MANAGEMENT OF HIV INFECTION

Federal Bureau of Prisons

Clinical Guidance

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WHAT'S NEW IN THIS DOCUMENT?

The following changes have been made since the July 2013 version of these guidelines.

MEDICAL EVALUATION

- The section on *Acute HIV Infection* has been expanded.
- New information is included regarding assessment and monitoring for cardiovascular disease and diabetes mellitus. The entire section describing the baseline medical evaluation has been expanded, as well.
  - ➜ See *Section 3, Baseline Medical Evaluation for HIV-Infected Inmates*.
  - ➜ See also the new *Appendix 3*, a checklist for reviewing symptoms and doing the physical exam.

TESTING AND TREATMENT

- New guidance is provided on the use and interpretation of *Fourth-Generation HIV Testing*.
- Treatment information throughout this document was updated to be in line with the February 9, 2016, DHHS *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*. In particular, revisions were made to *Section 6* (Initiating ART in Treatment-Naïve Patients) and *Section 7* (Initial Combination Regimens in ART-Naïve Patients).
  - ➜ *The DHHS Guidelines are updated regularly and should be consulted at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0. Providers can sign up to receive email update notifications.*
- The recommendations for *cervical cancer screening* in HIV-infected women have been updated (*Section 3)*. In addition, a new *Appendix 5b* summarizes the BOP recommendations.
- The new *Table 4* is designed to guide clinicians in choosing an initial antiretroviral regimen, based on patient and regimen characteristics and specific clinical scenarios.
- The new *Table 5* lists adverse effects associated with commonly used antiretroviral classes.
- Guidance regarding *hepatitis B* and *hepatitis C* coinfections has been expanded (*Section 12*).
- For detailed guidance regarding coinfection of HIV/TB, readers are now referred to the most recent BOP Clinical Practice Guidelines on the *Management of Tuberculosis*.
- A new section was added to address *management of the treatment-experienced patient*, including information on managing virological failure (*Section 8*).
- The *immunization recommendations* have been updated, based on the CDC immunization recommendations, available at: *http://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html*
- In addition, the new *Appendix 6* provides a decision-making chart for giving pneumococcal vaccinations to HIV-infected inmates.
- The new *Appendix 8* describes the advantages and disadvantages of antiretroviral (ARV) drug components by class.
- The new *Appendix 9* lists dosing for ARV drugs for patients with kidney disease and undergoing hemodialysis.

GENERAL

- Information has been added regarding documentation of *counseling* prior to HIV-testing.
- The availability of Regional HIV Clinical Pharmacist Consultants to consult with providers on the proper care of HIV patients is emphasized. See *Treatment Plan*.
- Other topics were expanded, including *Transition to Community* (*Section1*6) and *Transmission* (in *Section 17, Infection Control*).
- Some tables that contained the same information as one of the Appendices have been eliminated, and the reader is referred to the appropriate Appendix. Certain Appendices were eliminated, and the remaining Appendices—old and new—have been renumbered.

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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 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 for a list of guidelines for the medical care of HIV-positive persons.*

➜ *The* DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents *are updated regularly and should be consulted at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0. Providers can sign up to receive email update notifications.*

2. DIAGNOSIS AND REPORTING

INDICATIONS FOR TESTING FOR HIV

Testing of inmates for HIV infection must be a priority for the BOP: Almost one in seven persons living with HIV infection in the U.S. is unaware of being infected, and less than one-third of HIV-infected individuals in the U.S. have suppressed viral loads—a result commonly linked to undiagnosed HIV infection and failure to retain diagnosed patients in care.

The following HIV testing policies apply in the BOP:

- **OPT-OUT VOLUNTARY TESTING** is offered to all designated inmates after arrival to the designated institution.
- **VOLUNTARY TESTING** is also done when the inmate requests testing via an *Inmate Request to Staff Member*. This voluntary testing is available to all inmates—regardless of sentencing or duration of stay.
- **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. P6190.04 (7)
- **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*. P6190.04 (7)

➜ *Specific indications for HIV testing are described in Appendix 2.*

COUNSELING OF INMATES PRIOR TO HIV TESTING

All inmates tested for HIV infection should receive pre-test counseling from qualified health care personnel, in accordance with current BOP policy. Counseling should provide information on HIV transmission, methods for preventing the spread of the virus while in prison and upon release to the community, and the meaning of the test results.

➔ *The institution's Admission and Orientation program meets the HIV pre-test counseling requirement if documentation such as a sign-in roster is obtained and kept on file. Inmates are not required to sign an informed consent form during HIV counseling sessions.*

HIV SEROLOGICAL TESTING AND INTERPRETATION OF RESULTS

➔ *When the pre-test counseling is completed, HSD requires risk-based HIV testing per policy, but recommends testing ALL SENTENCED inmates unless they choose to opt out of HIV testing.*

Serological testing identifies HIV antigen and/or antibody generated as part of the immune response to infection with HIV. Third- and fourth-generation HIV testing algorithms are currently utilized by BOP laboratory processing facilities. Clinicians will not have the ability to specify which test is used since the test utilized will depend on the capabilities of the lab processing the specimen and the location of the requesting institution. Both tests are appropriate for diagnosing HIV infection. A brief description of each of these tests is provided below.

FOURTH-GENERATION HIV TESTING

CDC RECOMMENDATION:

The CDC recommends the use of an HIV-1/2 antigen/antibody combination immunoassay (fourth-generation) algorithm as the best method to accurately detect and diagnose an individual with early (< 6 months) or acute HIV infection.

BENEFITS OF FOURTH-GENERATION TESTING:

The conventional "third-generation" HIV testing algorithm begins with an HIV-1/HIV-2 antibody immunoassay, followed by supplemental testing (e.g., Western blot) to confirm repeatedly reactive results. This approach is highly sensitive and specific, but has several drawbacks: (1) It cannot detect acute infection; (2) it does not readily differentiate between HIV-1 and HIV-2; and (3) negative or indeterminate results on Western blots during early seroconversion can delay diagnosis.

Fourth-generation combination immunoassay detects HIV p24 antigen, as well as HIV antibodies. Because HIV p24 antigen is detectable before seroconversion, fourth-generation assays can detect HIV-1 during acute infection. In general, fourth-generation testing can confirm HIV infection 14–15 days after HIV RNA is detectable, which is 0–20 days (median, 5–7 days) sooner than third-generation testing.

➔ *Fourth-generation testing follows a series of reflex assays for HIV-1/2 antigen and antibodies, as shown below in* ***Table 1.***

TABLE 1. FOURTH-GENERATION TESTING

FOURTH-GENERATION ASSAYS FOR HIV-1/2 ANTIGEN AND ANTIBODIES			
➔ **Initial assay for HIV-1/2 antigen and antibodies:**			
RESULT: Nonreactive	➔ **Infection unlikely** (negative for p24 antigen & antibodies to HIV-1 and HIV-2)		
RESULT: Repeatedly reactive	➔ **Reflexes to HIV-1/2 antibody differentiation assay:**		
	RESULT: Reactive	➔ **HIV-1 or HIV-2 infection**	
	RESULT: Nonreactive or indeterminate	➔ **Reflexes to HIV-1 viral load:**	
		RESULT: Positive	➔ **Acute HIV infection**
		RESULT: Negative	➔ **HIV-1 infection unlikely** (*Consider testing for HIV-2 DNA if clinically indicated; see HIV-2 Infection below.*)

THIRD-GENERATION HIV TESTING

In the absence of an Ag/Ab combination immunoassay (fourth-generation), laboratories will utilize a sensitive IgM assay (third-generation). A viral RNA test should be ordered for any reactive results or if the medical provider suspects acute HIV infection. The third-generation algorithm includes using supplemental tests, such as a Western blot (WB) or immunofluorescent assay (IFA). Third-generation HIV assay algorithms are still commonly used, and WB is the most common supplemental test in this algorithm. Results of HIV WB are generally interpreted as outlined in ***Table 2*** below.

TABLE 2. INTERPRETATION OF WESTERN BLOT RESULTS

INTERPRETATION	WB 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

INDETERMINATE RESULTS:

Indeterminate WB results rarely occur, but can usually be evaluated through risk assessment and viral load measurement.

- **Patients evaluated as low-risk** are seldom infected with HIV, but may continue to show indeterminate results. These patients should be reassured that HIV infection is unlikely and should receive follow-up serology, including viral load, at three months.
- **Patients with risk factors who are in the process of seroconversion** will usually have positive WBs, as well as high viral loads, within one month. These patients should have repeat serology, including viral load, in one to two months. Viral detection methods may be used as an adjunctive diagnostic tool, but should not supplant antibody testing.

➔ ***Table 3*** *below outlines reasons for indeterminate WB results.*

TABLE 3. REASONS FOR INDETERMINATE WESTERN BLOT RESULTS

REASON	EXPLANATION
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 WB analysis.
Cross reactive antibodies	Autoimmune diseases, certain malignancies, injection drug use, HIV vaccination, and recent immunization may yield antibodies that are detectable on HIV WB analysis.
Advanced HIV infection	Loss of HIV antibodies because of AIDS itself may affect WB analysis.
Adapted from: Bartlett JG, Gallant JE. *Medical Management of HIV infection*. 2009-2010 ed. Baltimore: Johns Hopkins University; 2009.	

HIV-2 INFECTION

HIV-2 infections are rarely observed in the United States. The CDC reports that between 1988 and June 2010, 166 cases had met the CDC case definition of HIV-2 infection. The largest number of cases were from the Northeast, including 77 from New York City. The majority of cases had a West African origin or connection.

HIV-2 is associated with lower viral load levels, slower rates of CD4 decline, and slower rates of clinical progression, as compared with HIV-1; 86–95% of people infected with HIV-2 are long-term nonprogressors. Recent data show that survival of persons with undetectable HIV-2 viral load is similar to that of the general population. Nonetheless, HIV-2 infection can cause immunosuppression, as well as AIDS characterized by the same signs, symptoms, and opportunistic infections that are seen with HIV-1. Furthermore, AIDS resulting from HIV-2 infection is often associated with much lower viral load levels than AIDS resulting from HIV-1 infection (>10,000 copies/mL in HIV-2 cases, as compared to sometimes millions of copies/mL in HIV-1 cases).

In contrast to the detailed knowledge base for the management of HIV-1, no clinical trials have been conducted to date to guide decision-making in the management of HIV-2-related immunosuppression and progression of disease. Studies of virologic and immunologic responses to antiretroviral therapy (ART) have demonstrated a higher CD4 cell increase in HIV-1-infected patients after initiation of therapy, as compared to HIV-2-infected patients. These factors, combined with the absence of controlled trials of ART for HIV-2, contribute to the challenge of providing optimal treatment of HIV-2.

Commercially available HIV-1 viral load assays do not reliably detect or quantify HIV-2. Specialized labs are available to quantify HIV-2 plasma RNA viral load, but it should be noted that one-quarter to one-third of HIV-2-infected patients without ART will report viral loads below the limits of detection. It should also be noted that no validated HIV-2 genotypic or phenotypic resistance assays are available for clinical care and that HIV-2 is intrinsically resistant to NNRTIs and that several PIs lack ARV activity.

➔ *Treatment of HIV-2 infections should be conducted in consultation with experts in the management of HIV disease.*

ACUTE HIV INFECTION

Acute HIV-1 infection, the phase of HIV-1 disease that occurs two to four weeks after infection, is characterized by an initial burst of viremia. While anti-HIV-1 antibodies are undetectable during acute HIV infection, HIV-1 RNA or p24 antigen are nonetheless present.

Acute HIV infection should be suspected in patients who have had high-risk exposure within the past four weeks and are experiencing typical symptoms such as fever, lymphadenopathy, sore throat, rash, myalgia/arthralgia, and headache. Painful mucocutaneous ulceration is one of the most distinctive manifestations of acute HIV infection. The diagnosis of acute HIV infection requires a high level of clinical suspicion and should be considered in patients who present with consistent signs and symptoms.

When the possibility of acute or early HIV infection is being considered, providers should perform the most sensitive immunoassay available (ideally, a fourth-generation combination antigen/antibody immunoassay), in addition to an HIV viral load test or HIV-1 NAT. Acute or early infection can be defined by a negative immunoassay in the presence of a high viral load (>10,000 cps/mL). Viral loads in this setting are generally very high (>100,000 cps/mL). These patients should be counseled concerning the substantial risk of transmission during the acute phase of infection. Additional testing to confirm seroconversion may be warranted. Antiretroviral therapy, which is recommended for all individuals with HIV-1 infection, should normally be offered to those with early HIV-1 infection.

REPORTING

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

3. BASELINE MEDICAL EVALUATION FOR HIV-INFECTED INMATES

The baseline medical evaluation is indicated for inmates arriving with a history of HIV infection or who are diagnosed with HIV infection after arrival. This evaluation ordinarily includes a *history and physical examination*, *laboratory tests*, a review of the patient's *immunization status*, and a *treatment plan, with subspecialty referrals*, as needed—all discussed below.

➜ *See also Section 4, Periodic Medical Evaluations for HIV-Infected Inmates for guidance on periodic follow-up assessments.*

HISTORY AND PHYSICAL EXAMINATION

- **MEDICAL HISTORY AND ASSESSMENT OF RISK FACTORS**

  Obtain a comprehensive medical history, along with an assessment and documentation of HIV risk factors, including the following:

  - The date when HIV infection was diagnosed.
  - Pre-ART CD4 count (aka CD4 nadir), highest viral load, and most recent viral load/CD4 count.

(list continued on next page)

- When possible, estimated date of infection (based on history of prior negative results, history of symptoms of acute retroviral infection, or inmate's recollection of high-risk activities).
- History of prior HIV-related complications, 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 who have undergone ART. The medication history—preferably based on previous medical records—should include the antiretroviral (ARV) regimens prescribed, duration of treatment, response to each regimen, drug toxicities, reason for treatment changes, barriers to adherence, and prior resistance test results. Newly diagnosed patients should also be asked about any prior use of ARV agents for prevention of HIV infection, although prior medical records should be reviewed here, as well.

