, or primary CNS)
- Mycobacterium avium (disseminated)
- *M. tuberculosis* (pulmonary or extrapulmonary)
- Pneumocystis pneumonia (PCP)
- Pneumonia (bacterial, recurrent): ≥ 2 episodes within 12 months
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia (nontyphoid), recurrent
- Toxoplasmosis of internal organ

Note: *Category B conditions take precedence over those in Category A; and Category C conditions take precedence over those in Category B. For classification purposes, the lowest accurate CD4+ T cell count or percentage (not necessarily the most recent) should be used.*

Appendix 6. Prophylaxis for HIV-Related Opportunistic Infections

Drug/Dosages	Toxicities	Comments
Pneumocystis Pneumonia		
Indications: CD4+ T cells **<200 /mm^3** or oralpharyngeal candidiasis. Can stop primary and secondary PCP prophy if CD4+ T cells >200/mm^3 for 3 months.		
First Choice		
TMP-SMX (Bactrim, Septra) 1 DS PO daily ***or*** 1 SS daily	rash, fever, nausea, leukopenia, hepatitis	• Prevents toxoplasmosis and bacterial infections. • Use 1 DS/day if toxo IgG+.
Alternatives		
Dapsone 100 mg/day ***or*** 50 mg BID	hemolysis, methemoglobinemia	• Screening for G6-PD deficiency recommended in high-risk patients.
Pentamidine 300 mg q month aerosolized	bronchospasm/ cough (responds to bronchodilator tx)	• Obtain screening chest x-ray for TB. • Administer pentamadine by Respirgard II nebulizer.
Atovaquone 1500mg PO daily	rash, GI intolerance	• Must be taken with meals for absorption.
Toxoplasmosis		
Indication: Toxo IgG+ and CD4+ T cells **<100 cells/mm^3**. Can stop primary toxoplasmosis prophy if CD4+ T cell count is >200/mm^3 for >3 months; can stop secondary prophy if CD4+ T cell count is >200/mm^3 ***and*** asymptomatic for >6 months.		
First Choice		
TMP-SMX (Bactrim, Septra) 1 DS/day	rash, fever, nausea, leukopenia, hepatitis	• Repeat toxo IgG if titer was negative when CD4+ T cells were <100/mm^3. • Monitor for anemia/leukopenia; CBC q 3–4 months
Alternative		
Dapsone 50mg/day **& Pyrimethamine** 50mg/wk **& Leucovorin** 25mg/wk	hemolysis, anemia	• Monitor for anemia/leukopenia; CBC q 3–4 months.
Mycobacterium avium		
Indication: CD4+ T cell count <50 cells/mm^3. Can stop primary prophy if completed ≥12 months of therapy ***and*** no sx of MAC ***and*** CD4+ count >100 cells/mm^3 for ≥6 months.		
First Choices		
Azithromycin 1200 mg/week	nausea/vomiting	
Clarithromycin 500 mg BID	nausea/vomiting	
Aternative		
Rifabutin 300 mg/day	uveitis, arthralgias, hepatitis	• Uveitis when given with fluconazole; creates rifampin resistance; review drug interactions.

Appendix 7. DHHS Antiretroviral Guidelines: Rating Scheme and Acronyms

Below are the rating scheme and the acronyms used in Appendices 8–10 of these guidelines.

Rating Scheme for DHHS Recommendations	
Strength of Recommendation	**Quality of Evidence for Recommendation**
A: Strong recommendation for the statement	**I:** One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
B: Moderate recommendation for the statement	**II:** One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
C: Optional recommendation for the statement	**III:** Expert opinion

