

MANAGEMENT OF HIV INFECTION

**Federal Bureau of Prisons
Clinical Guidance**

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http://www.bop.gov/resources/health_care_mngmt.jsp

WHAT'S NEW IN THIS DOCUMENT?

This document updates the December 2017 version of the *BOP Clinical Guidance on the Management of HIV Infection*. Treatment information throughout this document was updated to be in line with the *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents* issued by the Department of Health and Human Services (DHHS) in 2018.

NOTEWORTHY CHANGES INCLUDE REVISIONS IN THE FOLLOWING AREAS:

- **INDICATIONS FOR HIV TESTING:** An opt out strategy of voluntary testing for HIV infection is recommended for all inmates, regardless of sentencing status, including new intakes and those already established in the population who have not declined testing.
- **MENINGOCOCCAL VACCINE:** Adults with HIV infection who have not been previously vaccinated should receive a 2-dose primary series of MenACWY (MCV4), available as Menactra® or Menveo®, at least 2 months apart, and then revaccinated every 5 years.
 - ➔ *Note that Menveo is the preferred formulary agent.*
- **COBICISTAT-CONTAINING REGIMENS:** Emerging data on cobicistat-containing regimens (e.g., elvitegravir-cobicistat, darunavir-cobicistat, and atazanavir-cobicistat) suggest that decreased drug levels occur during pregnancy, with an associated risk of loss of virologic suppression. Cobicistat-containing regimens should therefore not be initiated in treatment-naïve pregnant women.
- **DOLUTEGRAVIR:** DHHS recommends that dolutegravir not be used in women of child-bearing potential who have plans to conceive or who are not taking effective contraception. An observational study in Africa suggested an association between maternal use of dolutegravir at the time of conception and neural tube defects in the infant.
- **BICTEGRAVIR/TENOFOVIR (TAF)/EMTRICITABINE:** Bictegravir/tenofovir (TAF)/emtricitabine was added as a recommended initial regimen for most people with HIV infection.
- **HBV-HCV Co-INFECTION:** Individuals chronically infected with HBV, HCV, and HIV infection should receive a complete antiretroviral therapy (ART) regimen that includes two nucleoside reverse transcriptase inhibitors (NRTIs) that are active against both HIV and HBV, before starting HCV therapy.
- **LATENT TUBERCULOSIS INFECTION (LTBI):** In June 2018, the CDC issued updated guidance on the 12-week, once-weekly isoniazid-rifampentine regimen for LTBI, recommending the isoniazid-rifampentine regimen as an option for treatment of LTBI in HIV-infected patients whose antiretroviral regimens have acceptable drug-drug interactions with rifampentine.
- **DENTAL CARE:**
 - ▶ Regular periodontal appointments are recommended for inmates with HIV-associated periodontal disease.
 - ▶ Use HIV Dental Encounter code (7113) for assessment and treatment when co-managing patients with medical staff.

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1. PURPOSE AND OVERVIEW

The *BOP Clinical Guidance for the Management of HIV Infection* provides guidance on the screening, evaluation, and treatment of federal inmates with HIV infection, with a focus on primary care.

The BOP clinical guidance is 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:

- **An OPT OUT strategy of voluntary testing for HIV infection is recommended for all inmates, regardless of sentencing status, including new intakes and those already established in the population who have not declined testing.** An “opt out” approach involves an informed refusal of testing, rather than informed consent (or “opt in”) for testing. After informing a patient of the indications and plan for testing, the particular test is ordered and performed—unless the patient declines it. Testing in this situation is considered voluntary in that it is good clinical practice, but is not required by policy or law.
 - **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.*

FOURTH-GENERATION HIV 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.*

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: 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 - next page)	

HIV-2 INFECTION

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

IDENTIFYING 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.

- The possibility of HIV-2 infection should be considered in the appropriate epidemiologic setting in patients with serologically confirmed HIV infection, but low or undetectable HIV-1 RNA levels, or in those with declining CD4 T lymphocyte (CD4) cell counts despite apparent virologic suppression on antiretroviral therapy (ART).
- HIV-2 infections are identified during fourth-generation HIV testing.

DISEASE PROGRESSION: 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).

MANAGEMENT OF HIV-2: 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.

HIV-2 RNA TESTING

- ➔ *HIV-2 RNA testing should be conducted in consultation with the Regional Infectious Disease Coordinator and a specialized HIV provider.*

Laboratory monitoring for HIV-2 RNA viral load is problematic since testing availability is limited. Only two laboratories offer quantitative testing (see below), and both require pre-approval by Central Office.

- [Specialized labs](#) (see below) 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, that HIV-2 is intrinsically resistant to NNRTIs, and that several PIs (e.g., atazanavir) lack antiretroviral (ARV) activity against HIV-2.

Quantitative HIV-2 RNA viral load testing may be obtained from the laboratories listed below:

- University of Washington Lab Medicine Community Services (phone 800-713-5198 or email commserv@u.washington.edu):
<http://depts.washington.edu/labweb/AboutLM/Contact.htm>
<http://menu.labmed.washington.edu/oltg/display?mnemonic=HIV2VL>
- New York State Department of Health Lab (phone 518-473-6007):
<http://www.wadsworth.org/programs/id/bloodborne-viruses/clinical-testing/hiv-2-nucleic-acid>

EARLY (ACUTE AND RECENT) 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. **Recent HIV-1 infection** generally is considered the phase up to 6 months after initial infection, during which anti-HIV-1 antibodies are detectable.

Acute retroviral syndrome should be suspected in patients who have had high-risk exposure to HIV-1 within the past two to six weeks. Signs, symptoms, or laboratory findings may include—but are not limited to—fever, lymphadenopathy, skin rash, myalgia/arthralgia, headache, diarrhea, oral ulcers, leukopenia, thrombocytopenia, and transaminase elevation. 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 fourth-generation HIV testing in addition to an HIV viral load test. 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. Antiretroviral therapy, which is recommended for all individuals with HIV-1 infection, should normally be offered to those with early HIV-1 infection. Genotypic drug resistance testing should be performed before initiation of ART to guide the selection of the regimen.

COUNSELING OF INMATES TESTING POSITIVE FOR HIV INFECTION

Inmates who are newly diagnosed with HIV infection should be provided post-test counseling utilizing BP-A0492 Form – HIV Post-Test Counseling (Positive), available on Sallyport. The form will be signed by the inmate and retained in the medical record.

- Counseling messages include information about the meaning of the test results, the natural history of HIV disease, the benefits of antiretroviral treatment, and risk behaviors to avoid to prevent transmission.
- Pregnant inmates who test positive for HIV will be advised that the virus may be transmitted to the fetus and provided information on current treatment options to prevent perinatal transmission.
- All inmates testing positive will be referred to the Psychology Department for follow-up counseling.

In addition, all inmates with HIV infection should be given the following guidance about self-care:

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

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.
- 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. Comorbidities that may affect choice of therapy include peripheral neuropathy, gastrointestinal disease, chronic viral hepatitis, hyperlipidemia, diabetes mellitus, mental illness, cardiovascular disease (or risk), and kidney disease. 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 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.
- Focal or rapidly progressive lymphadenopathy.