- **COMPLETE PHYSICAL EXAMINATION**

➜ *For a more detailed checklist, see Appendix 3, HIV-Infected Inmates – Initial Assessment.*

The examination should include the following:

- Examination for evidence of wasting, obesity, evidence of ART-related lipohypertrophy (e.g., dorsocervical fat pad, gynecomastia, or visceral abdominal fat accumulation) and/or lipoatrophy (e.g., loss of subcutaneous fat in the face, extremities, or buttocks).
- Funduscopic examination for retinopathy.
- Oropharyngeal exam for candida and other significant oral manifestations.
- Careful skin exam for dermatologic conditions.
- Abdominal exam for hepatosplenomegaly.
- 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.
  ➜ *See Recommendations for Cervical Cancer Screening below.*
- For men and women, perform rectal examination, including visual inspection and digital rectal examination, to evaluate for anal warts, other STDs, and anal cancer, with screening for prostate abnormalities in men.
- Comprehensive cardiopulmonary examination, including examination for evidence of cardiovascular disease and diabetes. Family history for cardiovascular disease and diabetes should also be documented.
- Neurology and/or neuropsychology referral for assessment of neurocognitive disorders, dementia, and focal neuropathies may be indicated.

- **RECOMMENDATIONS FOR CERVICAL CANCER SCREENING – PAP SMEARS**
  - *Obtain Pap smears in accordance with the procedure outlined in Appendix 5a.*
  - *Recommendations for Cervical Screening for HIV-Infected Women are summarized in Appendix 5b.*
  - *Abnormal cervical screening (Pap) test results are briefly explained in the Definitions section.*

Pap smear results should be interpreted in accordance with the current CDC/NIH guidelines,[1] as outlined below:

AGE <30:

- *Co-testing for cervical cancer (Pap test and human papillomavirus [HPV] test) is not recommended for HIV-infected women <30 years of age.*
- **Baseline and routine Pap testing if normal:** HIV-infected women 21–29 years old should have a baseline Pap test at the time of initial diagnosis with HIV. Provided the initial Pap test for a young (or newly diagnosed) HIV-infected woman is normal, the next Pap test should be in 12 months. (Some experts recommend a Pap test at 6 months after the baseline test.) If the results of 3 consecutive Pap tests are normal, follow-up Pap tests should be every 3 years.
- **If ASC-US:** If a Pap test reveals atypical squamous cells of undetermined significance (ASC-US), and a reflex HPV test is positive, referral to colposcopy is recommended. If HPV testing is not available or not done, then repeat cytology in 6–12 months is recommended. For any result equal to or greater than ASC-US on repeat cytology, referral to colposcopy is recommended.
- **If LSIL or worse:** For low-grade squamous intraepithelial lesion (LSIL) or worse—including atypical squamous cells, cannot rule out high grade lesion (ASC-H), atypical glandular cells (AGC), and high grade squamous intraepithelial lesion **(**HSIL)—referral to colposcopy is recommended (regardless of reflex HPV result, if done).

AGE ≥30:

- *Either Pap testing alone or Pap and HPV co-testing is acceptable for cervical cancer screening for women age 30 and older. Cervical cancer screening in HIV-infected women should continue throughout a woman's lifetime (and not, as in the general population, end at 65 years of age).*
- **Baseline and routine Pap testing if normal:** If screening with Pap tests alone, the HIV-infected woman should have a baseline Pap test at the time of HIV diagnosis, then every 12 months. (Some experts recommend a Pap test at 6 months after the baseline test.) If the results of 3 consecutive Pap tests are normal, follow-up Pap tests should be every 3 years.
- **If baseline co-testing with Pap and HPV is available:** Co-testing can be done at the time of diagnosis or when a previously-diagnosed HIV infected woman turns 30. Co-test negative women (i.e., a normal Pap and negative HPV test) can have their next cervical cancer screening in 3 years. Those who have a normal Pap test, but are positive for HPV should have repeat co-testing in one year (unless HPV genotype testing for 16 or

[1] *Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents*. Updated 9-24-15. Available at: *https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/343/hpv*

16/18 is positive). If either of the co-tests at one year is abnormal (i.e., abnormal cytology or positive HPV), referral to colposcopy is recommended.

If the initial HPV results identify HPV16 or HPV16/18, then referral to colposcopy is recommended. If the HPV testing is positive, but the genotype-specific testing for HPV16 or HPV 16/18 is negative, then repeat co-testing in one year is recommended. If either of the co-tests at one year is abnormal (i.e., abnormal cytology or positive HPV), referral to colposcopy is recommended.

- **If ASC-US Pap test:** If reflex HPV testing is positive, then referral to colposcopy is recommended. If HPV testing is not available, repeat cytology in 6 to 12 months is recommended. For any result ≥ ASC-US on repeat cytology, referral to colposcopy is recommended.
- **If LSIL Pap test or worse:** If LSIL, ASC-H, AGC, or HSIL, referral to colposcopy is recommended (regardless of HPV result, if done).

ALL AGES

- 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

See Appendix 4a, HIV-Infected Inmates – Baseline Laboratory Evaluations for a more complete list, including additional tests that may be performed under certain circumstances.

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

- HIV serology (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).
- Complete blood count, chemistry profile, transaminase levels, blood urea nitrogen (BUN) and creatinine, urinalysis, and serologies for hepatitis A, B, and C viruses (HAV, HBV, and HCV).
- Fasting blood glucose and serum lipids.
- Screening tests for coinfections: Cytomegalovirus (CMV), gonorrhea, chlamydia, syphilis, latent Toxoplasma gondii, latent tuberculosis, varicella virus, trichomoniasis (women).

(list continued on next page)

- Genotypic resistance testing (at entry into care, regardless of whether ART will be initiated immediately). For patients who have HIV RNA levels <500 cps/mL, amplification of virus for resistance testing may not always be successful.
  - *Phenotype or combination Phenotype/Genotype (Phenosense GT) should generally **NOT** be used without expert consultation.*
- HLA B *5701 (if considering use of abacavir). A negative result suggests minimal risk of hypersensitivity reaction.
- Coreceptor tropism assay (if considering use of CCR5 co-receptor antagonist such as maraviroc). A "dual/mixed" (D/M) result suggests maraviroc will be ineffective.

IMMUNIZATION STATUS

Immunizations are an important part of preventive care for HIV-infected patients. Inactivated vaccines are generally safe and acceptable in HIV-infected individuals. It should be noted that vaccination of HIV-infected individuals may not confer the same degree of protection gained by immunocompetent persons. Guidance for immunizing persons with low CD4 counts is described under individual vaccines listed below. Certain live vaccines have sufficient safety data and are thus appropriate if indicated for HIV-infected individuals with CD4 counts ≥200 cells/μL.

- *It is recommended that providers frequently reference the CDC website for updated vaccine schedules established by the Advisory Committee on Immunization Practices (ACIP).*

RECOMMENDED IMMUNIZATIONS FOR ALL HIV-POSITIVE ADULTS

- **HEPATITIS A VACCINE**

  Recommended unless there is evidence of immunity. Single-antigen vaccine formulations should be administered in a two-dose schedule, depending on the manufacturer: at either 0 and 6-to-12 months (Havrix®), or 0 and 6-to-18 months (VAQTA®). Combination hepatitis A and B (Twinrx®) is not recommended due to hepatitis B dose being insufficient to elicit response.

- **HEPATITIS B VACCINE**

  Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels (anti-HBs) should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low. Patients should receive either:

  - One dose of 40 mcg/mL (Recombivax HB®) administered on a three-dose schedule at 0, 1, and 6 months

    OR

  - Two doses of 20 mcg/mL (Engerix®-B) administered simultaneously on a four-dose schedule at 0, 1, 2, and 6 months.

- **INFLUENZA VACCINE**

  Must be given every year. Only injectable (inactivated) flu vaccine should be given to those who are HIV-positive.

  - *The nasal spray vaccine (FluMist® LAIV) should not be used in this population.*

- **MENINGOCOCCAL VACCINE**

  Specific indications for meningococcal vaccination in HIV-infected individuals are the same as for uninfected patients: functional or anatomic asplenia, persistent complement component deficiency, travel exposure, ages 11–18 years, and exposure during an outbreak.

- **PNEUMOCOCCAL VACCINE**

  ➜ *See flow-chart in Appendix 6, Pneumococcal Vaccination for HIV-Infected Inmates.*

  Note: ***PCV13*** *= 13-valent pneumococcal conjugate vaccine (Prevnar 13)*
  PPSV23 *= 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23)*

HIV+ ADULTS, AGE 19–64:★

- **Pneumococcal vaccine-naïve persons** should first receive a dose of PCV13, followed by a dose of PPSV23—no sooner than 8 weeks after receiving the PCV13 dose. A second dose of PPSV23 should be given at least five years after the first dose of PPSV23.
- **Patients who have received one dose of PPSV23** should be given a PCV13 dose ≥1 year after the PPSV23 dose. A second PPSV23 is recommended—at least 8 weeks after the PCV13 dose, so long as it is at least 5 years after the first PPSV23 dose and the patient is >65 years of age.
- **Patients who have received two doses of PPSV23, but no PCV13,** should receive a PCV13 dose at least 1 year after the most recent dose of PPSV23.

HIV+ ADULTS, AGE > 64:★

- **Patients ≥ 65 who have not received PCV13 or PPSV23** should receive one dose of PCV13 followed by one dose of PPSV23 at least 8 weeks later.
- **Patients ≥ 65 who have received PPSC23 before age 65, but not PCV13,** should receive a PCV13 dose at least 1 year after the most recent dose of PPSV23. A second dose of PPSV23 should be given at least one year after the PCV13, so long as it is at least five years after the first dose of PPSV23.
- **Patients ≥ 65 who have received PPSV23 after age 65, but not PCV13,** should receive a PCV13 dose at least 1 year after the most recent dose of PPSV23.
- **Patients who received ≥ 1 dose of PPSV23 before age 65** should receive one additional dose at age 65 or later—at least 8 weeks after the PCV13 dose and at least 5 years after the previous PPSV23 dose.

> ★ ***PNEUMOCOCCAL VACCINES:***
> *If CD4 count is <200 cells/µL at the time of the vaccination, the vaccine may be less effective. Consider administering PPSV23 ≥ 8 weeks after PCV13, as described above, once the CD4 count increases to >200 cells/µL in response to ART.*

- **TETANUS AND DIPHTHERIA TOXOID (TD) AND TETANUS, DIPHTHERIA, AND PERTUSSIS (TDAP)**
  Adults with an unknown or incomplete history of completing a 3-dose primary Td-containing vaccination series should begin or complete the series, including one dose of Tdap.
  - **For unvaccinated adults**, administer the first 2 doses at least 4 weeks apart, and the third dose 6–12 months after the second dose. For incompletely vaccinated adults, administer remaining doses.
  - **Vaccinated persons** who have not received the Tdap vaccine or whose Tdap vaccine status is unknown should receive a single, one-time dose of Tdap. Tdap can be administered regardless of interval since the most recent tetanus or diphtheria-toxoid containing vaccine.
  - Boost with Td every 10 years.

- **HUMAN PAPILLOMAVIRUS (HPV)**
  Recommended for HIV-infected females and males, age 13–26, who did not get any or all doses when they were younger. Quadrivalent HPV vaccine is recommended. HPV vaccination is given in a series of three doses at 0, 1 to 2, and 6 months.

- **LIVE VACCINES**

  Varicella, zoster, and MMR vaccines are all contraindicated for patients with severe immunosuppression (CD4 counts <200 cell/µL) and during pregnancy.

  - **Measles, mumps, and rubella vaccine (MMR):** Recommended for adults with newly diagnosed HIV infections who are without acceptable evidence of measles, rubella, or mumps immunity. Two doses of MMR vaccine, given at least 28 days apart, are recommended unless patient has evidence of severe immunosuppression.
  - **Measles, mumps, rubella, and varicella (MMRV) combination vaccine:** Not recommended in HIV-infected patients, as it has not been studied in this population.
  - **Varicella:** All adults without *evidence of immunity* (as defined below) should receive 2 doses of single-antigen varicella vaccine, or a second dose if they have received only 1 dose.

    Evidence of immunity:
    - Documentation of 2 doses of varicella vaccine at least 4 weeks apart, *or*
    - U.S.-born before 1980, except for pregnant women, *or*
    - History of varicella or herpes zoster, based on diagnosis or verification of disease by a health care provider, *or*
    - Laboratory evidence of immunity or laboratory confirmation of disease.
  - **Zoster:** It is not yet clear which HIV-infected individuals at what age should receive the zoster vaccine.

RECOMMENDED IMMUNIZATIONS FOR SOME HIV-POSITIVE ADULTS

Refer to the CDC Immunization Schedule, *Vaccines That Might be Indicated for Adults Based on Medical and Other Indications*, and the ACIP recommendations available online and in printable PDF format at:

http://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html
http://www.cdc.gov/vaccines/acip/

TREATMENT PLAN AND SUBSPECIALTY REFERRALS

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).

> ***REGIONAL HIV CLINICAL PHARMACIST CONSULTANTS*** *are available to consult with providers on the proper care of HIV patients. Providers are encouraged to utilize these pharmacists when establishing a treatment plan, initiating or changing antiretroviral therapy, assessing possible treatment failure, etc. These pharmacists perform a quarterly review of all patients taking ART, with treatment recommendation being forwarded to the appropriate providers. Providers are encouraged to review these recommendations and adjust therapy as appropriate.*

4. PERIODIC MEDICAL EVALUATIONS FOR HIV-INFECTED INMATES

HIV-infected patients appear to have a higher risk of certain medical conditions compared to the general population. These include metabolic complications (e.g., dyslipidemia, diabetes mellitus, bone disease), neuropsychiatric disorders, certain malignancies, and certain coinfections. These may be associated with the HIV-infection itself, risk factors prevalent in HIV-infected populations, or the use of ART.