Acronyms			
Drug Classes			
EI	entry inhibitor	**NRTI**	nucleoside reverse transcriptase inhibitor
INSTI	integrase strand transfer inhibitor	**PI**	protease inhibitor
NNRTI	non-nucleoside reverse transcriptase inhibitor		
Antiretroviral Drugs			
3TC	lamivudine	**FPV/r**	fosamprenavir + ritonavir
ABC	abacavir	**FTC**	emtricitabine
ATV	atazanavir	**IDV**	indinavir
ATV/r	atazanavir + ritonavir	**LPV/r**	lopinavir + ritonavir
d4T	stavudine	**MVC**	maraviroc
ddC	zalcitabine	**NFV**	nelfinavir
ddI	didanosine	**NVP**	nevirapine
DLV	delaviridine	**RAL**	raltegravir
DRV	darunavir	**RTV**	ritonavir
DRV/r	darunavir + ritonavir	**SQV/r**	saquinavir + ritonavir
EFV	efavirenz	**TDF**	tenofovir
ETR	etravirine	**TPV**	tipranavir
FPV	fosamprenavir	**ZDV**	zidovudine
Other			
ALT	alanine aminotransferase	**GI**	gastrointestinal
ARV	antiretroviral	**HBV**	hepatitis B virus
AST	aspartate aminotransferase	**HCV**	hepatitis C virus
DM	diabetes mellitus		

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services*. January 10, 2011; 1–166. Available at: http://www.aidsinfo.nih.gov/guidelines/

Appendix 8. Initiating Antiretroviral Therapy in Treatment-Naïve Patients

Recommendations for Initiating Antiretroviral Therapy
(Ratings for the following recommendations are in parentheses. See *Appendix 7* for the rating scheme.)

General Recommendations

Based on the cumulative weight of evidence described above, the Panel recommends that:

- ART should be initiated in all patients with a history of an AIDS-defining illness or with a CD4 count of <350 cells/mm^3 **(AI)**.
- ART is also recommended for patients with CD4 counts between 350 and 500 cells/mm^3 **(A/B-II)**.*
- ART should also be initiated, regardless of CD4 count, in patients with the following conditions: HIV- associated nephropathy **(AII)** and HBV coinfection when treatment of HBV is indicated **(AIII)**.
- A combination ARV drug regimen is also recommended for pregnant women who do not meet criteria for treatment with the goal to prevent perinatal transmission **(AI)**.
- For patients with CD4 counts >500 cells/mm^3, 50% of the DHHS Panel members favor starting ART (B); the other 50% of members view treatment as optional (C) in this setting **(B/C-III)**.**
- Patients initiating ART should be willing and able to commit to lifelong treatment and should understand the benefits and risks of therapy and the importance of adherence (**AIII**).
- Patients may choose to postpone therapy, and providers, on a case-by-case basis, may elect to defer therapy based on clinical and/or psychosocial factors.

* The DHHS Panel is divided on the strength of this recommendation: 55% of Panel members voted for strong recommendation **(A)** and 45% voted for moderate recommendation **(B)**.
** BOP Guidelines recommend that patients with CD4>500 be considered on a case-by-case basis.

Conditions Favoring More Rapid Initiation of Therapy

Deferring ART may be appropriate in some cases. However, several conditions increase the urgency for therapy, including:

- Pregnancy **(AI)** (Clinicians should refer to the DHHS ***Perinatal Guidelines*** for more detailed recommendations for the management of HIV-infected pregnant women. See *Appendix 1*.)
- AIDS-defining conditions **(AI)**
- Acute opportunistic infections (see discussion below)
- Lower CD4 counts (e.g., <200 cells/mm^3) **(AI)**
- Rapidly declining CD4 counts (e.g., >100 cells/mm^3 decrease per year) **(AIII)**
- Higher viral loads (e.g., >100,000 copies/ml) **(BII)**
- HIV- associated nephropathy **(AII)**
- HBV coinfection when treatment for HBV is indicated **(AIII)**

Acute Opportunistic Infections

In patients with opportunistic conditions for which there is no effective therapy (e.g., cryptosporidiosis, microsporidiosis, progressive multifocal leukoencephalopathy), but for which ART may improve outcomes by improving immune responses, the benefits of ART outweigh any increased risk, and therefore treatment should be started as soon as possible **(AIII)**.

In the setting of opportunistic infections, such as cryptococcal meningitis or non-tuberculous mycobacterial infections, for which immediate therapy may increase the risk of immune reconstitution inflammatory syndrome (IRIS), a short delay may be warranted before initiating ART **(CIII)**.