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.
- **For 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

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>

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.

- **For 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 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.

INITIAL TESTING

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 cell counts**
- **Plasma HIV RNA levels** (viral load)
- **Complete blood count** with differential white blood cell count and basic chemistry panel with calculated creatinine clearance or estimated glomerular filtration rate (eGFR)
- **Fasting lipid profile**
- **Fasting glucose or hemoglobin A1C**
- **HLA B *5701** (if considering use of abacavir). A negative result suggests minimal risk of hypersensitivity reaction.
- **Genotypic resistance testing** (Genosure Prime preferred) 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.*
- **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.
 - *Coreceptor tropism assay should generally NOT be ordered without expert consultation.*
- **Urinalysis**

SCREENING FOR COINFECTIONS

The following screening tests are recommended to identify coinfections:

- **Testing for Mycobacterium tuberculosis infection** by tuberculin skin test (TST) if there is no history of tuberculosis or a prior positive tuberculosis screening test. A baseline chest radiograph should be obtained in all HIV-infected patients to rule out active tuberculosis; it may also be useful in other patients who are likely to have preexisting lung abnormalities.
- **Serologic testing for Toxoplasma gondii** for prior exposure to T. gondii by measuring anti-Toxoplasma IgG upon initiation of care.
- **Viral hepatitis screening:**
 - ▶ **Hepatitis B virus (HBV):** Screen for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and antibody to hepatitis B total core antigen (anti-HBc or HBcAb). HBsAb should be repeated in 1–2 months or at the next scheduled visit after the third HBV vaccine was given, to assess for immunogenicity.

- ▶ **Hepatitis C virus (HCV):** Screen for HCV antibody. HCV RNA should be ordered on all patients with a positive HCV antibody test to assess for active HCV disease.
 - ➔ *For management of HCV infection, see the BOP Clinical Guidance on Evaluation and Management of Chronic Hepatitis C Virus (HCV) Infection.*
- ▶ **Hepatitis A virus (HAV):** Screen for anti-HAV total or IgG antibody.
- **Screening for herpes viruses:**
 - ▶ Patients at lower risk of cytomegalovirus (CMV) infection (e.g., populations other than men who have sex with men [MSM] or injection drug users, both of which may be assumed to be seropositive) should be tested for latent CMV infection with an anti-CMV IgG upon initiation of care. If transfusions are required, CMV-negative or leukocyte-reduced blood or blood products reduce the risk of CMV transmission to CMV-seronegative patients with HIV infection.
 - ▶ Obtain varicella IgG for HIV-infected patients. This is particularly helpful information in managing exposures to varicella infections.
- **Screening for sexually transmitted diseases:**
 - ▶ All patients should be screened for syphilis upon initiation of care, using RPR.
 - ▶ All women should be screened for trichomoniasis.
 - ▶ Men and women should be screened for gonorrhea and chlamydia infection at initial presentation.

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 cell 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/ μ L.

- ➔ *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 HIV-POSITIVE ADULTS

- **HEPATITIS A VACCINE**

Recommended for HAV-susceptible patients with chronic liver disease, or who are injection-drug users or MSM.

- ▶ **Vaccine formulations should be administered in a two or three-dose schedules, depending on the manufacturer:** Two doses at 0 and 6-to-12 months (Havrix[®]); two doses at 0 and 6-to-18 months (Vaqta[®]); or three doses at 0, 1, and 6 months using combination hepatitis A and B vaccine (Twinrix[®]).
- ▶ **Antibody response should be assessed 1 month after vaccination is complete.** If HAV antibody immunoglobulin (HAV Ab IgG) is negative, the patient should be revaccinated when CD4 cell count >200 cells/ μ L.

- **HEPATITIS B VACCINE**

- ▶ **Recommended unless there is evidence of immunity (positive HBsAb) or active hepatitis.** If HBsAg, HBsAb, and HBcAb are negative, hepatitis B vaccine series should be administered.
 - ➔ See [Hepatitis B/HIV Coinfection](#) in Section 12.
- ▶ **Dosing:** Patients should receive one dose (1.0 mL) of Engerix-B[®] (20 µg/mL), Recombivax HB[®] (10 µg/mL), or combined HAV and HBV vaccine Twinrix (if HAV vaccine is also indicated) administered on a 3-dose schedule at 0, 1, and 6 months.
 - ➔ *Anti-HBs should be obtained 1–2 months after completion of the vaccine series. Anti-HBs <10 IU/mL will be considered as nonresponders.*
 - ➔ *Adults on hemodialysis should receive a 3-dose series of 40 µg Recombivax HB at 0, 1, and 6 months or a 4-dose series of 40 µg Engerix-B at 0, 1, 2, and 6 months.*
- ▶ **For Vaccine Non-Responders:** Revaccinate with a second vaccine. An alternate double-dose schedule may be considered for non-responders (a 3-dose series of 40 mcg Recombivax HB at 0, 1, and 6 months *or* a 4-dose series of 40 mcg Engerix-B at 0, 1, 2, and 6 months).

- **INFLUENZA VACCINE**

Recommended to 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**

- ➔ *Adults with HIV infection are not routinely recommended to receive MenB because meningococcal disease in this population is caused primarily by serogroups C, W, and Y.*
- ▶ **Adults with HIV infection who have not been previously vaccinated** should receive a 2-dose primary series of MenACWY (MCV4), available as Menactra[®] or Menveo[®], at least 2 months apart, and then revaccinated every 5 years.
 - ➔ *Note that Menveo is the preferred formulary agent.*
- ▶ **Those who previously received 1 dose of MCV4** should receive a second dose at least 2 months after the first dose, and then revaccinated every 5 years.

- **PNEUMOCOCCAL VACCINE**

Note: PCV13 = 13-valent pneumococcal conjugate vaccine (Prevnar 13)

PPSV23 = 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23)

- ▶ **The dosing schedule** of pneumococcal vaccine depends on the patient's immunization history.
- ▶ **Primary series for adults who have not previously received PCV13:**
 - For patients who have previously received one or more doses of PPSV23, a single dose of PCV13 should be given at least one year after the last PPSV23 dose was received.
 - For patients who have not previously received PPSV23, a single dose of PCV13 should be given, followed by a single dose of PPSV23 at least eight weeks later. The CD4 cell count may influence timing of the PPSV23 dose (see [box](#) - next page).★

★ **PNEUMOCOCCAL VACCINES:**

If CD4 count is <200 cells/ μ L at the time of the vaccination, the vaccine may be less effective. Consider administering PPSV23 \geq 8 weeks after PCV13, as described above, once the CD4 count increases to >200 cells/ μ L in response to ART.

▶ **Revaccination:**

- A second dose of PPSV23 should be given five years after the initial PPSV23 dose.
- An additional single dose of PPSV23 should be given after age 65, at least five years after the preceding PPSV23 dose.
- No more than three lifetime doses of PPSV23 are generally given.