To reduce chronic non-AIDS morbidity and mortality, care of HIV-positive patients must focus on: (1) maintaining ART-mediated viral suppression; **(2)** addressing strategies to reduce risk factors (e.g., smoking cessation, healthy diet, and exercise); and **(3)** managing chronic comorbidities such as hypertension, hyperlipidemia, chronic kidney disease, and diabetes.

➜ *Guidelines regarding periodic medical evaluations are provided in Appendix 4b.*

➜ *For additional guidance, see the following:*

Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. First published online November 13, 2013.
Available at: http://cid.oxfordjournals.org/content/early/2013/11/12/cid.cit665.full

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. Updated April 16, 2015.
Available at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0

MONITORING FOR POTENTIAL COMPLICATIONS

Optimal care of the HIV-infected patient requires knowledge about and evaluation for potential complications:

- Patient interviews and physical examinations targeting the diagnosis of complications of HIV infection associated with suppression of T cell-mediated immunity and the primary disorders likely resulting from the direct effects of the virus (e.g., HIV-associated neurocognitive disorder, peripheral polyneuropathy, musculoskeletal impairments, malignancies).

  ➜ *See the DHHS guidelines at*: *https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/0*

- Dental referrals for co-management should continue with any new oral manifestation.
- Evaluation and follow-up for both AIDS-defining- and non-AIDS-defining complications, such as HIV-associated kidney disease, liver disease, cardiovascular disease (CVD), neurologic complications, and malignancies.
- CVD evaluations should include risk assessments and monitoring for hyperlipidemia.

  ➜ *Use the DAD risk assessment tool, available at:* *http://www.hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/eid/0/lid/0/Default.aspx*

PERIODIC LABORATORY AND DIAGNOSTIC STUDIES

A number of periodic laboratory tests are important during follow-up for evaluating HIV-infected patients, as follows:

- If ART is not initiated.
- Before and after initiation of therapy, or modification of therapy, to assess the virologic and immunologic efficacy of ART.
- To monitor for laboratory abnormalities that may be associated with ARV drugs.

Two surrogate markers are used routinely to assess immune function and level of HIV viremia: CD4 count and plasma HIV RNA (viral load), respectively.

Resistance testing should be used to guide selection of an ARV regimen. A viral tropism assay should be performed before initiation of a CCR5 coreceptor antagonist, or at the time of virologic failure that occurs while a patient is receiving a CCR5 antagonist. HLAB* 5701 testing should be performed before initiation of abacavir (ABC).

➜ *See Appendix 4b, which outlines the 2016 DHHS recommendations on the frequency of testing. As noted in that table, some tests may be repeated more frequently if clinically indicated.*

5. 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 count) to prevent acute illnesses that may require hospitalization. Prophylaxis should be prescribed in accordance with the most recent DHHS recommendations.

➜ **Pneumocystis jiroveci[2] *pneumonia (PCP),* Toxoplasma gondii*-associated encephalitis, and disseminated infection with* Mycobacterium avium *complex (MAC):*** *For recommendations for initiating prophylaxis for these infections, see* *Appendix 7, Prophylaxis for HIV Related Opportunistic Infections*.

Primary prophylaxis for OTHER opportunistic infections should be initiated as indicated below:

- **PROPHYLAXIS FOR LATENT TUBERCULOSIS INFECTION (LTBI):**
  Persons with HIV infection who are exposed to *M. tuberculosis* have a high risk of developing active TB disease. Treatment of LTBI is indicated for HIV-positive inmates who have tuberculin skin test results of 5 millimeters or greater, or positive Interferon-Gamma Release Assay (IGRA), e.g., QuantiFERON®-TB Gold In-Tube. In addition, inmates who are close contacts of a contagious TB case require treatment for latent TB, regardless of their tuberculin skin test measurement. Immune reconstitution with ART may result in unmasking of LBTI, resulting in the conversion of a previously negative tuberculin skin test to a positive result. Patients with a negative tuberculin skin test and advanced HIV disease (i.e., CD4 count <200 cells/µL) should have a repeat test after initiation of ART and CD4 count increase to >200 cells/µL.

  The preferred treatment regimen for LTBI is as follows:

  - Isoniazid (300 mg) daily by mouth, administered under direct observation for 9 months.
  - Pyridoxine (usually 50 mg per dose of isoniazid).
  - Baseline liver transaminases tests with monthly assessments for clinical signs and symptoms of hepatotoxicity. Regular monitoring is required only if the inmate is at high risk for hepatotoxicity.
  - Rifapentime is NOT recommended due to concerns of multiple ART drug interactions.

  ➜ *For more complete information, see the LTBI section in the BOP Clinical Practice Guidelines for Management of Tuberculosis, available at: http://www.bop.gov/resources/health_care_mngmt.jsp.*

- **PROPHYLAXIS FOR CYTOMEGALOVIRUS (CMV)**
  Primary prophylaxis for CMV infection with oral valgancyclovir is not routinely indicated, despite severe immunosuppression (CD4 count <50 cells/µL) and positive CMV IgG titers. Although oral valgancyclovir has efficacy as a prophylactic agent, valgancyclovir treatment does not increase survival, may promote CMV resistance, and requires a significant pill burden for the patient.

[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.

- **PROPHYLAXIS FOR 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 count <100 cells/µL) 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 DHHS guidelines.

➜ *Specific recommendations for discontinuing prophylaxis for* Pneumocystis jiroveci *pneumonia (PCP),* Toxoplasma gondii-*associated encephalitis, and disseminated infection with* Mycobacterium avium *complex (MAC) are outlined in* *Appendix 7**. Please note that prophylaxis for LTBI is a standard 9-month course.*

- **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 count increases to >100 cells/µL 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 count decreases to <100 cells/µL.

- **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 who have received at least one year of maintenance therapy and whose CD4 count increases to ≥100 cells/µL for at least 3 months in response to ART. Reinitiate fluconazole if the CD4 count declines to <100 cells/µL.
  - **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/µL for >6 months in response to ART; and **(4)** Serum histoplasma antigen <2 units. Reinitiate itraconazole if CD4 count declines to <150 cells/µL.
  - **Coccidioidomycosis:** Inmates with prior diffuse pulmonary, disseminated non-meningeal, or meningeal diseases, ordinarily require indefinite suppressive therapy with either oral fluconazole (400 mg daily) or oral itraconazole (200 mg twice daily). Inmates with only focal coccidioidal pneumonia can discontinue secondary prophylaxis with clinical response to ≥12 months antifungal therapy, with CD4 count >250 cells/µL, and receiving ART. However, monitoring for recurrence should continue with serial chest radiographs and coccidioidal serology.

➜ *Addition information on treating patients diagnosed with OIs related to HIV infection is available from current DHHS guidelines, available at: http://www.aidsinfo.nih.gov/guidelines/.*

6. INITIATING ART IN TREATMENT-NAÏVE PATIENTS

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, all of which are important treatment goals.

- Deferring ART until CD4 count declines puts an individual at risk of AIDS-defining conditions and has been associated with higher risk of morbidity and mortality.
- High plasma HIV RNA is a major risk factor for HIV transmission; effective ART can reduce viremia and transmission of HIV to sexual partners by more than 96%.

PRIMARY GOALS FOR INITIATING ART:

★ To prevent HIV-associated morbidity and prolong the duration and quality of survival.

★ To restore and preserve immunologic function.

★ To maximally and durably suppress plasma HIV viral load.

★ To prevent HIV transmission.

Achieving viral suppression requires the use of ARV regimens with three active drugs from two or more drug classes. Baseline resistance testing and patient characteristics should guide the specific regimen design. All currently recommended initial ARV regimens for the treatment naïve patient include three active drugs. 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.

➜ *The increasing number of drugs and drug classes makes viral suppression below detection limits an appropriate goal in all patients.*

Viral load reduction to below detection limits in ART-naïve patients usually occurs within the first 8–24 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.

Sustaining viral suppression and maintaining higher CD4 count levels—mostly as a result of effective combination ART—may delay, prevent, or reverse some non-AIDS-defining complications such as HIV-associated kidney disease, liver disease, CVD, neurologic complications, and malignancies.

RECOMMENDATIONS FOR INITIATING THERAPY

ART is recommended by DHHS for all HIV-infected patients to reduce the risk of disease progression and to prevent transmission of HIV. Regardless of CD4 count, the decision to initiate ART should always include consideration of a patient's comorbid conditions, his or her willingness and readiness to initiate therapy, and available resources.

CONDITIONS FAVORING MORE URGENT INITIATION OF THERAPY:

- *Pregnancy*
- *AIDS-defining conditions*
- *Acute opportunistic infections (OIs)*
- *Lower CD4 counts (<200 cells/µL)*
- *HIV-associated nephropathy (HIVAN)*
- *Acute/early HIV infection*
- *HIV/HBV coinfection*
- *Rapidly declining CD4 counts (>100 cells/µL decrease per year)*
- *Higher viral loads (>100,000 cps/mL)*

For some asymptomatic patients, the potential risks of short- or long-term drug-related complications—as well as non-adherence to long-term therapy—may offset the benefits of early initiation of therapy. Some asymptomatic patients may choose to postpone therapy; providers, on a case-by-case basis, may elect to defer therapy based on clinical and/or psychosocial factors.

HIV GENOTYPIC 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 for guiding therapy in ARV-naïve patients.

- *Phenotypic or combination phenotype/genotype (Phenosense GT) is NOT generally recommended without expert consultation.*
- *Drug-resistance testing should also be performed when managing suboptimal viral load reduction, i.e., failure to maintain viral load of <200 cps/mL. Successful resistance testing generally require a viral load of >500 cps/mL.*

7. INITIAL COMBINATION REGIMENS FOR THE ART-NAÏVE PATIENT

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. The DHHS guidelines are available at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0.*

➜ *Consultation with a regional HIV clinical pharmacist consultant or other HIV expert is required prior to selecting ART not listed in the DHHS guidelines as a preferred or alternate regimen for ARV-naïve patients.*

GENERAL CONSIDERATIONS WHEN SELECTING AN INITIAL ARV REGIMEN

INSTI *= integrase strand transfer inhibitor;* ***NNRTI*** *= non-nucleoside reverse transcriptase inhibitor;*
NRTI *= nucleoside reverse transcriptase inhibitor;* ***PI*** *= protease inhibitor*

➜ *See Appendix 8 for advantages and disadvantages of ARV components used in initial ART.*

➜ *See Appendix 9 for information on dosing of ARV drugs in adults with chronic kidney disease and hemodialysis.*

- **INITIAL THERAPY** generally consists of two ***NRTIs*** combined with an ***INSTI***, a pharmacologically boosted ***PI***, or an ***NNRTI*** (alternative regimen).
  - The ***NRTI*** combination in all recommended and alternative regimens is either tenofovir/emtricitabine or abacavir/lamivudine.
  - The choice of an ***INSTI***, an ***NNRTI***, or a ***PI*** as the third drug in an initial ARV regimen should be guided by the regimen's efficacy, genetic barrier to resistance, adverse effects profile, and convenience; the patient's comorbidities; and the patient's concomitant medications and the potential for drug-drug interactions.

- **POSSIBLE DRUG-DRUG INTERACTIONS** should be taken into consideration when selecting an ARV regimen. Several ARV medications have been identified as inducers, inhibitors, and/or substrates of the hepatic cytochrome P450 enzyme system, frequently responsible for clinically significant drug interactions. A detailed review of concomitant medications is vital to creating a regimen that minimizes undesirable interactions. The potential for drug interactions should be assessed when initiating ARV therapy—or when any new drug (including over-the-counter agents) is added to an existing regimen.

RECOMMENDED INITIAL REGIMENS

➔ *The DHHS guidelines provide tables listing characteristics of the drug classes mentioned below, as well as guidance on selecting regimens for specific clinical scenarios. In addition, the DHHS has included the pharmacokinetic enhancer cobicistat for use in recommended INSTI-based regimens and in alternative PI-based regimens.*

The following regimens have been studied in randomized controlled trials and have been shown to have optimal and durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Given the large number of excellent options for initial therapy, selection of a regimen for a particular patient should be guided by factors such as virologic efficacy, toxicity, pill burden and dosing frequency, the potential for drug-drug interaction, the patient's resistance testing results and comorbid conditions, and cost.

➔ ***Prescribers should consult with the institution pharmacist or regional HIV clinical consultant pharmacist in selecting the most cost-effective, patient specific option.***

INSTI-BASED REGIMENS

INSTI-based regimens are recommended because of their high virologic efficacy and their excellent safety and tolerability profiles.

- **RALTEGRAVIR** 400 mg (*twice daily)* **+ TENOFOVIR** 300mg **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Low number of drug-drug interactions.*

- **ELVITEGRAVIR** 150 mg **/ COBICISTAT** 150 mg / **TENOFOVIR** 300 mg (disoproxil TDF) **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Only for patients with pre-ART CrCl >70 mL/min. Must be taken with food.*

- **ELVITEGRAVIR** 150 mg **/ COBICISTAT** 150 mg / **TENOFOVIR** 10 mg (alafenamide TAF) **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Only for patients with pre-ART CrCl >30 mL/min. Must be taken with food.*

- **DOLUTEGRAVIR** 50 mg **/ ABACAVIR** 600 mg **/ LAMIVUDINE** 300 mg (*once daily)*
  - *Low number of drug-drug interactions.*
  - *Only for patients who are HLA-B 5701 negative. Positive status should be recorded as an allergy to abacavir.*

- **DOLUTEGRAVIR** 50 mg **+ TENOFOVIR** 300 mg **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Low number of drug-drug interactions*.

PI-BASED REGIMENS

A PI-based regimen may be preferred for patients who are at high risk for intermittent therapy because of poor adherence or who have shown NRTI drug resistance. PI-based treatment is also preferred for patients who must start ART before the genotype is available, due to a relatively high genetic barrier to resistance.