In the setting of other opportunistic infections, such as *Pneumocystis jiroveci* pneumonia (PCP), early initiation of ART is associated with increased survival, and therapy should not be delayed **(AI)**.

In patients who have active tuberculosis, initiating ART within the first 1−2 months of treatment for tuberculosis appears to confer a significant survival advantage. (See section on ***Mycobacterium Tuberculosis*** **Disease with HIV Coinfection** in the January 2011 DHHS guidelines cited below.)

Clinicians should refer to the **DHHS *Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents*** (available at http://www.aidsinfo.nih.gov/guidelines/) for more detailed discussion on when to initiate ART in the setting of a specific opportunistic infection.

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services*. January 10, 2011; 1–166. Available at: http://www.aidsinfo.nih.gov/guidelines/

Appendix 9. Preferred Treatment Regimens for Antiretroviral-Naïve Patients

Recommended Treatment Regimens for Antiretroviral-Naïve Patients

Regimens should be individualized, based on the advantages and disadvantages of each combination. Considerations should include: pill burden, dosing frequency, toxicities, drug-drug interaction potential, co-morbid conditions, and level of plasma HIV-RNA.

Clinicians should refer to the *DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents* referenced below to review the pros and cons of the different components of a regimen, as well as the adverse effects and dosages of individual antiretroviral agents.

Ratings for the DHHS Panel's recommendations are in parentheses. See *Appendix 7* for the rating scheme and a list of the acronyms used. See the section on *Where to Start* for the BOP recommended dosages for each regimen.

Preferred Regimens

The following regimens are preferred because they have optimal and durable efficacy, a favorable tolerability and toxicity profile, and ease of use. Except for the recommendation for pregnant women, the preferred regimens are arranged by duration of clinical experience.

NNRTI-Based Regimen • EFV/TDF/FTC1 **(AI)** **PI-Based Regimens** *(in alphabetical order)* • ATV/r + TDF/FTC1 **(AI)** • DRV/r (once daily) + TDF/FTC1 **(AI)** **INSTI-Based Regimen** • RAL + TDF/FTC1 **(AI)** **Preferred Regimen for Pregnant Women** • LPV/r (twice daily) + ZDV/3TC1 **(AI)**	**Comments:** **EFV** should *not* be used during the first trimester of pregnancy or in women trying to conceive or not using effective and consistent contraception. **ATV/r** should *not* be used in patients who require >20 mg omeprazole equivalent per day. Refer to Table 15a of the *DHHS Guidelines* (referenced below) for dosing recommendations regarding interactions between ATV/r and acid-lowering agents.

Alternative Regimens

The following regimens are effective and tolerable, but have potential disadvantages compared to the preferred regimens. An alternative regimen may be the preferred regimen for some patients.

NNRTI-Based Regimens *(in alphabetical order)* • EFV + (ABC or ZDV)/3TC1 **(BI)** • NVP + ZDV/3TC1 **(BI)** **PI-Based Regimens** *(in alphabetical order)* • ATV/r + (ABC or ZDV)/3TC1 **(BI)** • FPV/r (once or twice daily) + either [(ABC or ZDV)/3TC1] or TDF/FTC1 **(BI)** • LPV/r (once or twice daily) + either [(ABC or ZDV)/3TC1] or TDF/FTC1 **(BI)**	**Comments:** **NVP** • NVP should *not* be used in patients with moderate to severe hepatic impairment (Child-Pugh B) • NVP should *not* be used in women with pre-ARV CD4 count >250 cells/mm^3 or men with pre-ARV CD4 count >400 cells/mm^3. **ABC** • ABC should *not* be used in patients who test positive for HLA-B*5701. • Use ABC with caution in patients with high risk of cardiovascular disease or with pretreatment HIV RNA >100,000 copies/mL. **LPV/r** • Once-daily LPV/r is *not* recommended in pregnant women.