- ▶ **Administration:** Both pneumococcal vaccines are administered as a 0.5 mL dose. PCV13 should be given intramuscularly, whereas PPSV23 can be given either intramuscularly or subcutaneously. Intradermal administration can cause severe local reactions and should be avoided.

• **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.
- ▶ **Tdap:** 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 the 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. The ACIP recommends any vaccine in HIV-infected females and the 9-valent and quadrivalent vaccines in HIV-infected males. HPV vaccination is given in a series of three doses at 0, 1 to 2, and 6 months.

• **LIVE VACCINES**

MMR vaccines are all contraindicated for patients with severe immunosuppression (CD4 counts <200 cells/ μ L) 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.

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, and bone disease), cardiovascular disease, chronic kidney disease, neuropsychiatric disorders, certain malignancies (e.g., lymphoma, Kaposi's sarcoma), 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.

➔ **For additional guidance, see the following FOUR resources:**

(1) 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>

(2) 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 October 17, 2017.

Available at: <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0>

(3) U.S. Department of Health and Human Services, Health Resources and Services Administration, Guide for HIV/AIDS Clinical Care – 2014 Edition. Rockville, MD: U.S. Department of Health and Human Services, 2014.

Available at: <https://aidsetc.org/guide/contents>

(4) Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV Medicine Association of the Infectious Diseases Society of America. Lucas GM, Ross MJ, Stock PG, et al. *Clin Infect Dis*. 2014;59(9):e96–e138.

Available at: http://www.natap.org/2014/HIV/Clin2014-Lucas-cid_ciu617.pdf

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.
 - ➔ See the National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia, available at: [http://www.lipidjournal.com/article/S1933-2874\(15\)00059-8/fulltext](http://www.lipidjournal.com/article/S1933-2874(15)00059-8/fulltext)

PERIODIC LABORATORY AND DIAGNOSTIC STUDIES

- ➔ 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.
- **Recommended 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.
 - ▶ **Note:** HLA-B* 5701 testing should be performed before initiation of abacavir (ABC).
- **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.**
 - ➔ See also [HIV Genotypic Drug Resistance Testing](#) in Section 6.
 - ▶ **Preferred:** HIV-1 GenoSure Prime – baseline test for resistance to all major classes of HIV medications, may not be available in all areas

- ▶ **Other resistance testing**, available in consultation with HIV specialist, typically ordered together:
 - HIV-1 Genotype (resistance mutation analysis): Baseline test for resistance to three of the four major classes of HIV medications.
 - HIV-1 Integrase Resistance: Baseline test for resistance to one of the four major classes of HIV medication.
- ▶ **The following resistance tests may have significant costs and are not commonly required.** These tests should ONLY be ordered in consultation with HIV specialist:
 - HIV-1 Co-Receptor Tropism (Trofile)
 - HIV-1 Entry Inhibitor (Fuzeon)
 - HIV-1 Phenotype (Phenosense)
 - HIV-1 Phenotype/Genotype

5. PROPHYLAXIS FOR OPPORTUNISTIC INFECTIONS (OIs)

- ➔ 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/>.

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.

- ➔ **For recommendations for initiating prophylaxis for *Pneumocystis jiroveci*² pneumonia (PCP), *Toxoplasma gondii*-associated encephalitis, and disseminated infection with *Mycobacterium avium* complex (MAC), see [Appendix 6, Prophylaxis for HIV Related Opportunistic Infections](#).**

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

- **PROPHYLAXIS FOR LATENT TUBERCULOSIS INFECTION (LTBI)**

- ➔ See BOP Clinical Guidance Management of on Tuberculosis.

Persons with HIV infection who are exposed to *M. tuberculosis* have a high risk of developing active TB disease. Risk of progression from LTBI to TB disease in HIV-infected persons is reduced by both antiretroviral treatment and treatment of LTBI. 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 persons with no clinical or radiographic evidence of TB disease. 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 LTBI, 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.

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.

The preferred treatment regimen for LTBI is as follows:

- ▶ Isoniazid (300 mg) daily or (900 mg) twice weekly, by mouth, administered under direct observation for 9 months.
 - ▶ Pyridoxine (usually 50 mg per dose of isoniazid) to prevent peripheral neuropathy.
 - ▶ 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. Chemoprophylaxis should be stopped if the serum aminotransferase level increases to greater than:
 - Five times the upper limit of normal without symptoms *or*
 - Three times the upper limit of normal with symptoms *or*
 - Two times the upper limit of normal among patients with baseline abnormal transaminases.
 - ▶ Rifapentine is generally NOT recommended due to concerns of multiple ART drug interactions. Only efavirenz or raltegravir-based regimens—in combination with either abacavir/lamivudine OR tenofovir disoproxil fumarate (TDF)/emtricitabine (NOT tenofovir alafenamide TAF)—can be used with once-weekly isoniazid plus rifapentine
- ➔ 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)**

CMV end-organ disease is best prevented using ART to maintain the CD4 count >100 cells/ μ L and recognizing the early symptoms of CMV disease. Since retinitis is the most common sign of CMV disease, patients with low CD4 counts should be monitored for changes in visual acuity, such as increased floaters, and then referred to an ophthalmologist for evaluation and proper therapy.

• **PROPHYLAXIS FOR FUNGAL INFECTIONS**

Primary prophylaxis for fungal infections is not routinely indicated for patients with AIDS. Acute therapy with fluconazole for one to two weeks for oral candidiasis and two to three weeks for esophageal disease is highly effective; long-term fluconazole use may promote candidal resistance. Secondary prophylaxis with oral fluconazole should only be considered if recurrences are frequent or severe. Primary itraconazole prophylaxis for histoplasmosis (CD4 count <150 cells/ μ L) may be considered for inmates with unique indications.

COCCIDIOIDOMYCOSIS: Yearly or twice-yearly serological testing for coccidioidomycosis is reasonable for serologically negative HIV-infected individuals who live in regions endemic for coccidioidomycosis. Testing is also advised for individuals who have traveled to or lived in endemic areas (southwestern United States, Mexico, and South America) in the past. Both IgM and IgG antibody testing using either an EIA or immunodiffusion technique are recommended. A new positive test suggests possible active disease in patients with low CD4 cell counts, and further clinical evaluation should be undertaken.

- ▶ If no signs, symptoms or laboratory abnormalities compatible with active coccidioidomycosis are identified, antifungal therapy with fluconazole 400 mg daily is

recommended for those with CD4 counts <250 cells/ μ L. This should be continued until the CD4 count is \geq 250 cells/ μ L and ART has fully suppressed HIV replication.

- ▶ Outside endemic regions, routine testing does not appear to be useful and should not be performed.

DISCONTINUATION OF OI PROPHYLAXIS

Discontinuation of primary and secondary prophylaxis of OIs should be considered on an individual basis, using the DHHS guidelines outlined below.

- ➔ **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 6](#). 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/ μ L 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/ μ L.