- **DARUNAVIR** 800 mg **+ RITONAVIR** 100 mg **+ TENOFOVIR** 300 mg **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Must be taken with food.*

ALTERNATIVE INITIAL REGIMENS

The following regimens are effective and tolerable, but have potential disadvantages, limitations for use in certain patient populations, or less supporting data than ***recommended regimens***. In certain situations, depending on individual patient characteristics and needs, an ***alternative regimen*** may actually be the optimal and preferred regimen for a specific patient.

➜ *Patients who are doing well on a particular alternative regimen should NOT generally be switched to other agents.*

NNRTI-BASED REGIMENS

- **EFAVIRENZ** 600 mg **/ TENOFOVIR** 300 mg **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Reclassified due to the high rate of central nervous system (CNS)-related toxicities and a possible association with suicidality with efavirenz. Efavirenz may exacerbate psychiatric illness.*

- **RILPIVIRINE** 25 mg / **TENOFOVIR** 300 mg / **EMTRICITABINE** 200 mg (*once daily)*
  - *Only for patients with pre-treatment HIV RNA <100,000 cps/mL and CD4 count >200 cells/µL.*
  - *Must be taken with food.*
  - *Contraindicated in patients receiving proton pump inhibitors.*
  - *Smaller tablet size offers better tolerance than efavirenz.*

PI-BASED REGIMENS

- **ATAZANAVIR** 300 mg **+ RITONAVIR** 100 mg **+ TENOFOVIR** 300 mg **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Greater rate of discontinuation due to toxicities, when compared to darunavir or raltegravir.*
  - *Must be taken with food.*

- **DARUNAVIR** 800 mg **+ RITONAVIR** 100 mg **+ ABACAVIR** 600 mg **/ LAMIVUDINE** 300 mg (*once daily)*
  - *Only for patients who are HLA-B5701 negative.*
  - *Must be taken with food*.

- **DARUNAVIR** 800 mg **/ COBICISTAT** 150 mg **+ TENOFOVIR** 300 mg **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Only for patients with pre-treatment estimated CrCl >/ 70 mL/min.*
  - *Must be taken with food.*

- **ATAZANAVIR** 300 mg **/ COBICISTAT** 150 mg **+ TENOFOVIR** 300 mg **/ EMTRICITABINE** 200 mg (*once daily)*
  - *Only for patients with pre-treatment estimated CrCl >/ 70 mL/min.*
  - *Must be taken with food.*

- **DARUNAVIR** 800 mg **/ COBICISTAT** 150 mg **+ ABACAVIR** 600 mg **/ LAMIVUDINE** 300 mg (*once daily)*
  - *Only for patients who are HLA-B5701 negative.*
  - *Must be taken with food*.

PREFERRED REGIMENS FOR PREGNANT WOMEN

➜ *Please refer to the DHHS Perinatal Guidelines at: http://www.aidsinfo.nih.gov/guidelines/.*

INITIAL ARV REGIMEN THERAPY: CONSIDERATIONS BASED ON CLINICAL SCENARIOS

Table 4 is designed to guide clinicians in choosing an initial ARV regimen according to various patient and regimen characteristics and specific clinical scenarios.

- When more than one scenario applies to a patient, clinicians should review considerations for the relevant scenarios and select the most appropriate regimen.
- However, if a patient is doing well on a particular regimen, it is not generally necessary to switch to another regimen based on the scenarios outlined in the table.

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. The most up-to-date DHHS guidelines are available at:* *https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0*

TABLE 4. INITIAL ARV REGIMEN CONSIDERATIONS BASED ON SPECIFIC CLINICAL SCENARIOS

PATIENT/REGIMEN CHARACTERISTICS	CLINICAL SCENARIO	CONSIDERATION(S)	RATIONALE/COMMENTS
Pre-ART Characteristics	CD4 count <200 cells/µL	***Do not use the following regimens:*** • RPV-based regimens	Higher rate of virologic failure observed in those with low pre-treatment CD4 cell count.
	HIV RNA >100,000 cps/mL	***Do not use the following regimens:*** • RPV-based regimens • ABC/3TC with EFV or ATV/r	Higher rates of virologic failure observed in those with high pre- treatment HIV RNA.
	HLA-B*5701 positive	***Do not use ABC-containing regimen.***	Abacavir hypersensitivity, a potentially fatal reaction, is highly associated with positivity for the HLA-B*5701 allele.
	Must treat before HIV drug resistance results are available	***Avoid NNRTI-based regimen.***	Transmitted mutations conferring NNRTI resistance are more likely than mutations associated with PI or INSTI resistance.
	CrCl <70 ml/min	***Avoid coformulation regimens containing TDF.***	TDF has been associated with renal tubulopathy.
	CrCl <50 ml/min	***Avoid coformulation regimens containing 3TC.***	3TC requires dose adjustment.
	CrCl <30 ml/min	***Avoid coformulation regimens containing FTC.***	Dosage adjustment required.

(Table 4 continues on next page. See KEY TO ACRONYMS at the end of the table.)

PATIENT/REGIMEN CHARACTERISTICS	CLINICAL SCENARIO	CONSIDERATION(S)	RATIONALE/COMMENTS
ART-Specific Characteristics	One-pill, once-daily regimen desired	***ART options include:*** • DTG/ABC/3TC • EFV/TDF/FTC • EVG/c/TDF/FTC • EVG/c/TAF/FTC • RPV/TDF/FTC *(if HIV RNA <100,000 cps/mL and CD4 count >200/µL)*	Available as fixed-dose combination tablets.
	ARV regimens that must be taken with food	***ART options include:*** • ATV/r or ATV/c-based regimens • DRV/r or DRV/c-based regimens • EVG/c/TDF/FTC • EVG/c/TAF/FTC • RPV/TDF/FTC	
Presence of Coinfections	HBV infection *(Hepatitis B algorithm completion/non-formulary approval required)*	***Use TDF/FTC (or TDF plus 3TC) whenever possible.*** ***If TDF is contraindicated:*** • For treatment of HBV, use FTC or 3TC with entecavir or another drug active against HBV	TDF, FTC, and 3TC are active against both HIV and HBV. However, 3TC- or FTC-associated HBV mutations can emerge rapidly when these drugs are used without another HBV- active agent.
	HCV treatment required	Refer to recommendations for *Hepatitis C/HIV Coinfection* in Section 12.	
	TB infection	***If rifampin is used:*** • EFV-based regimens have the least drug- drug interactions. • If RAL is used, increase RAL dose to 800 mg BID. • Use DTG at 50 mg BID dose ***only*** in patients without selected INSTI mutations (refer to product label). • If using a PI-based regimen, rifabutin should be used in place of rifampin in the TB regimen.	• Rifampin is a strong inducer of CYP3A4 and UGT1A1 enzymes, causing significant decrease in concentrations of PI, INSTI, and RPV. • Rifampin has a less significant effect on EFV concentration than on other NNRTIs, PIs, and INSTIs. • Rifabutin is a less potent inducer and is a good option for patients receiving non- EFV-based regimens.

***KEY TO ACRONYMS*:**
3TC = lamivudine; **ABC** = abacavir; **ATV/r** = ritonavir-boosted atazanavir; **ARV** = antiretroviral; **c** = cobicistat; **CKD** = chronic kidney disease; **CrCl** = creatinine clearance; **DRV/r** = ritonavir-boosted darunavir; **DTG** = dolutegravir; **eGFR** = estimated glomerular filtration rate; **EFV** = efavirenz; **EVG/c/TDF/FTC** = elvitegravir/cobicistat/tenofovir/emtricitabine; **FDA** = Federal Drug Administration; **FTC** = emtricitabine; **HBV** = hepatitis B virus; **HCV** = hepatitis C virus; **INSTI** = integrase strand transfer inhibitor; **LPV/r** = ritonavir-boosted lopinavir; **NNRTI** = non-nucleoside reverse transcriptase inhibitor; **NRTI** = nucleoside reverse transcriptase inhibitor; **PI** = protease inhibitor; **PI/r** = ritonavir-boosted protease inhibitor; **RAL** = raltegravir; **RPV** = rilpivirine; **RTV** = ritonavir; **TDF** = tenofovir disoproxil fumarate

ADAPTED FROM: Table 7, 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, AIDS info Web site*. Updated April 8, 2015. Available at: *https://aidsinfo.nih.gov/contentfiles/lvguidelines/AA_Tables.pdf*

8. Management of the Treatment-Experienced Patient

Assessment of Virologic Failure

Virologic failure is the inability to achieve or maintain suppression of viral replication to an HIV RNA level <200 cps/mL within 8 to 24 weeks of starting a new regimen. It is important to determine the reasons for a patient's virologic failure, because the approaches to therapy will differ. **The following potential causes of a patient's virologic failure should be explored in depth:**

- **Adherence**
  Assess the patient's adherence to the regimen and address the underlying causes for lack of adherence. Simplify the regimen if possible.
- **Medication intolerance**
  Assess the patient's tolerance of the current regimen and consider the following management strategies:
  - Treating the symptoms (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 supplements resulting in drug interaction; make appropriate substitutions.
  - Changes in hepatic or renal functions.

  ➔ *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 is discontinued if the plasma HIV RNA level is >500 cps/mL.
  - A standard genotypic resistance assay is generally preferred for patients experiencing virologic failure on their first or second regimens. Phenotype should be done with expert consultation.
  - Evaluate the degree of drug resistance from the current resistance test, with the 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.
  - In persons failing INSTI-based regimens, additional genotypic testing for INSTI resistance should be performed to determine whether to include a drug from this class in subsequent regimens.
  - A phenotypic assay may be preferred in patients with known or suspected complex drug-resistance patterns, particularly to PIs.
  - The Stanford University HIV Drug Resistance Database provides helpful guidance for interpreting genotypic resistance test results.
    ➔ *See http://sierra2.stanford.edu/sierra/servlet/JSierra.*

  ➔ *If no drug resistance is identified, a "failing regimen" is almost always associated with suboptimal adherence.*

The time required (8 to 24 weeks) for viral load to reach <20 cps/mL (viral suppression) after a change in ART, and the interpretation of viral response to ART, will vary based on interpatient variability and/or viral characteristics. *Clinicians should use good clinical judgement in assessing effectiveness of new ART. Samples of two clinical scenarios are described below*:

1) A treatment-experienced patient is started on new ART, based on genotype results, and within 8 weeks achieves an undetectable viral load. Eight weeks later, the patient is found to have a viral load of 2500 cps/mL; adherence to ART is >90%. It is likely that this patient was harboring an undetected resistant viral strain prior to the treatment change, and ART should NOT be continued for the above-mentioned 24 weeks. The virus will not be suppressed with current ART. Resistance testing should be ordered, and ART adjusted again based on genotype results.

2) Another treatment-experienced patient is started on new ART, based on genotype results, and experiences a one-log drop in viral load within the first 8 weeks. Eight weeks later, the patient experiences another one-log drop, but has not reached undetectable levels. It is reasonable to continue current ART for another 8 weeks (total of 24 weeks) in an attempt to achieve viral suppression.

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.
- Drug resistance does not appear to occur in patients with persistent HIV RNA levels suppressed to ≤50 cps/mL.
- Persistent HIV RNA levels >200 cps/mL often are associated with evidence of viral evolution and drug-resistance mutation accumulation. Persistent plasma HIV RNA levels in the 200-1,000 cps/mL range should therefore be considered as virologic failure.
- Viremia "blips" (e.g., viral suppression followed by a detectable HIV RNA level, and then a subsequent return to undetectable levels) usually are not associated with subsequent virologic failure.
- Patients on older regimens with agents that are no longer recommended, due to higher risk of chronic toxicity, may be considered for a switch to recommended and alternative regimens.

MANAGEMENT OF VIROLOGIC FAILURE

➜ For the complete DHHS discussion of virologic failure, including clinical scenarios, see: *https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/15/virologic-failure-and-suboptimal-immunologic-response*

Below is a brief summary of DHHS guidance on managing virologic failure:

- Once virologic failure is confirmed, generally the regimen should be changed as soon as possible to avoid progressive accumulation of resistance mutations.
- A 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 generally 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 from the same class may not mean that the drug is fully active, even if the patient has not previously taken the "new" drug..
- 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-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 count, which increases the risk of clinical progression. Therefore, this strategy is not recommended.

9. 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 improves when the number of daily doses is reduced.

➜ *Review the DHHS Guidelines for suggested candidates for regimen simplification and the types of treatment simplification. See the information available at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/16/regimen-switching-in-the-setting-of-virologic-suppression.*

➜ *ART simplification should normally be done in consultation with a physician who has HIV-treatment expertise and/or with a BOP HIV Clinical Consultant Pharmacist.*

10. Discontinuation or Interruption of ART

Discontinuing ART may result in viral rebound, immune decompensation, and clinical progression.

- An unplanned interruption of ART may become necessary in cases of severe drug toxicity, intervening illness, surgery that precludes oral therapy, or unavailable antiviral medication.
- Discontinuing ART should normally be undertaken in consultation with a physician who has HIV treatment expertise and/or a BOP HIV Clinical Pharmacist.

11. ADVERSE DRUG REACTIONS

Clinicians must carefully consider the toxicity potential of an antiretroviral regimen, as well as the individual patient's underlying conditions, concomitant medication, and prior history of drug intolerances. However, in general, the overall benefits of ART outweigh its risks. Furthermore, some conditions not related to AIDS (e.g., anemia, cardiovascular disease, renal impairment) may be more likely in the absence of ART.

Prior to prescribing or changing antiretroviral therapy, review the DHHS guidelines[3] 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.
  - ➜ *See Table 5, Adverse Effects Associate with Commonly Used Antiretroviral Classes, below.*
  - ➜ *See also Appendix 8 for disadvantages of ARV components used in initial ART.*
- Rates of treatment-limiting adverse events in ART-naïve patients enrolled in randomized trials appear to be declining with the newer ARV regimens, and are generally now less than 10%.