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services*. January 10, 2011; 1–166. Available at: http://www.aidsinfo.nih.gov/guidelines/

Appendix 10. Antiretroviral Drugs and Components *Not* Recommended

Do Not Offer *at Any Time*	Do Not Offer *as Initial Therapy*
• Monotherapy with NRTI • Dual therapy NRTI regimens • Abacavir + tenofovir + lamivudine (or emtricitabine) as a triple-NRTI regimen • Tenofovir + didanosine + lamivudine (or emtricitabine) combination as a triple-NRTI regimen • Atazanavir + indinavir • Didanosine + stavudine • Didanosine + tenofovir • Emtricitabine + lamivudine • Stavudine + zidovudine • 2-NNRTI combinations • Evavirenz (in first trimester of pregnancy or in women with significant child-bearing potential) • Nevirapine (initiation with CD4+ T cell counts >250 cells/mm^3 for women or >400 cells/mm^3 for men • Etravirine + unboosted PI • Etravirine + ritonavir-boosted atazanavir or fosamprenavir • Etravirine + ritonavir -boosted tipranavir • Unboosted darunavir, saquinavir, or tipranavir ➧ **Review *DHHS Guidelines* (referenced below) for possible exceptions to the above recommendations.**	• ABC/3TC/ZDV (coformulated) as triple-NRTI combination regimen ► *Inferior virologic efficacy* • ABC + 3TC + ZDV + TDF as quadruple-NRTI combination ► *Inferior virologic efficacy* • ABC + ddI or TDF ► *Insufficient data in ART-naïve patients* • DRV (unboosted) ► *Use without RTV has not been studied* • DLV ► *Inferior virologic effacy* • ddI + TDF ► *High rate of early virologic failure* ► *Rapid selection of resistant mutations* ► *Potential for immunologic nonresponse* • T-20 ► *No trial experience in ART-naïve* • ETR ► *Insufficient data in ART-naïve patients* • IDV (unboosted) ► *Inconvenient dosing* • IDV (RTV-boosted) ► *High incidence of nephrolithiasis* • NFV ► *Inferior virologic efficacy* • RTV as sole PI ► *Gastrointestinal intolerance* • SQV (unboosted) ► *Inferior virologic efficacy* • d4T + 3TC ► *Significant toxicities including lipoatrophy; peripheral neuropathy; and hyperlactatemia, including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis* • TPV (ritonavir-boosted) ► *Inferior virologic efficacy*

Note: Acronyms are defined in Appendix 7.
Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services*. January 10, 2011; 1–166. Available at: http://www.aidsinfo.nih.gov/guidelines/

Appendix 11. Procedure for Pap Smears

Pap Smear Instructions
The cervix is scraped circumflexually with an *Ayer* spatula or a curved brush; a sample from the posterior fornix or the vaginal pool may also be included. The endocervical sample is taken with a saline-moistened, cotton-tipped applicator or a straight ectocervical brush, which is rolled on a slide and *immediately* fixed in ethyl ether plus 95% ethyl alcohol, or in 95% ethyl alcohol alone. The yield is 7-fold higher with the brush specimen. ***Important points for obtaining an adequate sample are below:*** • Collect the Pap smear prior to the bimanual exam, to avoid contaminating the sample with lubricant. • Obtain the Pap before testing for sexually transmitted diseases. • If a large amount of vaginal discharge is present, carefully remove it with a large swab before collecting the Pap smear. • Obtain the ectocervical sample before obtaining the endocervical sample. • Small amounts of blood will not interfere with cytologic sampling; defer Pap if bleeding is heavy. • Collected material should be applied uniformly to the slide, without clumping, and should be fixed immediately to avoid air-drying. • If spray fixatives are used, the spray should be held at least 10 inches away from the slide to prevent disruption of cells by the propellant. • When performing speculum examination, if an ulcerative or exophytic lesion is detected and is suspicious for cancer, a referral for possible biopsy is warranted. ***Note:*** *New liquid-based collection and thin layer processing methods decrease the frequency of inadequate smears and provide more sensitive and specific results.*
Adapted from: Bartlett JG, Gallant JE. *Medical Management of HIV infection*. 2009-2010 ed. Baltimore: Johns Hopkins University; 2009.