- **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 \geq 100 cells/ μ L after having an undetectable viral load for 3 months in response to ART. Reinitiate fluconazole if the CD4 count declines to <100 cells/ μ L.
- ▶ **Histoplasmosis:** Inmates with prior histoplasmosis ordinarily require prolonged maintenance therapy with oral itraconazole (200 mg twice daily) for 12 months. This is followed by secondary prophylaxis with itraconazole 200 mg once daily. Secondary prophylaxis/chronic maintenance therapy can be discontinued if the following criteria are fulfilled:
(1) itraconazole for \geq 1 yr; **(2)** negative blood cultures; **(3)** CD4 count \geq 150 cells/ μ L for >6 months in response to ART; and **(4)** Serum histoplasma antigen <2 units. Reinitiate itraconazole if CD4 count declines to <150 cells/ μ L.
- ▶ **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 asymptomatic disease, but positive serology or focal coccidioidal pneumonia, can discontinue secondary prophylaxis with clinical response to \geq 6 months antifungal therapy, with CD4 count >250 cells/ μ L, and receiving ART. However, monitoring for recurrence should continue with serial chest radiographs and coccidioidal serology. Inmates from

endemic areas selected to receive primary prophylaxis due to positive serologic testing should be continued until the CD4 count is ≥ 250 cells/ μ L and ART has fully suppressed HIV replication.

- ▶ **Oral Candidiasis:** Secondary fluconazole prophylaxis (chronic suppressive therapy) can be discontinued when the CD4 count has risen >200 cells/ μ L with ART.

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 counts, 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%.
- The magnitude of CD4 recovery is directly correlated with CD4 count at ART initiation.
- START and TEMPRANO trials demonstrated a decreased risk of severe HIV-related illness or death in patients who initiated ART with baseline CD4 counts >500 cells/ μ L.

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.

The key to successful ART in maintaining viral suppression is adherence to the prescribed regimen. Achieving viral suppression requires the use of ARV regimens with three active drugs from two or more drug classes. Baseline genotype resistance testing and patient characteristics should guide the specific regimen design. Specific antiretroviral regimens are discussed below.

- ➔ *When viral suppression is not achieved, or is lost, prompt genotype resistance testing and 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 individuals. 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. Thus, on a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors. **However, initiation of therapy is recommended as soon as possible, regardless of CD4 count.**

CONDITIONS FAVORING MORE URGENT INITIATION OF THERAPY:

- *Pregnancy*
- *AIDS-defining conditions*
- *Acute opportunistic infections (OIs)*
- *Lower CD4 counts (<200 cells/ μ L)*
- *HIV-associated nephropathy (HIVAN)*
- *Acute/early HIV infection*
- *HIV/HBV or HIV/HCV coinfection*

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 7](#) for advantages and disadvantages of ARV components used in initial ART.
- See [Appendix 8](#) 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** backbone component in all recommended and alternative regimens is either tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)/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, convenience, the patient comorbidities, 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 metabolic pathways. 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.
 - Providers can review the Drug-Drug Interactions section of DHHS guidelines and the drug-interactions website of the University of Liverpool (<http://www.hiv-druginteractions.org/>). Since information on drug-drug interactions are updated as new information becomes available, medical literature and drug interaction websites should be routinely checked.
- **POSSIBLE DRUG-DISEASE INTERACTIONS** should be taken into consideration when selecting an ARV regimen, including when there are concurrent disease states such as viral hepatitis, CVD, CKD, DM, cancer, etc.

RECOMMENDED INITIAL REGIMENS FOR MOST PEOPLE WITH HIV

- 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 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, 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.** → See the end of [TABLE 2](#) for a key to **DRUG ACRONYMS**.

PLEASE NOTE:

- “Tenofovir” as listed below refers to either the alafenamide (TAF) or disoproxil fumarate (TDF) form. TAF and TDF are the two forms of tenofovir approved by the FDA. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels AIDS-defining conditions.
- Avoid use of abacavir-containing NRTI backbone combinations in chronic hepatitis B co-infected patients unless combined with effective hepatitis antiviral therapy.
- Raltegravir can be given as 400 mg twice daily, or 1200 mg (two 600 mg tablets) once daily. The 600 mg and 400 mg tablets are not interchangeable.
- Emerging data on cobicistat-containing regimens (e.g., elvitegravir-cobicistat, darunavir-cobicistat, and atazanavir-cobicistat) suggest that decreased drug levels occur during pregnancy, with an associated risk of loss of virologic suppression. Cobicistat-containing regimens should therefore NOT be initiated in treatment-naïve pregnant women.
- DHHS recommends that dolutegravir not be used in women of child-bearing potential who have plans to conceive or who are not taking effective contraception. An observational study in Africa suggested an association between maternal use of dolutegravir at the time of conception and neural tube defects in the infant.

INSTI-BASED REGIMENS

INSTI-based regimens are recommended as initial therapy for most people with HIV. In large clinical trials and in clinical practice, INSTI-based regimens have achieved high rates of virologic suppression and often have greater tolerability than PI- or NNRTI-based regimens.

➔ When only one of the NRTIs is fully active, or if adherence is a concern, dolutegravir is preferred over elvitegravir and raltegravir containing regimens.

- **ELVITEGRAVIR / COBICISTAT / TENOFOVIR / EMTRICITABINE (once daily)**
 - ▶ TAF containing version (Genvoya®) is only for patients with pre-ART CrCl >30 mL/min.
 - ▶ TDF containing version (Stribild®) is only for patients with pre-ART CrCl >70 mL/min.
 - ▶ Must be taken with food.
- **BICTEGRAVIR / TENOFOVIR (TAF) / EMTRICITABINE (once daily)**
 - ▶ Low number of drug-drug interactions.
 - ▶ High barrier to resistance.
 - ▶ TAF is not recommended if CrCL <30 ml/min.
- **DOLUTEGRAVIR / ABACAVIR / LAMIVUDINE (TRIUMEQ®) (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 PLUS TENOFOVIR / EMTRICITABINE (once daily)**
 - ▶ Low number of drug-drug interactions.
 - ▶ Higher barrier to resistance.
 - ▶ TDF/FTC (Truvada®) requires renal dosing when CrCL ≤50 ml/min; consider using TAF/FTC.
 - ▶ TAF/FTC (Descovy®) is not recommended if CrCL <30 ml/min.
- **RALTEGRAVIR PLUS TENOFOVIR / EMTRICITABINE (once daily)**
 - ▶ Low number of drug-drug interactions.
 - ▶ TDF/FTC (Truvada) requires renal dosing when CrCL ≤50 ml/min; consider using TAF/FTC.
 - ▶ TAF/FTC (Descovy) is not recommended if CrCL <30 ml/min.