TABLE 5. ADVERSE EFFECTS ASSOCIATED WITH COMMONLY USED ANTIRETROVIRAL CLASSES

ARV CLASS	ADVERSE EFFECTS
NRTIs	• Loss of bone mineral density/renal effects (TDF) • Bone marrow suppression (ZDV) • Cardiovascular disease (ABC) • Diabetes/insulin resistance (ZDV) • Dyslipidemia (ZDV>ABC) • Gastrointestinal effects (ZDV) • Hypersensitivity (ABC: contraindicated if HLA-B 5701 positive)
NNRTIs	• Dyslipidemia (EFV) • Hepatotoxicity/hypersensitivity (NVP) • Nervous system/psychiatric effect (EFV) • Rash (all NNRTIs) • Stevens-Johnson Syndrome (NVP>EFV>ETR>RPV)
PIs	• Associated with MI/stroke in some cohorts (SQV/r, ATV/r, LPV/r) • Cholelithiasis (ATV – median onset is 42 months) • Diabetes/insulin resistance (IDV, LPV/r) • Dyslipidemia (all ritonavir boosted PIs can increase LDL, TG and HDL) • Gastrointestinal effects (LPV/r > DRV/r & ATV/r) • Hepatic effects (has been reported with all PIs; ATV: indirect hyperbilirubinemia) • Renal effects (ATV and LPV/r: increased chronic kidney disease risk)
(Table 5 continues on next page. See KEY TO ACRONYMS at the end of the table.)	

[3] 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. April 8, 2015. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf.

ARV CLASS	ADVERSE EFFECTS
INSTIs	• Dyslipidemia (EVG/c/TDF/FTC: increased TG, LDL, HDL) • Gastrointestinal effects (EVG/c/TDF/FTC: nausea and diarrhea) • Elevated creatine phosphokinase (RAL) • Insomnia (all INSTIs)

KEY TO ACRONYMS:
3TC = lamivudine; **ABC** = abacavir; **ATV** = atazanavir; **c** = cobicistat; **DRV** = darunavir; **EFV** = efavirenz; **ETR** = etravirine; **EVG/c/TDF/FTC** = elvitegravir/cobicistat/tenofovir/emtricitabine; **FTC** = emtricitabine; **IDV** = indinavir; **INSTI** = integrase strand transfer inhibitor; **LPV** = lopinavir; **NNRTI** = non-nucleoside reverse transcriptase inhibitor; **NRTI** = nucleoside reverse transcriptase inhibitor; **NVP** = nevirapine; **PI** = protease inhibitor; **RAL** = raltegravir; **RPV** = rilpivirine; **r** = ritonavir; **SQV** = saquinavir; **TDF** = tenofovir; **ZDV** = zidovudine

ADAPTED FROM:
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. (Table 14. Antiretroviral Therapy-Associated Common and/or Severe Adverse Effects.) Department of Health and Human Services. February 9, 2016.
Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf.

12. CONSIDERATIONS FOR ARV USE IN PATIENTS WITH COINFECTIONS

HEPATITIS B/HIV COINFECTION

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. *Conversely*, chronic HBV does not substantially alter the progression of HIV infection and does not influence HIV suppression or CD4 cell responses following ART initiation.

The DHHS guidance on HBV/HIV coinfection is summarized below:

➜ *Review the DHHS Guidelines for additional information.*

- **Prior to initiation of ART**, all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for HBV DNA using a quantitative assay to determine the level of HBV replication.
- **All patients with chronic HBV** should be assessed for immunity to HAV infection (anti-HAV antibody total) and vaccinated if nonimmune.
- Emtricitabine (FTC), lamivudine (3TC), and tenofovir (TDF) each have activity against both HIV and HBV**.** Therefore, if HBV or HIV treatment is needed—
  - **Preferred regimen:** ART should be initiated with the combination of TDF + FTC *or* TDF + 3TC as the NRTI backbone of a fully suppressive ARV regimen, as well as for treating the HBV infection.
  - **Alternative regimens:** If TDF cannot be used safely, a different fully suppressive ARV regimen should be used along with entecavir for treating the HBV infection.
- **HBV DNA testing** should be done every 6–12 months to determine the effectiveness of therapy in suppressing HBV replication. Refer to BOP HBV Clinical Practice Guideline (CPG) for recommended monitoring schedule following initiation of HBV treatment.
- **If ART needs to be modified due to HIV virologic failure**—and the patient has adequate HBV suppression—the ARV drugs being used successfully against HBV should be continued, but combined with other suitable ARV agents to achieve HIV suppression.

HEPATITIS C/HIV COINFECTION

The management of HCV-infected patients is rapidly evolving as new drug regimens become approved. Practitioners are encouraged to refer regularly to the frequently updated HCV website (*www.hcvguidelines.org*) sponsored by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). The BOP Central Office Medical staff continues to monitor the website and provide revised guidance as necessary.

➜ *Consult the latest version of the BOP Clinical Practice Guidelines on Evaluation and Management of Chronic Hepatitis C Virus (HCV) Infection at: http://www.bop.gov/resources/health_care_mngmt.jsp.*

➜ *Prioritization for treatment of HCV in HIV/HCV-coinfected patients should follow the policies described in the BOP HCV guidelines.*

➜ *Data suggest that HIV/HCV-coinfected patients treated with all-oral HCV regimens have sustained virologic response rates comparable to those of HCV-monoinfected patients.*

DHHS GUIDANCE

The DHHS guidance on HBV/HIV coinfection is summarized below:

➜ *Review the DHHS Guidelines for additional information.*

- **All HIV-infected patients should be screened for HCV infection**, preferably before starting ART.
- **ART may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation.** For most HIV/HCV-coinfected patients, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury (DILI). Therefore, ART should be considered for HIV/HCV-coinfected patients, regardless of CD4 count.
- **Drug-induced liver injury following the initiation of ART is more common in HIV/HCV-coinfected patients than in those with HIV monoinfection.** The greatest risk of DILI may be observed in coinfected individuals with advanced liver disease (e.g., cirrhosis or end-stage liver disease). Eradication of HCV infection with treatment may decrease the likelihood of ARV-associated DILI.
- **Mild to moderate fluctuations in ALT and/or AST are typical in individuals with chronic HCV infection.** In the absence of signs and/or symptoms of liver disease or increases in bilirubin, these fluctuations do not warrant interruption of ART.
- **In patients with lower CD4 counts (e.g., <200 cells/µL), it may be preferable to initiate ART and delay HCV therapy** until the patient is stable on HIV treatment.

CONCURRENT TREATMENT OF HIV AND HCV

Initial ART combination regimens for most HIV/HCV-coinfected patients are the same as those for individuals without HCV infection. However, when treatment for both HIV and HCV is indicated, consideration of potential drug-drug interactions and overlapping toxicities should guide ART regimen selection or modification. See ***Table 6*** below.

➜ *Refer to the BOP Guidelines on Evaluation and Management of Chronic Hepatitis C Virus (HCV) Infection for more information on specific drug interactions.*

TABLE 6. CONSIDERATIONS IN CONCURRENT TREATMENT OF HIV AND HCV

MEDICATION	CONSIDERATIONS
Didanosine (DDI)	• Should not be given with RBV because of the potential for drug-drug interactions.
Zidovudine (ZDV)	• Use with RBV should be avoided when possible because of higher rates of anemia.
Abacavir (ABC)	• Has been associated with decreased response to peginterferon plus RBV in some, but not all, retrospective studies; current evidence is insufficient to recommend avoiding this combination.
Growth Factors ***(e.g., filgrastim, erythropoietin)***	• May be required to manage interferon-associated neutropenia and RBV-associated anemia.
Sofosbuvir (SOF)	• Can be used with most ART agents except TPV, which lowers SOF levels.
Simeprevir (SMV)	• Can be coadministered with RAL, DTG, RPV, 3TC, FTC, ABC, MVC, and TDF. • Coadministration is **NOT** recommended with EFV, ETR, HIV PIs, cobicistat, or EVG/c/TDF/FTC.
Ledipasvir (LDV) ***(currently coformulated with SOF)***	• Can be co-administered with ABC, DTG, EFV, FTC, 3TC, RAL, and RPV. • Boosted PIs (except for TPV) can also be co-administered with LDV/SOF when TDF is excluded from ART. • LDV increases TDF levels, which are further increased when combined with RTV-boosted PIs and cobicistat-containing regimens. Thus, LDV/SOF should be avoided when TDF is combined with boosted (RTV or cobicistat) PIs or with EVG/c/TDF/FTC. • When LDV/SOF is co-administered with other TDF-containing regimens, renal function should be closely monitored for TDF toxicity. Patients at high risk for renal toxicity (CrCl <60ml/min or evidence of Fanconi syndrome) should generally **NOT** use TDF-containing regimens. TAF may be an alternative to TDF during LDV/SOF treatment for patients who take EVG/c or boosted PIs as part of their ART. • Co-administration with ZDV and DDI should also be avoided.
Daclatasvir (DCV)	• Dose adjustments are necessary when co-administered with some ARVs. • DCV dose is decreased to 30 mg daily when co-administered with indinavir, nelfinavir, saquinavir, or RTV-boosted ATV, or with any cobicistat-containing regimens except darunavir. • DCV dose is increased to 90 mg daily when coadministered with EFV or nevirapine. • Pending further data, avoid use with ETR because of the potential for lower DCV levels.
Elbasvir/Grazoprevir (EBR/GZR)	• Can be used with ABC, FTC, 3TC, RAL, DTG, and RPV. • EBR/GZR is contraindicated with EFV, or with HIV PIs, and is not recommended with ETR or EVG/c/FTC/TDF (or EVG/c/FTC/TAF).
Paritaprevir/Ritonavir/ Ombitasvir + Dasabuvir (PrOD)	• Has been safely used with TDF/FTC co-formulation plus RAL or ATV. When used with PrOD, the ATV dose is 300 mg once daily with no additional RTV added during treatment with this HCV regimen. • Based on pathway metabolism extrapolation, ABC, DTG, and 3TC should also be safe for use. • PrOD is not recommended for co-administration with NNRTIs, EVG, MVC, or any of the HIV PIs except ATV.

***KEY TO ACRONYMS*:**
3TC = lamivudine; **ABC** = abacavir; **ATV** = atazanavir; **ARV** = antiretroviral; **ART** = antiretroviral therapy; **c** = cobicistat; **CrCl** = creatinine clearance; **DTG** = dolutegravir; **EFV** = efavirenz; **ETR** = etravirine; **EVG** = elvitegravir**;** **FTC** = emtricitabine; **HCV** = hepatitis C virus; **MVC**= maraviroc; **NRTI** = nucleoside reverse transcriptase inhibitor; **PI** = protease inhibitor; **RAL** = raltegravir; **RBV** = ribavirin; **RPV** = rilpivirine; **RTV** = ritonavir; **TAF** = tenofovir alafenamide fumarate; **TDF** = tenofovir disoproxil fumarate; **TPV** = tipranavir

TUBERCULOSIS/HIV COINFECTION

HIV infection significantly increases the risk of progression from latent to active TB disease. The CD4 count influences both the frequency and severity of active TB disease. Similarly, active TB may be associated with a higher HIV viral load and more rapid progression of HIV disease. Active pulmonary or extrapulmonary TB disease requires prompt initiation of TB treatment. Management of HIV-related tuberculosis is complex and requires consultation with experts in the management of both HIV disease and tuberculosis.

➜ *The treatment of active TB disease in HIV-infected patients should follow the guidance provided in the most recent BOP Clinical Practice Guidelines on the Management of Tuberculosis, available at http://www.bop.gov/resources/health_care_mngmt.jsp.*

13. IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

The term *immune reconstitution inflammatory syndrome* (IRIS) describes a collection of inflammatory disorders associated with paradoxical worsening of the symptoms of preexisting infections in HIV-positive individuals following the initiation of ART. The presumed mechanism is qualitative and quantitative recovery of pathogen-specific cellular and humoral response to multiple opportunistic pathogens—primarily mycobacteria, fungi, and viruses.

OCCURRENCE AND DIAGNOSIS

- Preexisting infections in individuals with IRIS may have been previously diagnosed and treated, or they may have been subclinical and later unmasked by the host's regained capacity to mount an inflammatory response, due to ART. This inflammatory reaction is usually self-limited, especially if the preexisting infection is treated effectively. However, in rare cases, long-term sequelae and fatal outcomes may occur, particularly when neurologic structures are involved.
- Most patients with IRIS develop symptoms within one week to a few months after the initiation of ART. Although it is reasonable to perform studies looking for unmasked subclinical opportunistic infection, the diagnosis of IRIS is generally one of exclusion. Investigations to rule out the possibility of drug reaction, patient noncompliance, persistently active infection, and/or drug resistance are usually warranted before concluding that IRIS is present.

TREATMENT

- Treatment for the underlying pathogen should generally be started or continued in patients who develop IRIS. This is particularly important when treating patients with IRIS associated with HBV.
- Corticosteroids or nonsteroidal anti-inflammatory agents (NSAIDS) may be added to help decrease the inflammatory response in some patients with IRIS. The decision to use corticosteroids should be individualized and should take into account the risks of therapy. Providers may consider initiating prednisone at a dose of 1 mg/kg/day (maximal dose 60–80 mg), and then tapering steroid therapy while monitoring for recurrence of clinical symptoms over the ensuing weeks to months.

  ➜ *Steroid therapy should normally not be used unless or until symptoms of IRIS appear.*

- In the case of underlying infections that have an effective antimicrobial therapy (e.g., PCP, tuberculosis, HBV, and cryptococcosis), it may be possible to avoid IRIS by treating the infection for one to two months prior to initiating ART. However, current evidence shows that in order to decrease the risk of clinical progression to AIDS and possibly death, **initiation of ART should generally not be delayed for more than two weeks after starting treatment of the underlying infection**.

IRIS IN HIV-POSITIVE PATIENTS WITH PREEXISTING TUBERCULOSIS INFECTION

INDICATIONS FOR EARLIER INITIATION OF ART

- As described above, a *minimal* delay in initiating ART (within two to four weeks of starting TB treatment) should be strongly considered for patients with CD4 cell counts from 50–200 cells/µL who have evidence of clinical disease of major severity—as indicated by clinical evaluation, low Karnofsky or Eastern Cooperative Oncology Group (ECOG) performance score, low BMI, low hemoglobin, low albumin, or organ system dysfunction.
- Initiation of ART within two to four weeks of TB treatment also should be considered for patients with CD4 counts >200 cells/µL who present with evidence of severe disease.

OCCURRENCE AND TREATMENT

- IRIS may occur after initiation of ART. Both ART and TB treatment should be continued while managing IRIS. Predictors of IRIS include CD4 count <50 cells/µL; higher on-ART CD4 counts; higher pre-ART and lower on-ART HIV viral loads; severity of TB disease, especially high pathogen burden; and less than 30-day interval between initiation of TB and HIV treatments.
- Most IRIS in HIV/TB disease occurs within three months of the start of TB treatment. Mild or moderately severe IRIS can be managed symptomatically or treated with NSAIDS. Patients with more severe IRIS can be treated successfully with corticosteroids.

➜ *See the discussion above in this section on the use of corticosteroids to treat IRIS*.

14. DENTAL MANAGEMENT

➜ *See Table 7 below for an overview of dental management of HIV-infected patients.*

The provision of dental care to patients with HIV disease should be based on the overall health status of the patient, not solely on HIV status (CD4 counts).[4] A thorough review of a patient's health history should be conducted. Knowing the progression of HIV is important, as there is a broad spectrum of associated diseases and oral manifestations.[5]

➜ ***It is essential that dental staff work collaboratively with medical providers in fostering a team approach to patient care.***

It is important to note that patients may not know their HIV status. Dental providers may be the first health care provider to encounter symptomatic disease. Keen oral health examination, including soft tissue palpation of the head and neck, is important in identifying and managing the effects of this disease. Oftentimes, signs of declining immune status can first be identified in the oral cavity or during the head and neck exam.

- Prompt identification and referral to medical providers facilitates the team management of these patients. Likewise, medical staff should refer HIV inmates to the dental clinic for co-management when oral conditions have been identified at the time of their medical encounters.
- The presence of rampant caries, aggressive periodontal disease, and soft tissue lesions/conditions require attentive treatment management or referral. Frequent periodontal evalutaions—every three to six months—may be warranted for some patients.
- Emphasis on self-care and prevention is critical in this patient population.
- Any prescriptions must be based on careful consideration of the possibility of adverse drug effects.[6]

Pretreatment considerations: There are some general pretreatment considerations for HIV-infected patients. Special attention to medications is particularly important when prescribing antibiotics, as patients may already be on aggressive regimens. Some medications may cause xerostomia, resulting in extensive caries. Patients on long-term antiretroviral medications should be evaluated for neutropenia. Patients with severe neutropenia (absolute neutrophil counts < 500) should be provided prophylactic antimicrobials for all dental procedures.[4,5]

Moreover, it should be noted that the presence of oral lesions in patients who otherwise appear to have responded well to antiviral therapy and have undetectable HIV viral load may suggest treatment failure. Referral to the patient's primary care provider is indicated.[7] Once the

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[4] http://www.hivdent.org/_dentaltreatment_/DT_treatment1.htm

[5] Abel SN, Croser D, Fischman S, Glick M, Phelan JA, eds. *Principles of Oral Health Management for the HIV/AIDS Patient*. Dental Alliance for AIDS/HIV Care (DAAC); 2000. Available at: http://www.aids-ed.org/pdf/curricula/Princ_Oral_Health_HIV.pdf

[6] Little JW, Falace DA, Miller CS, Rhodus NL. *Dental Management of the Medically Compromised Patient*, 8th ed. St. Louis, MO: Elsevier, Inc; 2013.

[7] Rezneck D, Bednarsh H. HIV and the dental team: the role of the dental professional in managing patients with HIV/AIDS. *Dimensions of Dental Hygiene*. 2006;4(6):14–16. Available at: http://www.dimensionsofdentalhygiene.com/ddhright.aspx?id=849

possibility of significant immunosuppression, neutropenia, or thrombocytopenia has been ruled out, HIV-infected patients usually do not require special consideration when providing dental treatment.

TABLE 7. DENTAL MANAGEMENT

DISEASE PROGRESSION: CD4 CELLS/μL	MANAGEMENT CONSIDERATIONS
400–600: Initial immune suppression **200–400: Emergence of opportunistic infections**	• Review health history. • Check recent labs (CBC with differential current within 6 months). • Emphasize preventive dentistry. • Use chlorhexidine rinses before dental procedures to reduce microbial load. • Consult with primary care provider if opportunistic infections are present. • Treat oral candidiasis and ulcerative lesions. • Consider biopsy for non-responsive oral lesions.
≤ 200: Severe immune suppression	• All of the above. • Primary care provider should be contacted for pretreatment medical consultation. • Review health history and labs: ► *Determine if patient is neutropenic (absolute neutrophil counts <500): Prophylactic antimicrobials for severe neutropenic patients.* ► *Determine if patient has Idiopathic Thrombocytopenia Purpura (ITP): Obtain pre-surgical platelet counts for patient procedures, which include scaling and curettage.* • Avoid aspirin and NSAIDs as analgesics. • Patients with rampant caries and or poor salivary flow are not good candidates for extensive restorations. Consider glass ionomers. • Regular periodontal appointments should be provided for inmates with HIV-associated periodontal disease.

15. 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.

16. 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.

  ➔ *Staff and inmates can utilize the Re-Entry Medication Acquisition Guide, available on Sallyport, for a concise list of medication assistance programs and resources for individuals re-entering society post-incarceration*.

- Consultation with BOP social workers should be pursued on a case-by-case basis to assist with release planning efforts. Social workers can connect inmates transitioning into the community with systems that will provide appropriate and needed services, resources, and opportunities to ensure continuity of HIV care. If the institution is without a staff social worker, regional social workers are available to assist with this transition.

- 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.

17. INFECTION PREVENTION AND CONTROL

TRANSMISSION

HIV is spread primarily through percutaneous 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.

For HIV-infected patients without other STDs, who are adherent to ART with continuous viral suppression (viral load <20–75 cps/mL, depending on assay used), the risk of HIV transmission is low. However, the threshold at which transmission becomes impossible is unknown. There has been at least one reported case of HIV transmission from a patient with suppressed plasma viral load to a monogamous uninfected sexual partner.

➔ *Therefore, while a sustained viral load below the limits of detection will dramatically reduce the possibility of HIV transmission, it does not absolutely assure the absence of HIV in the genital and blood compartments and, hence, the inability to transmit HIV to others.*

INMATE COUNSELING

- **All inmates should be counseled about the importance of preventing blood exposures**—during orientation to the institution and when appropriate during clinical evaluations.

- **All inmates diagnosed with HIV infection should be counseled about preventing transmission. The following messages should be reinforced:**
  - Do not have sex while in prison; do not have unprotected sex upon release to the community.
  - Do not shoot (inject) 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 if you have an open, draining wound.
  - Do not donate blood, body organs or other tissue, or semen.

- **All inmates with HIV infection should be given the following guidance about self-care:**
  - Always wash your 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: Infection Control Precautions*) 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 CDC and WHO guidelines for hand hygiene in healthcare settings, both available at *http://www.cdc.gov/handhygiene/Guidelines.html*.

DEFINITIONS: GENERAL

ART is highly active, **ANTIRETROVIRAL THERAPY** that can achieve sustained, undetectable HIV RNA levels in infected persons.

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.

CERVICAL SCREENING (PAP) TEST RESULTS can be normal or can include one of the following abnormal findings:[8]

- **ASC-US:** *Atypical squamous cells of undetermined significance* means that changes in the cervical cells have been found. The changes are almost always a sign of an HPV infection. ASC-US is the most common abnormal Pap test result.
- **LSIL:** *Low-grade squamous intraepithelial lesion* means that the cervical cells show changes that are mildly abnormal. LSIL usually is caused by an HPV infection that often goes away on its own.
- **HSIL:** *High-grade squamous intraepithelial lesion* suggests more serious changes in the cervix than LSIL. It is more likely than LSIL to be associated with precancer and cancer.
- **ASC-H:** *Atypical squamous cells, cannot exclude HSIL* means that changes in the cervical cells have been found that raise concern for the presence of HSIL.
- **AGC:** *Atypical glandular cells* means that changes have been found in the glandular cells that raise concern for the presence of precancer or cancer.

CLINICIAN is a physician, dentist, mid-level provider, or pharmacist with a collaborative practice agreement.

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

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 **ART,** and may paradoxically be associated with inflammatory reactions to certain preexisting pathogens such as *M. tuberculosis*, cytomegalovirus, and *M. avium* complex. The term **IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)** refers to the occurrence of these inflammatory disorders.

➜ *See Section 13 for more information on IRIS.*

[8] *Abnormal Cervical Cancer Screening Test Results*. American College of Obstetricians and Gynecologists website. Updated January 2015. Available at: *http://www.acog.org/Patients/FAQs/Abnormal-Cervical-Cancer-Screening-Test-Results*

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.

➜ *See HIV Genotypic Drug Resistance Testing in Section 6 for more information*.

UNDETECTABLE HIV is the measurement of HIV RNA at levels that are below the level of detectability of specific assays.

VIRAL SUPPRESSION is defined by DHHS as the measurement of HIV RNA persistently below the levels of detection, <20–75 cps/mL, depending on the assay used.

DEFINITIONS: INFECTION CONTROL PRECAUTIONS

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.
- Full surface disinfection of the dental operatory when invasive procedures are performed, exacerbated by the aerosolization of blood and saliva.

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/resources/health_care_mngmt.jsp*

APPENDIX 1. GUIDELINES REGARDING MEDICAL CARE OF HIV-INFECTED PERSONS

NOTE: Many of the following resources, or more recent updates, can also be accessed at the AIDS*info* website's list of Federally approved HIV/AIDS medical practice guidelines at : http://www.aidsinfo.nih.gov/guidelines/

TOPIC	NAME	LINK	AGENCY
Antiretroviral Therapy	*Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents (2015)*	http://www.aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0/	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 (2015)*	http://www.aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0/	DHHS
HIV Testing	*Revised Recommendations for HIV Testing in Health-Care Settings (2006)*	http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm	CDC
Immunizations	*Immunization Schedule, Adult Version*	http://www.cdc.gov/vaccines/schedules/index.html	CDC ACIP
Non-Occupational Exposures	*Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States (2005)*	http://aidsinfo.nih.gov/contentfiles/NonOccupationalExposureGL.pdf	CDC
Occupational Exposures	*Clinical Practice Guidelines on Medical Management of Exposures: HIV, HBV, HCV Human Bites, and Sexual Assaults (2014)*	https://www.bop.gov/resources/health_care_mngmt.jsp	BOP
	PEPline: Clinician Consultation Center Post-Exposure Prophylaxis Hotline *(Call 888-448-4911 for a phone consultation, 9AM–2AM. ET, seven days a week.)*	*For PEP Quick Guide to frequently asked questions:* http://nccc.ucsf.edu/clinician-consultation/post-exposure-prophylaxis-pep/	UCSF
Opportunistic Infections	*Guidelines for Preventing Opportunistic Infections among HIV-Infected Persons (2015)*	http://www.aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi_041009.pdf	CDC NIH IDSA
Oral Health Care	*HIVdent: HIV/AIDS Oral Healthcare Resource on the Internet*	http://www.hivdent.org/	Non-profit coalition
Resistance Testing	*Diagnostic, Monitoring, and Resistance Laboratory Tests for HIV (2011)*	http://www.guideline.gov/content.aspx?id=34267	IAS-USA NYS
Risk Assessment	*Risk Screening and Risk-Reduction Interventions*	http://www.cdc.gov/hiv/prevention/programs/pwp/risk.html	CDC
Sexually Transmitted Diseases	*Sexually Transmitted Diseases Treatment Guidelines (2015)*	http://www.cdc.gov/std/treatment/	CDC

ABBREVIATIONS:

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; **NYS** = New York State Department of Health; **UCSF** = University of California, San Francisco; **USPHS** = U.S. Public Health Service

APPENDIX 2. CRITERIA FOR TESTING FOR HIV INFECTION

Test all inmates with the following CONDITIONS, 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*: Candida, 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.

Mandatory-test★ all sentenced (6 months or more) inmates with the following RISK FACTORS:

- Injected illegal drugs and shared equipment.
- (For males) had sex with another man.
- Had unprotected intercourse with a person with a 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.

★ ***Inmates must participate in mandatory HIV testing programs.***

Offer voluntary testing to ALL sentenced inmates at the time of incarceration:

Opt-out voluntary testing is offered to all sentenced inmates after arrival to the designated institution. Many persons with HIV infection are asymptomatic and are unaware of their infection; therefore, consistent with CDC guidelines and the issued memorandum from the BOP Medical Director, all sentenced inmates should universally be offered HIV testing at the time of incarceration.

Voluntary testing via an Inmate Request to Staff Member (BP-S148) form is also available to all inmates regardless of sentencing or duration of stay.