RECOMMENDED INITIAL REGIMENS IN CERTAIN CLINICAL SITUATIONS

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

PI-BASED REGIMENS

A boosted 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 OR COBICISTAT PLUS TENOFOVIR / EMTRICITABINE (once daily)**
 - ▶ *Must be taken with food.*
 - ▶ *DRV/c plus TDF is NOT recommended for patients with CrCl <70 mL/min.*
 - ▶ *TDF/FTC (Truvada®) requires renal dosing when CrCL ≤50 ml/min; consider using TAF/FTC.*
 - ▶ *TAF/FTC (Descovy®) is not recommended if CrCL <30 ml/min.*
 - ▶ *Tenofovir/emtricitabine can be substituted with abacavir/lamivudine (Epzicom®) if HLA-B*5701-negative.*
- **ATAZANAVIR 300 MG + RITONAVIR OR COBICISTAT PLUS TENOFOVIR/EMTRICITABINE (once daily)**
 - ▶ *Must be taken with food.*
 - ▶ *ATV/c plus TDF is not recommended for patients with CrCl <70 mL/min.*
 - ▶ *Greater rate of discontinuation due to toxicities, when compared to darunavir or raltegravir.*
 - ▶ *TDF/FTC (Truvada®) requires renal dosing when CrCL ≤50 ml/min; consider using TAF/FTC.*
 - ▶ *TAF/FTC (Descovy®) is not recommended if CrCL <30 ml/min.*
 - ▶ *Tenofovir/emtricitabine can be substituted with abacavir/lamivudine (Epzicom) if HLA-B*5701-negative and HIV RNA <100,000 copies/ml and CD4 >200 cells/μL.*

NNRTI-BASED REGIMENS

- **EFAVIRENZ 600 MG / TENOFOVIR / EMTRICITABINE (once daily)**
 - ▶ *Reclassified due to the high rate of central nervous system (CNS)-related toxicities and a possible association of efavirenz with suicidality. Efavirenz may exacerbate psychiatric illness.*
 - ▶ *EFV/TDF/FTC (Atripla®) is NOT recommended when CrCL ≤50 ml/min; consider using TAF/FTC.*
 - ▶ *EFV plus TAF/FTC (Descovy®) not recommended if CrCL <30 ml/min.*
- **RILPIVIRINE / TENOFOVIR / EMTRICITABINE (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.*
 - ▶ *RPV/TDF/FTC (Complera®) is not recommended when CrCL ≤50 ml/min; consider using RPV/TAF/FTC (Odefsey®).*
 - ▶ *RPV/TAF/FTC (Odefsey) is not recommended if CrCL <30 ml/min.*

INSTI-BASED REGIMENS

- **RALTEGRAVIR 400 MG PLUS ABACAVIR / LAMIVUDINE (EPZICOM®) (once daily)**
 - ▶ *Use if HLA-B*5701-negative and HIV RNA <100,000 copies/ml.*

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 2 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 2. 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	<i>Do not use the following regimens:</i> <ul style="list-style-type: none"> • RPV-based regimens • DRV/r + RAL 	Higher rate of virologic failure observed in those with low pre-treatment CD4 cell count.
	HIV RNA >100,000 cps/mL	<i>Do not use the following regimens:</i> <ul style="list-style-type: none"> • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r + RAL 	Higher rates of virologic failure observed in those with high pre-treatment HIV RNA.
	HLA-B*5701 positive	<i>Do not use ABC-containing regimen.</i>	Abacavir hypersensitivity, a potentially fatal reaction, is highly associated with positivity for the HLA-B*5701 allele.
	Must treat patient before HIV drug resistance results are available	<i>Use:</i> <ul style="list-style-type: none"> • DRV/(r or c) plus TAF/FTC or • DTG plus TAF/FTC 	Transmitted mutations conferring NNRTI resistance are more likely than mutations associated with PI or INSTI resistance.
	CrCl <60 ml/min	<i>Avoid coformulation regimens containing TDF.</i> <i>Consider avoiding ATV.</i>	TDF has been associated with renal tubulopathy. ATV has been associated with chronic kidney disease in some observational studies
	CrCl <50 ml/min	<i>Avoid coformulation regimens containing 3TC.</i>	3TC requires dose adjustment.
	CrCl <30 ml/min	<i>Avoid coformulation regimens containing FTC.</i>	Dosage adjustment required.
	CrCl <30 ml/min	<i>Avoid coformulation regimens containing TAF</i>	Use is not recommended

(TABLE 2, page 1 of 3. 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	<i>ART options include:</i> <ul style="list-style-type: none"> • DTG/ABC/3TC • EFV/TDF/FTC • EVG/c/TDF/FTC • EVG/c/TAF/FTC • RPV/TDF/FTC • RPV/TAF/FTC • BIC/TAF/FTC 	Do not use RPV-based regimens if HIV RNA >100,000 copies/mL and CD4 count <200 cells/μL. Do not use a regimen including ABC if HLAB* 5701 positive
	ARV regimens that must be taken with food	<i>ART options include:</i> <ul style="list-style-type: none"> • ATV/r or ATV/c-based regimens • DRV/r or DRV/c-based regimens • EVG/c/TDF/FTC • EVG/c/TAF/FTC • RPV-based regimens 	
	Psychiatric illnesses	<i>Consider avoiding EFV- and RPV-based regimens. Patients on INSTI-based regimens with pre-existing psychiatric conditions should be closely monitored.</i>	EFV and RPV can exacerbate psychiatric symptoms and may be associated with suicidality.
	Hyperlipidemia	<i>The following ARV drugs have been associated with dyslipidemia:</i> <ul style="list-style-type: none"> • PI/r or PI/c • EFV • EVG/c 	DTG and RAL have fewer lipid effects. TDF has been associated with more favorable lipid effects than ABC or TAF.
	High cardiac risk	<i>DTG-, RAL- or RPV-based regimens may be advantageous in this setting. Consider avoiding ABC- and LPV/r -based regimens. An ATV-based regimen may have advantages over a DRV-based regimen.</i>	Increased cardiovascular risk in some studies
	Pregnancy	<i>Refer to the Perinatal Guidelines.</i>	
Presence of Coinfections	HBV infection <i>(Hepatitis B algorithm completion/non-formulary approval required)</i>	<i>Use TDF or TAF/FTC (or TDF or TAF plus 3TC) whenever possible. If TDF is contraindicated, treat HBV with FTC or 3TC with entecavir or another drug active against HBV.</i>	TDF/TAF, 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.	

(TABLE 2, page 2 of 3. See [KEY TO ACRONYMS](#) at the end of the table.)

PATIENT/REGIMEN CHARACTERISTICS	CLINICAL SCENARIO	CONSIDERATION(S)	RATIONALE/COMMENTS
Presence of Coinfections (continued)	TB infection	<i>If rifampin is used:</i> <ul style="list-style-type: none"> • EFV can be used without dosage adjustment. • 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. • If rifapentine once weekly is used: EFV or RAL (twice daily) with TDF/FTC or ABC/3TC can be used without dosage adjustment • TAF is not recommended with any rifamycin-containing regimen. 	<ul style="list-style-type: none"> • 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. • Rifapentine is both CYP3A4 substrate and inducer. Do not use with TAF • Rifamycins may significantly reduce TAF exposure
Adherence concerns	Patients with history of poor adherence	<i>Consider boosted PI- or DTG-based regimens.</i>	PIs and DTG have a higher relative barrier to resistance
<p>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 = elvitegravir; 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/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate</p> <p>ADAPTED FROM: Table 7, in Panel on Antiretroviral Guidelines for Adults and Adolescents. <i>Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents.</i> 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</p>			
(TABLE 2, page 3 of 3.)			

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 copies. 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.

➔ *Consider therapeutic drug monitoring when pharmacokinetic issues or impaired drug absorption are suspected.*

- **SUSPECTED DRUG RESISTANCE**

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

- ▶ 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>.

➔ See also http://www.iasusa.org/resistance_mutations.

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. Providers should seek expert consultation for patients with viral loads >200 cps/ml for more than 24 weeks. 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 or increased pill burden, 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 to a failing regimen is NOT generally recommended because of the risk of rapid development of resistance.

- Factors associated with better virologic responses to subsequent regimens:
 - ▶ Lower HIV RNA level and/or higher CD4 count at the time of therapy change.
 - ▶ Using a new (i.e., not yet taken) class of ARV drugs.
 - ▶ Using ritonavir or cobicistat-boosted PIs in PI-experienced patients.
- Discontinuing or briefly interrupting therapy is not generally recommended and may lead to a rapid increase in HIV RNA, decrease in CD4 count, and risk of clinical progression
- When switching an ARV regimen in a patient with chronic hepatitis B virus (HBV)/HIV coinfection, the new regimen must continue to provide effective Hepatitis antiviral therapy. Discontinuation of these drugs may cause serious hepatocellular damage resulting from reactivation of HBV.

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. To achieve sustained viral suppression over a lifetime, both long-term and short-term ART toxicities must be anticipated and overcome. The clinician must consider potential adverse effects when selecting an ARV regimen, as well as the individual patient’s comorbidities, concomitant medications, and prior history of drug intolerances.

Prior to prescribing or changing antiretroviral therapy, review the DHHS guidelines³ 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 3, Adverse Effects Associate with Commonly Used Antiretroviral Classes, below.**
 - ➔ See also [Appendix 7](#) 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 3. ADVERSE EFFECTS ASSOCIATED WITH COMMONLY USED ANTIRETROVIRAL CLASSES

ARV CLASS	ADVERSE EFFECTS
NRTIs	<ul style="list-style-type: none"> • Loss of bone mineral density/renal effects (TDF) • Smaller declines in BMD and less impact on renal biomarkers (TAF) • 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) • Hepatic effect (reported with most NRTIs) HBV coinfecting may experience severe hepatic flares when TAF, TDF, FTC or 3TC is withdrawn
NNRTIs	<ul style="list-style-type: none"> • Dyslipidemia (EFV) • QTc prolongation (EFV, RPV) • Hepatotoxicity/hypersensitivity (NVP) • Nervous system/psychiatric effect (EFV) • Rash (all NNRTIs) • Stevens-Johnson Syndrome (NVP>EFV>ETR>RPV)
PIs	<ul style="list-style-type: none"> • Associated with MI/stroke in some cohorts (SQV/r, ATV/r, LPV/r) • Increased CV risk (DRV) • Cholelithiasis (ATV – median onset is 42 months) • Diabetes/insulin resistance (IDV, LPV/r) • Dyslipidemia (all ritonavir or COBI boosted PIs) • 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) • Spontaneous bleeding (TPV)
(TABLE 3, page 1 of 2. 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	<ul style="list-style-type: none"> • Dyslipidemia (EVG/c/TDF/FTC: increased TG, LDL, HDL) • Gastrointestinal effects (EVG/c/TDF/FTC: nausea and diarrhea) • Elevated creatine phosphokinase (RAL) • Insomnia, depression and suicidality (infrequently reported with INSTIs)
<p>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; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine</p> <p>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.</p>	
(TABLE 3, page 2 of 2.)	

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 the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents for additional information: <https://aidsinfo.nih.gov/guidelines>
- **Prior to initiation of ART**, all patients with chronic HBV/HIV coinfection (as determined by a positive HBsAg or HBV DNA test) 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.
- **To avoid viral resistance, both HIV and HBV must be treated.** Emtricitabine (FTC), lamivudine (3TC), tenofovir (TAF or TDF), and entecavir—each has activity against both HIV and HBV. Therefore, if HBV or HIV treatment is needed:
 - ▶ **Preferred regimen:** ART should be initiated with the fixed-dose combination of TDF/FTC or TAF/FTC, or the individual drug combinations of TDF plus 3TC as the NRTI backbone of a fully suppressive antiretroviral regimen. 3TC or FTC have a low barrier to HBV resistance and should only be used in combination with other anti-HBV drugs to prevent the emergence of HBV resistance.

- ▶ **Alternative regimens:** If TDF or TAF cannot be used safely, a different fully suppressive ARV regimen should be used along with entecavir for treating the HBV infection.
- ▶ **FTC or 3TC monotherapy should not be used due to high HBV failure rate.**
- **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 regardless of HIV sensitivity, 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 Guidance 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 recommendations 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.
- **All HIV-infected patients should be screened for HCV infection.**
 - ➔ See BOP Clinical Guidance on Evaluation and Management of Chronic Hepatitis C Virus Infection.
- **Benefits of ART:** Even in the potent HIV antiretroviral therapy era, HIV infection remains independently associated with advanced liver fibrosis and cirrhosis in patients with HIV/HCV coinfection, but 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 initiated in all HIV/HCV-coinfected patients, regardless of CD4 count.
- **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. Although ART should be initiated for all HCV/HIV-coinfected patients regardless of CD4 count, in ART-naive patients with CD4 counts >500 cells/μL, some clinicians may choose to defer ART until HCV treatment is completed.
- ➔ **Review these two DHHS Guidelines for additional information:**
 - (1) Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of

Health, and the HIV Medicine Association of the Infectious Diseases Society of America.
Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf.

(2) Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. Department of Health and Human Services. Available at: <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.

TESTING FOR HBV BEFORE TREATING FOR HCV

- HBV reactivation has been observed in persons with HBV infection during HCV treatment. For that reason, all patients initiating HCV therapy should be tested for HBV.
- Persons with chronic HCV/HIV coinfection should be screened for active and prior hepatitis B virus (HBV) infection by testing for the presence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B surface (HBsAb) and core (HBcAb total). Persons who are not immune to HBV infection (HBsAb-negative) should receive anti-HBV vaccination.
- Persons with HCV/HIV coinfection and active HBV infection (determined by a positive HBsAg test) should receive a complete ART regimen that includes two nucleoside reverse transcriptase inhibitors (NRTIs) with activity against both HIV and HBV, usually tenofovir with emtricitabine or lamivudine, prior to initiating HCV therapy. Treatment should be selected in consultation with a Hepatitis Clinical Pharmacist Consultant or Hepatitis/ Infectious Disease specialist.

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.