APPENDIX 3. HIV-INFECTED INMATES – INITIAL ASSESSMENT

REVIEW OF SYMPTOMS	PHYSICAL EXAMINATION
A complete review of systems should be performed, with special attention given to the following areas:	***A complete physical examination should be performed, with special attention given to the following areas:***
☐ **GENERAL:** Unexplained weight loss, night sweats, fever, changes in body habitus	☐ **VITAL SIGNS:** Including height and weight
☐ **SKIN:** Skin discoloration, rash, ulcers, or lesions	☐ **GENERAL:** Including body habitus; evidence of obesity, wasting, lipodystrophy; assessment of frailty and ambulatory ability
☐ **LYMPH NODES:** Localized or generalized enlargement of lymph nodes	☐ **SKIN:** Seborrheic dermatitis, ecchymoses, purpura, petechiae, Kaposi sarcoma, herpes simplex or zoster, psoriasis, molluscum contagiosum, onychomycosis, folliculitis, condylomata, cutaneous fungal infections
☐ **EYES:** Vision change or loss	☐ **LYMPH NODES:** Generalized or localized lymphadenopathy
☐ **MOUTH:** Gum disease, ulcers, oral lesions or pain	☐ **EYE:** Retinal exudates or cotton wool spots, hemorrhages, pallor, icterus
☐ **CARDIOPULMONARY:** Chest pain, shortness of breath, palpitations, wheezing, dyspnea, orthopnea	☐ **OROPHARYNX:** Oral hairy leukoplakia, candidiasis (thrush, palatal erythema, angular cheilosis), aphthous ulcers, gingivitis, periodontal disease, Kaposi sarcoma, tonsillar or parotid gland enlargement
☐ **GASTROINTESTINAL:** Diarrhea, nausea, pain	☐ **CARDIOVASCULAR**: Heart exam, peripheral pulses, presence/absence of edema
☐ **ENDOCRINOLOGY:** Symptoms of hyperglycemia, thyroid disease, hypogonadism	☐ **CHEST:** Lung examination
☐ **NEUROLOGIC AND PSYCHIATRIC:** Persistent and severe headaches; memory loss, loss of concentration, cognitive difficulties, depression, apathy, anxiety, mania, mood swings; lower extremity paresthesias, pain, numbness; paralysis or weakness; dizziness; seizures; sleep disorders	☐ **BREAST:** Nodules, nipple discharge
☐ **GENITOURINARY:** Dysuria, urethral or vaginal discharge or lesions, hematuria	☐ **ABDOMEN**: Hepatomegaly, splenomegaly, masses, tenderness
☐ **ORTHOPEDIC:** Hip pain, joint pain, fractures; diagnosis of, or risk factors for, osteopenia/ osteoporosis	☐ **GENITOURINARY**: Ulcers, warts, chancres, rashes, abnormal gynecologic exam, discharge
	☐ **ANORECTAL:** Ulcers, warts, fissures, internal or external hemorrhoids, masses, Kaposi sarcoma
	☐ **NEUROPSYCHIATRIC**: Depression, mania, anxiety, signs of personality disorder; difficulties in concentration, attention, and memory; signs of dementia; speech problems; gait abnormalities, focal deficits (motor or sensory); lower extremity vibratory sensation (distal sensory neuropathy, abnormal reflexes)

APPENDIX 4A. HIV-INFECTED INMATES – BASELINE LABORATORY EVALUATIONS

BASELINE TESTS	COMMENTS
HIV serology	If diagnosis is not previously confirmed, and viral load is low or undetectable.
CD4 cell count and percentage	To assess urgency of ART and need for OI prophylaxis.
Plasma HIV RNA	To assess viral load.
HIV resistance testing	HIV genotype testing is preferred over phenotype testing for ARV-naive patients or patients not on ART.
Coreceptor tropism assay	If use of CCR5 antagonist is being considered.
HLA B*5701	If use of abacavir is being considered.
Complete blood cell count with differential	
Alanine aminotransferase, aspartate, aminotransferase; total bilirubin, alkaline phosphatase	To assess for evidence of liver damage, hepatitis, or systemic infection (e.g., elevated alkaline phosphatase occurs with some OIs)
Total protein/albumin	High total protein is common with untreated HIV infection due to increased immunoglobulin fraction secondary to B-cell hyperplasia. Low albumin may indicate nutritional deficiency or nephrotic syndrome.
Electrolytes, blood urea nitrogen/creatinine	To assess kidney function; use creatinine to calculate estimated GFR. May consider calcium, magnesium, and phosphorous.
Fasting lipid profile and blood glucose or hemoglobin A1c	
Urinalysis	To assess for evidence of proteinuria, hematuria.
CMV screening	Use anti-CMV IgG for patients at low risk of CMV infection.
Gonorrhea, chlamydia screening	NAAT testing (preferred) or culture with sites based on exposure history (e.g., urine, urethral, vaginal, cervical, rectal, oropharyngeal).
Syphilis screening	Use local protocol (either RPR or treponemal-specific antibody tests).
Screening for latent Toxoplasma gondii infection	Use anti-toxoplasma IgG.
Screening for latent Mycobacterium tuberculosis infection	Use tuberculin skin test or IGRA. IGRA is preferred if patient has history of BCG vaccination.
Varicella virus screening	Use anti-varicella IgG if patient has no known history of chickenpox or shingles.
Viral hepatitis screening	HBsAg, HBsAb, anti-HBc, HCV antibody, HAV total (or IgG antibody). • If HBsAg+, order HBV RNA level. • If HCVAb+, order HCV RNA level and HCV genotype.

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BASELINE TESTS	COMMENTS
Tests that may be performed under certain circumstances:	
Chest radiography	To rule out active pulmonary tuberculosis in patients with evidence of latent M. tuberculosis infection and in those individuals who are close contacts of persons with infectious TB (regardless of the results of the screening test). Also consider for patients with underlying lung disease, as a baseline for evaluating future respiratory illness.
Cytology: Pap test	Cervical; anal as indicated on a case-by-case basis. Abnormal results require follow-up with colposcopy and high-resolution anoscopy, respectively.
Glucose-6-phosphate dehydrogenase	Screen for deficiency in appropriate racial or ethnic groups (persons of African, Asian, or Mediterranean descent) to avoid use of oxidant drugs.
Serum testosterone level	In males with fatigue, weight loss, loss of libido, erectile dysfunction, or depression, or who have evidence of reduced bone mineral density. Morning free testosterone test is preferred.
Trichomoniasis screening	In all HIV+ women.

ABBREVIATIONS:

anti-HBc = hepatitis B core antibody; **ART** = antiretroviral therapy; ARV = antiretroviral; **CMV** = cytomegalovirus; **HAV** = hepatitis A virus; **HbsAb** = hepatitis B surface antibody; **HbsAg** = hepatitis B surface antigen; **HCV** = hepatitis C virus; **HIV** = human immunodeficiency virus; **GFR** = glomerular filtration rate; **IgG** = immunoglobulin G; **IGRA** = interferon-γ release assay; **NAAT** = nucleic acid amplification test; **OI** = opportunistic infection; **RPR** = rapid plasma reagin

Appendix 4a, Baseline Laboratory Evaluations, page 2 of 2

APPENDIX 4B. HIV-INFECTED INMATES – LABORATORY MONITORING SCHEDULE, PRIOR TO AND AFTER INITIATION OF ART

TESTING	Entry into care	Follow-up (before ART is initiated)	If initiation or modification of ART is indicated	2-8 wks after ART initiated or modified	Every 3-6 months	Every 6 months	Every 12 months	Treatment failure
HIV serology	X							
CD4 count	X	q 3-6 mo.	X		during 1st 2 years of ART		X *(optional if on ART & CD4>500 & VL<20)*	X
Viral load	X	optional	X	X	X	X[1]		X
Resistance testing	X		X					X
HLA-B 5701			if considering ABC					
Tropism testing			if considering CCR5 antagonist					if considering CCR5 antagonist
Hep B serology	X		may repeat if negative at baseline					
Hep C serology	X							
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			
Fasting lipid profile	X	if normal, annually	X	consider at 4-8 wk. w/ new ART		if last measure-ment was abnormal	if last measure-ment was normal	
Fasting glucose or hemoglobin A1C	X	if normal, annually	X		if last measure-ment was abnormal		if last measure-ment was normal	
UA	X		X			if on TDF	X	
Pregnancy test			in women of child-bearing potential					
Coagulation testing	As needed. Needed prior to invasive dental procedures for high-risk HIV patients.							

1. For patients adherent to ART with consistently suppressed viral load and stable immunologic status for more than 2 years, monitoring can be extended to 6 month intervals.

Adapted from:

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. Updated April 16, 2015. Available at: *https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0*.

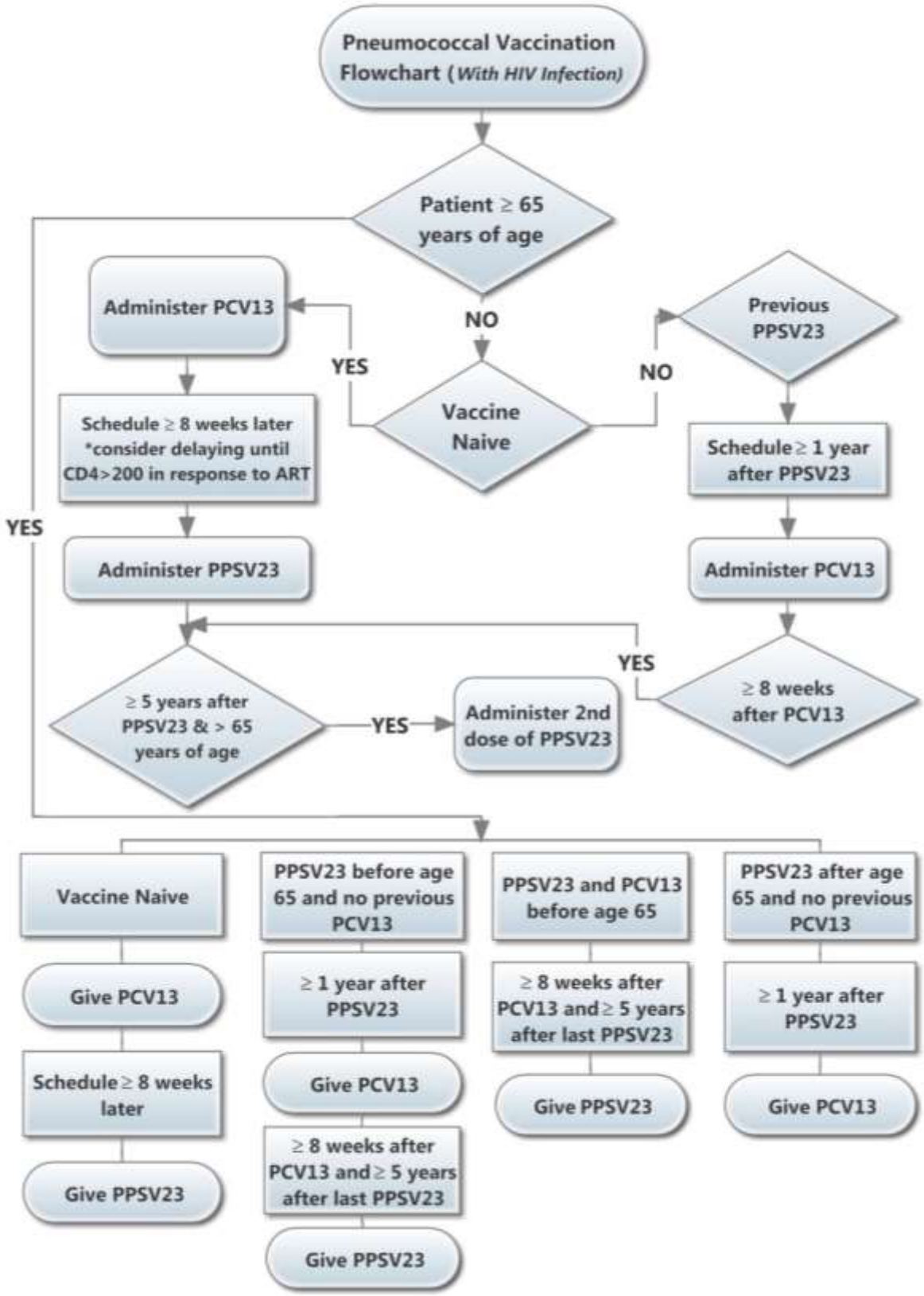
APPENDIX 5A. PAP SMEAR INSTRUCTIONS

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:*** • Collect the Pap smear prior to the bimanual exam, to avoid contaminating the sample with lubricant. • Obtain the Pap smear 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.

APPENDIX 5B. BOP RECOMMENDED CERVICAL SCREENING FOR HIV-INFECTED WOMEN

HIV-INFECTED WOMEN AGED <30 YEARS:
• If younger than age 21, known to be HIV-infected or newly diagnosed with HIV, and sexually active, screen within 1 year of onset of sexual activity regardless of mode of HIV infection. • HIV-infected women aged 21–29 should have a Pap test following initial diagnosis. • Pap test should be done at baseline and every 12 months. Some experts recommend a Pap test at 6 months after the baseline test. • If results of 3 consecutive Pap tests are normal, follow-up Pap tests can be performed every 3 years. ➔ *Co-testing (Pap test and HPV test) is not recommended for women younger than 30.*
HIV-INFECTED WOMEN AGED ≥30 YEARS
IF PAP TESTING ONLY:
• Pap test should be done at baseline and every 12 months. Some experts recommend a Pap test at 6 months after the baseline test. • If results of 3 consecutive Pap tests are normal, follow-up Pap tests can be performed every 3 years.
IF PAP TEST AND HPV CO-TESTING:
• Pap test and HPV co-testing should be done at baseline. • If result of the Pap test is normal and HPV co-testing is negative, follow-up Pap test and HPV co-testing can be performed every 3 years. • If the result of the Pap test is normal, but HPV co-testing is positive, follow-up Pap test and HPV co-testing should be performed in one year. • If the one year follow-up Pap test is abnormal or HPV co-testing is positive, referral to colposcopy is recommended.
Adapted from: *Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents*. Updated 9-24-15. Available at: *https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/343/hpv*

APPENDIX 6. PNEUMOCOCCAL VACCINATION FOR HIV-INFECTED INMATES



APPENDIX 7. PROPHYLAXIS FOR HIV-RELATED OPPORTUNISTIC INFECTIONS

DRUG/DOSAGES★	TOXICITIES	COMMENTS
PNEUMOCYSTIS PNEUMONIA		
INDICATIONS: CD4+ T cells <200/µL ***OR*** oralpharyngeal candidiasis ➜ *Can stop primary and secondary PCP prophylaxis if CD4+ T cells >200/µL for 3 months.*		
FIRST CHOICE		
TMP-SMX (Bactrim, Septra) 1 DS 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 1500 mg daily	rash, GI intolerance	• Must be taken with meals for absorption.
TOXOPLASMOSIS		
INDICATION: Toxo IgG+ and CD4+ T cells <100/µL ➜ *Can stop primary toxoplasmosis prophylaxis if CD4+ T cell count is >200/µL for >3 months.* *Can stop secondary prophylaxis if CD4+ T cell count is >200/ µL* ***AND*** *asymptomatic for >6 months.*		
FIRST CHOICE		
TMP-SMX (Bactrim, Septra) 1 DS daily	rash, fever, nausea, leukopenia, hepatitis	• Repeat toxo IgG if titer was negative when CD4+ T cells were <100/µL. • Monitor for anemia/leukopenia; CBC q 3–4 months
ALTERNATIVE		
Dapsone 50 mg/day ***AND*** **Pyrimethamine** 50 mg/wk ***AND*** **Leucovorin** 25 mg/wk	hemolysis, anemia	• Monitor for anemia/leukopenia; CBC q 3–4 months.
MYCOBACTERIUM AVIUM COMPLEX (MAC)		
INDICATION: CD4+ T cell count <50/µL ➜ *Can stop primary prophylaxis if completed ≥12 months of therapy* ***AND*** *no symptoms of MAC* ***AND*** *CD4+ count >100/µL for ≥6 months.*		
FIRST CHOICES		
Azithromycin 1200 mg/week	nausea/vomiting	
Clarithromycin 500 mg bid	nausea/vomiting	
ALTERNATIVE		
Rifabutin 300 mg/day	uveitis, arthralgias, hepatitis	• Uveitis when given with fluconazole; creates rifampin resistance; review drug interactions.
★ **q** = "every"; **bid** = twice daily		

APPENDIX 8. ADVANTAGES AND DISADVANTAGES OF ARV COMPONENTS RECOMMENDED AS INITIAL ANTIRETROVIRAL THERAPY

ARV CLASS	ARV AGENT(S)	ADVANTAGES	DISADVANTAGES
DUAL-NRTI	**ABC/3TC**	• Co-formulated with DTG as an STR.	• Inferior virologic responses in patients with baseline HIV RNA ≥100,000 cps/mL when given with EFV or ATV/r, as compared with TDF/FTC in ACTG 5202 study. This difference was not seen when ABC/3TC was used in combination with DTG. • May cause life-threatening hypersensitivity reaction in patients positive for the HLA B*5701 allele. As a result, HLA-B*5701 testing is required before use. • ABC use has been associated with cardiac events in some, but not all, observational studies.
	TDF/FTC	• Co-formulated with EFV, EVG/c, and RPV as an STR. • Active against HBV; recommended dual-NRTI for HIV/HBV coinfected patients. • Better virologic responses than with ABC/3TC in patients with baseline viral load ≥100,000 cps/mL, when combined with ATV/r or EFV.	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency. • Decreases BMD more than other NRTI combinations.
INSTI	**DTG**	• Once-daily dosing. • May have higher barrier to resistance than EVG or RAL. • Co-formulated with ABC and 3TC as an STR. • No food requirement. • No CYP3A4 interactions.	• Oral absorption can be reduced by simultaneous administration with products containing polyvalent cations (e.g., Al, Ca, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). • Inhibits renal tubular secretion of Cr and can increase serum Cr, without affecting glomerular function. • UGT substrate; potential for drug interactions.
	EVG/c	• Co-formulated as an STR with TDF/FTC. • Once-daily dosing. • Compared with ATV/r, causes smaller increases in total and LDL cholesterol.	• EVG/c/TDF/FTC is only recommended for patients with baseline CrCl ≥70 mL/min; therapy should be discontinued if CrCl decreases to <50 mL/min. • Cobicistat is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • Oral absorption of EVG can be reduced by simultaneous administration with antacids containing polyvalent cations such as Al, Ca, or Mg. • Cobicistat inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. • May have lower genetic barrier to resistance than boosted PI- or DTG-based regimens • Food requirement.

Appendix 8, Advantage/Disadvantages of ARV Components, page 1 of 3
(See KEY TO ACRONYMS on page 3 of Appendix.)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
INSTI	**RAL**	• Compared to other INSTIs, has longest post-marketing experience. • No food requirement. • No CYP3A4 interactions.	• May have lower genetic barrier to resistance than boosted PI- or DTG-based regimens. • Increases in creatine kinase, myopathy, and rhabdomyolysis have been reported. • Rare cases of severe hypersensitivity reactions (including SJS and TEN) have been reported. • Oral absorption of RAL can be significantly impaired by antacids containing Al or Mg; co-administration is not recommended. • UGT substrate; potential for drug interactions.
NNRTI	**EFV**	• Once-daily dosing. • Co-formulated with TDF/FTC. • Long-term clinical experience. • EFV-based regimens (except for EFV plus ABC/3TC) have well-documented efficacy in patients with high HIV RNA.	• Transmitted resistance more common than with PIs and INSTIs. • Short- and long-term neuropsychiatric (CNS) side effects, including depression and, in some studies, suicidality. • Teratogenic in non-human primates; avoid use in women who are trying to conceive or who are sexually active and not using contraception. • Dyslipidemia. • Greater risk of resistance at the time of treatment failure than with PIs. • Skin rash. • Potential for CYP450 drug interactions. • Should be taken on an empty stomach (food increases drug absorption and CNS toxicities).
	RPV	• Once-daily dosing. • Co-formulated with TDF/FTC. • Smaller pill size than co-formulated DTG/ABC/3TC, EFV/TDF/FTC, and EVG/c/TDF/FTC. • Compared with EFV, fewer discontinuations for CNS adverse effects. • Fewer lipid effects. • Fewer rashes.	• Not recommended in patients with pre-ART HIV RNA >100,000 cps/mL or CD4 count <200 cells/µL because of higher rate of virologic failure in these patients. • Transmitted resistance more common than with PIs and INSTIs. • More NNRTI-, TDF-, and 3TC-associated mutations at virological failure than with regimen containing EFV and two NRTIs • Potential for CYP450 drug. • Meal requirement (>390 kcal). • Requires acid for adequate absorption. • Contraindicated with PPIs. • Use with caution when co-administered with H2 antagonists or antacids. • Use with caution when co-administered with a drug known to increase the risk of torsades de pointes.

Appendix 8, Advantage/Disadvantages of ARV Components, page 2 of 3
(See Key to Acronyms on page 3 of Appendix.)

ARV CLASS	ARV AGENT(S)	ADVANTAGES	DISADVANTAGES
PI	**ATV/c or ATV/r**	• Once-daily dosing. • Higher genetic barrier to resistance than NNRTIs, EVG, and RAL. • PI resistance at the time of treatment failure uncommon with pharmacologically-boosted PIs. • ATV/c and ATV/r have similar virologic activity and toxicity profiles.	• Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice. • Food requirement. • Absorption depends on food and low gastric pH. • Nephrolithiasis, cholelithiasis, nephrotoxicity. • GI adverse effects. • Potential for drug interactions with CYP3A4 inhibitors and substrates.
	DRV/c or DRV/r	• Once-daily dosing. • Higher genetic barrier to resistance than NNRTIs, EVG, and RAL. • PI resistance at the time of treatment failure uncommon with pharmacokinetically-boosted PIs.	• Skin rash. • Food requirement. • GI adverse effects. • Potential for drug interactions with CYP3A4 inhibitors and substrates.
	LPV/r	• Only RTV co-formulated PI. • No food requirement. • Once- or twice-daily dosing.	• Requires 200 mg per day of RTV. • Once-daily dosing not recommended in pregnant women. • Possible higher risk of MI associated with cumulative use of LPV/r. • PR and QT interval prolongation have been reported. Use with caution in patients at risk of cardiac conduction abnormalities or receiving other drugs with similar effect. • Possible nephrotoxicity. • Potential for drug interactions with CYP3A4 inhibitors and substrates.

***KEY TO ACRONYMS*:**

ABC/3TC = abacavir/lamivudine; **ATV/c** = cobicistat-boosted atazanavir; **ATV/r** = ritonavir-boosted atazanavir; **ARV** = antiretroviral; **BMD** = bone mineral density; **CNS** = central nervous system; **CrCl** = creatinine clearance; **DRV/c** = cobicistat-boosted darunavir; **DRV/r** = ritonavir-boosted darunavir; **DTG** = dolutegravir; **EFV** = efavirenz; **EVG/c** = elvitegravir/cobicistat; **HBV** = hepatitis B virus; **HCV** = hepatitis C virus; **INSTI** = integrase strand transfer inhibitor; **LPV/r** = ritonavir-boosted lopinavir; **NNRTI** = non-nucleoside reverse transcriptase inhibitor; **NRTI** = nucleoside reverse transcriptase inhibitor; **PI** = protease inhibitor; **RAL** = raltegravir; **RPV** = rilpivirine; **RTV** = ritonavir; **STR** = single tablet regimen; **TDF/FTC** = tenofovir disoproxil fumarate/emtricitabine

Appendix 8, Advantage/Disadvantages of ARV Components, page 3 of 3

APPENDIX 9. DOSING OF ARV DRUGS IN ADULTS WITH CHRONIC KIDNEY DISEASE (CKD) AND/OR HEPATIC IMPAIRMENT

ARV	USUAL DAILY DOSE★	DOSING IN RENAL INSUFFICIENCY/ HEMODIALYSIS (HD)★	DOSING IN HEPATIC IMPAIRMENT
NRTI REQUIRING NO RENAL DOSAGE ADJUSTMENT			
Abacavir	600 mg qd ***or*** 300 mg bid	No dosage adjustment necessary	No dosage adjustment necessary
NRTI REQUIRING DOSAGE ADJUSTMENT			
Emtricitabine	200 mg qd	CrCl 30–49: 200 mg q48 hours 120mg q24 hours (solution) CrCl 15–29: 200 mg q72 hours 80mg q24 hours (solution) CrCl <15/HD: 200 mg q96 hours 60mg q24 hours (solution)	No dosage adjustment necessary
Lamivudine	300 mg qd ***OR*** 150 mg bid	CrCl 30–49: 150 mg q24 hours CrCl 15–29: 150 mg, then 100 mg q24 hours CrCl 5-14: 150 mg, then 50 mg q24 hours CrCl <5/HD: 50 mg, then 25 mg q24 hours	No dosage adjustment necessary
Tenofovir (TDF)	300 mg qd	CrCl 30–49: 300 mg q48 hours CrCl 10–29: 300 mg twice weekly CrCl <10 On HD: 300 mg q7 days or after dialysis No HD: ➔ Not recommended	No dosage adjustment necessary
TDF+FTC (Truvada®)	1 tablet qd	CrCl 30–49: 1 tablet q48 hours CrCl <30/HD: ➔ Not recommended	No dosage adjustment necessary
Zidovudine	300 mg bid	CrCl <15/HD: 100 mg tid ***OR*** 300 mg qd	No dosage adjustment necessary
NNRTI REQUIRING NO RENAL DOSAGE ADJUSTMENT			
Efavirenz	600mg qd	No dosage adjustment necessary	No dosage adjustment necessary
Etravirine	200mg bid	No dosage adjustment necessary	No dosage recommendation
Rilpavirine	25mg qd	No dosage adjustment necessary	No dosage recommendation
NNRTI REQUIRING RENAL DOSAGE ADJUSTMENT			
Atripla®	1 tablet qd	CrCl <50: ➔ Not recommended	No dosage adjustment necessary
Complera®	1 tablet qd	CrCl <50: ➔ Not recommended	No dosage recommendation
Nevirapine	200 mg bid	Patient on HD: Limited data; no dosage recommendation	Child-Pugh Class B or C: ➔ Contraindicated
PIS REQUIRING NO RENAL DOSAGE ADJUSTMENT			
Darunavir	800 mg qd ***OR*** 600 mg bid, if DRV mutation	No dosage adjustment necessary	Severe hepatic impairment: ➔ Not recommended

★ **q** = "every"; **qd** = once daily; **bid** = twice daily; **tid** = three times a day

Appendix 9, Dosing of ARV Drugs with CKD and Hepatic Impairment, page 1 of 2

ARV	Usual Daily Dose*	Dosing in Renal Insufficiency/ Hemodialysis (HD)*	Dosing in Hepatic Impairment
PIs requiring renal dosage adjustment			
Atazanavir	300 mg + RTV 100 mg qd	No dosage adjustment for patients with renal dysfunction who do not require HD ➜ Not recommended for ARV-experienced patients on HD	Child-Pugh Class B: 300 mg qd Child-Pugh Class C: ➜ Not recommended Patients with hepatic impairment (Child-Pugh Class B or C): ➜ RTV boosting not recommended
Atazanavir + cobicistat (Evotaz®)	1 tablet qd	➜ If used with TDF, not recommended if CrCl <70	No dosage recommendation ➜ Not recommended in patients with hepatic impairment
Darunavir + cobicistat (Prezcobix®)	1 tablet qd	➜ If used with TDF, not recommended if CrCl<70	Child-Pugh Class C: ➜ Not recommended
Lopinavir/RTV (Kaletra®)	2 tablets bid *OR* 4 tablets qd	➜ Avoid once-daily (qd) dosing in patients on HD	No dosage recommendation ➜ Use with caution in patients with hepatic impairment
INSTIs requiring no renal dosage adjustment			
Dolutegravir	50 mg qd	No dosage adjustment necessary	Child-Pugh Class C: ➜ Not recommended
Elvitegravir	—	No dosage adjustment necessary	Child-Pugh Class C: ➜ Not recommended
Raltegravir	400 mg bid	No dosage adjustment necessary	Severe hepatic insufficiency: No dosage recommendation
INSTIs requiring renal dosage adjustment			
Stribild®	1 tablet qd	➜ Stribild should not be initiated in patients with CrCl <70 mL/min. ➜ Discontinue Stribild if CrCl declines to <50 mL/min while patient is on therapy.	No dosage recommendation
CCR5 antagonist			
Maraviroc	—	➜ Not recommended with potent CYP3A inducers or inhibitors	No dosage recommendation

* **q** = "every"; **qd** = once daily; **bid** = twice daily; **tid** = three times a day

Appendix 9, Dosing of ARV Drugs with CKD and Hepatic Impairment, page 2 of 2