The following are links to tables showing drug interactions between the HIV antiretrovirals and the HCV Direct Acting Antivirals (DAAs):

- <https://aidsinfo.nih.gov/guidelines/htmltables/1/5536> (Table 12)
- <https://www.hcvguidelines.org/unique-populations/hiv-hcv> (scroll to the bottom of the page)

After HCV treatment is completed, if ART was modified, the modified ART regimen should be continued for at least 2 weeks before reinitiating the original regimen. Continued use of the modified regimen is necessary because of the prolonged half-life of some HCV drugs and the potential risk of drug-drug interactions if a prior HIV regimen is resumed too soon after HCV treatment is completed.

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.

INH administered daily or twice weekly for 9 months has been the cornerstone of treatment for latent tuberculosis infection (LTBI) to prevent active TB. It can be coadministered with any antiretroviral (ARV) regimen and is safe to use in pregnant women and is the preferred treatment for HIV infected patients in the BOP already taking suppressive antiretroviral regimens with unacceptable drug-drug interactions with rifapentine.

For other cases, INH plus rifapentine administered once weekly for 12 weeks is the preferred BOP treatment for LTBI. In June 2018, the CDC issued updated guidance on the 12-week, once-weekly isoniazid-rifapentine regimen for LTBI, recommending the isoniazid-rifapentine regimen for treatment of LTBI in HIV-infected patients whose antiretroviral regimens have acceptable drug-drug interactions with rifapentine. Although rifapentine induces cytochrome P 450 isoenzymes, and can potentially cause significant drug-drug interactions, there are now pharmacokinetic data supporting its use with EFV and RAL (400 mg twice daily) in combination with either ABC/3TC or TDF/FTC in HIV-infected patients. Note that tenofovir alafenamide (TAF) cannot be co-administered with rifampin, rifabutin, or rifapentine.

- *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)

- *Refer to DHHS guidelines for the Prevention and Treatment of Opportunistic Infections for specific monitoring and management procedures for IRIS, available at: <https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/0>*

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 central nervous system or pulmonary 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 symptoms of IRIS appear.*
- In the setting of some OIs, such as cryptococcal and tuberculous meningitis, for which immediate initiation of ART may increase the risk of serious IRIS, a short delay before initiating ART may be warranted (expert consultation recommended). When ART is initiated in a patient with an intracranial infection, the patient should be closely monitored for signs and symptoms associated with IRIS. In the setting of other OIs, such as *Pneumocystis jirovecii* pneumonia, early initiation of ART is associated with increased survival; therefore, therapy should not be delayed.
- In patients who have active non-meningeal tuberculosis, initiating ART during treatment for tuberculosis confers a significant survival advantage; therefore, ART should be initiated as recommended below.

IRIS IN HIV-POSITIVE PATIENTS WITH PREEXISTING TUBERCULOSIS INFECTION

- ➔ *Refer to DHHS guidelines for the Prevention and Treatment of Opportunistic Infections for specific monitoring and management procedures for IRIS, available at:*
<https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/0>

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 counts from 50–200 cells/ μ L 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/ μ L 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/ μ L; 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](#) in treating IRIS.

14. DENTAL MANAGEMENT

- See [TABLE 4](#) 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 evaluations—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 possible 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 and increases the possibility of drug interactions. 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

⁴ http://www.hivdent.org/_dental_treatment_/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.

treatment failure. Referral to the patient’s primary care provider is indicated.⁷ Once the 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 4. DENTAL MANAGEMENT

DISEASE PROGRESSION: CD4 CELLS/ μ L	MANAGEMENT CONSIDERATIONS
<p>400–600: Initial immune suppression</p> <p>200–400: Emergence of opportunistic infections</p>	<ul style="list-style-type: none"> • 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. • Regular periodontal appointments are recommended for inmates with HIV-associated periodontal disease. • Use HIV Dental Encounter code (7113) for assessment and treatment when co-managing patients with medical staff.
<p>≤ 200: Severe immune suppression</p>	<ul style="list-style-type: none"> • All of the above. • Primary care provider should be contacted for pretreatment medical consultation. • Review health history and update labs: <ul style="list-style-type: none"> ▶ <i>Determine if patient is neutropenic (absolute neutrophil counts <500): Prophylactic antimicrobials for severe neutropenic patients.</i> ▶ <i>Determine if patient has Idiopathic Thrombocytopenia Purpura (ITP): Obtain pre-surgical platelet counts for invasive patient procedures, which include scaling and curettage.</i> • Avoid aspirin and NSAIDs as analgesics.

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.

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>

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.

GENERAL DEFINITIONS

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/integrase). **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.

VIROLOGIC FAILURE is defined by DHHS as the inability to achieve or maintain suppression of viral replication to an HIV RNA level <200 copies/ml with ART.

INFECTION CONTROL DEFINITIONS: STANDARD PRECAUTIONS

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 relevant to the correctional setting 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.

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 AIDSinfo website's list of Federally approved HIV/AIDS medical practice guidelines at: http://www.aidsinfo.nih.gov/guidelines/			
TOPIC	NAME	LINK	AGENCY
Antiretroviral Therapy	<i>Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents (2018)</i>	http://www.aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0/	DHHS
Antiretroviral Therapy for Pregnant Women	<i>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 (2018)</i>	http://www.aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0/	DHHS
HIV Testing	<i>Revised Recommendations for HIV Testing in Health-Care Settings (2006)</i> AND <i>Laboratory Testing for the Diagnosis of HIV Infection: Update Recommendations (2014)</i>	https://www.cdc.gov/hiv/guidelines/testing.html	CDC
Immunizations	<i>Immunization Schedule, Adult Version</i>	http://www.cdc.gov/vaccines/schedule/index.html	CDC ACIP
	<i>Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents (2018)</i>	http://www.aidsinfo.nih.gov/contentfiles/vguidelines/adult_oi_041009.pdf	NIH IDSA
Non-Occupational Exposures	<i>Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States (2017)</i>	https://stacks.cdc.gov/view/cdc/38856	CDC
Occupational Exposures	<i>Clinical Practice Guidelines on Medical Management of Exposures: HIV, HBV, HCV Human Bites, and Sexual Assaults (2014)</i>	https://www.bop.gov/resources/health_care_mngmt.jsp	BOP
	<i>PEPline: Clinician Consultation Center Post-Exposure Prophylaxis Hotline</i> <i>(Call 888-448-4911 for a phone consultation, 11AM–8PM ET, seven days a week.)</i>	<i>For PEP Quick Guide to frequently asked questions:</i> http://nccc.ucsf.edu/clinician-consultation/post-exposure-prophylaxis-pep/	UCSF
Opportunistic Infections	<i>Guidelines for Preventing Opportunistic Infections among HIV-Infected Persons (2018)</i>	http://www.aidsinfo.nih.gov/contentfiles/vguidelines/adult_oi_041009.pdf	CDC NIH IDSA
Oral Health Care	<i>HIVdent: HIV/AIDS Oral Healthcare Resource on the Internet</i>	http://www.hivdent.org/	Non-profit coalition
Online Education & Clinic Tools	<i>AETC AIDS Education & Training Center Program</i>	https://aidsetc.org/nhc	DHHS- HRSA

(Appendix 1, Guidelines Regarding Medical Care of HIV-Infected Persons, page 1 of 2. **ABBREVIATIONS** defined at the end.)

TOPIC	NAME	LINK	AGENCY
Risk Assessment	<i>Preventing New HIV Infections</i>	https://www.cdc.gov/hiv/guidelines/preventing.html	CDC
Sexually Transmitted Diseases	<i>Sexually Transmitted Diseases Treatment Guidelines (2015)</i>	http://www.cdc.gov/std/treatment/	CDC
<p>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</p>			
<p><i>(Appendix 1, Guidelines Regarding Medical Care of HIV-Infected Persons, page 2 of 2.)</i></p>			

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	<i>Including, but not limited to:</i> Fever, adenopathy, pharyngitis, rash, myalgias, diarrhea, and headache.
Signs/symptoms of HIV-related condition	<i>Including, but not limited to:</i> 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	<i>Follow-up HIV-antibody testing should be performed at the following intervals after the exposure date:</i> 6 weeks, 12 weeks, and 6 months (and 12 months for those who become infected with HCV after exposure to a source coinfecting 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:	
<ul style="list-style-type: none"> • 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. <p>* Inmates must participate in mandatory HIV testing programs.</p>	
Offer voluntary testing to ALL sentenced inmates at the time of incarceration:	
<p>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.</p> <p>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.</p>	

APPENDIX 3. HIV-INFECTED INMATES – INITIAL ASSESSMENT

REVIEW OF SYMPTOMS	PHYSICAL EXAMINATION
<p>A complete review of systems should be performed, with special attention given to the following areas:</p> <ul style="list-style-type: none"> <input type="checkbox"/> GENERAL: Unexplained weight loss, night sweats, fever, changes in body habitus <input type="checkbox"/> SKIN: Skin discoloration, rash, ulcers, or lesions <input type="checkbox"/> LYMPH NODES: Localized or generalized enlargement of lymph nodes <input type="checkbox"/> EYES: Vision change or loss <input type="checkbox"/> MOUTH: Gum disease, ulcers, oral lesions or pain <input type="checkbox"/> CARDIOPULMONARY: Chest pain, shortness of breath, palpitations, wheezing, dyspnea, orthopnea <input type="checkbox"/> GASTROINTESTINAL: Diarrhea, nausea, pain <input type="checkbox"/> ENDOCRINOLOGY: Symptoms of hyperglycemia, thyroid disease, hypogonadism <input type="checkbox"/> 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 <input type="checkbox"/> GENITOURINARY: Dysuria, urethral or vaginal discharge or lesions, hematuria <input type="checkbox"/> ORTHOPEDIC: Hip pain, joint pain, fractures; diagnosis of, or risk factors for, osteopenia/osteoporosis 	<p>A complete physical examination should be performed, with special attention given to the following areas:</p> <ul style="list-style-type: none"> <input type="checkbox"/> VITAL SIGNS: Including height and weight <input type="checkbox"/> GENERAL: Including body habitus; evidence of obesity, wasting, lipodystrophy; assessment of frailty and ambulatory ability <input type="checkbox"/> SKIN: Seborrheic dermatitis, ecchymoses, purpura, petechiae, Kaposi sarcoma, herpes simplex or zoster, psoriasis, molluscum contagiosum, onychomycosis, folliculitis, condylomata, cutaneous fungal infections <input type="checkbox"/> LYMPH NODES: Generalized or localized lymphadenopathy <input type="checkbox"/> EYE: Retinal exudates or cotton wool spots, hemorrhages, pallor, icterus <input type="checkbox"/> OROPHARYNX: Oral hairy leukoplakia, candidiasis (thrush, palatal erythema, angular cheilosis), aphthous ulcers, gingivitis, periodontal disease, Kaposi sarcoma, tonsillar or parotid gland enlargement <input type="checkbox"/> CARDIOVASCULAR: Heart exam, peripheral pulses, presence/absence of edema <input type="checkbox"/> CHEST: Lung examination <input type="checkbox"/> BREAST: Nodules, nipple discharge <input type="checkbox"/> ABDOMEN: Hepatomegaly, splenomegaly, masses, tenderness <input type="checkbox"/> GENITOURINARY: Ulcers, warts, chancres, rashes, abnormal gynecologic exam, discharge <input type="checkbox"/> ANORECTAL: Ulcers, warts, fissures, internal or external hemorrhoids, masses, Kaposi sarcoma <input type="checkbox"/> 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 SCREENING AND DIAGNOSTIC EVALUATIONS

BASELINE TESTS	COMMENTS
HIV serology	If diagnosis is not previously confirmed, and viral load is low or undetectable.
CD4 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 <i>Toxoplasma gondii</i> infection	Use anti-toxoplasma IgG.
Screening for latent <i>Mycobacterium tuberculosis</i> infection	Use tuberculin skin test or IGRA. IGRA is preferred if patient has history of BCG vaccination.
Chest radiography	A chest x-ray (CXR) is recommended for all HIV-infected inmates at intake. A PA view is sufficient for asymptomatic inmates; PA and lateral views are recommended for symptomatic inmates.
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). <ul style="list-style-type: none"> • If HBsAg+, order HBV RNA level. • If HCVAb+, order HCV RNA level and HCV genotype.

Appendix 4a, Baseline Screening and Diagnostic Evaluations, page 1 of 2

BASELINE TESTS	COMMENTS
Tests that may be performed under certain circumstances:	
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.
<p>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</p>	
<i>Appendix 4a, Baseline Screening and Diagnostic Evaluations, page 2 of 2</i>	

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

TESTING	Entry into care	If ART initiation is delayed *	ART initiation or modification	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		if VL<20 & CD4≥300 after 2 years on ART	X
Viral load	X	optional	X	X	X	X**		X
Resistance testing	X	optional	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 non-immune & no chronic HBV infection				may repeat if non-immune & no chronic HBV infection	
Hep C serology	X		may repeat if negative at baseline				repeat HCV screening for at-risk patients	
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	if on ZDV or if CD4 is tested			
Fasting lipid profile	X	if normal, annually	X			if last measurement was abnormal	if last measurement was normal	
Fasting glucose or hemoglobin A1C	X	if normal, annually	X		if last measurement was abnormal		if last measurement was normal	
UA	X		X			if on TAF or 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.							

* q = "every"

** 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 July 14, 2016. 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:
<ul style="list-style-type: none"> • 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. <p>➔ <i>Co-testing (Pap test and HPV test) is not recommended for women younger than 30.</i></p>
HIV-INFECTED WOMEN AGED ≥30 YEARS
IF PAP TESTING ONLY:
<ul style="list-style-type: none"> • 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:
<ul style="list-style-type: none"> • 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.
<p>Adapted from: <i>Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents.</i> Updated August 10, 2017. Available at: https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection-prevention-and-treatment-guidelines/343/hpv</p>

APPENDIX 6. PROPHYLAXIS FOR HIV-RELATED OPPORTUNISTIC INFECTIONS

→ See *Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents* for complete information. Available at: <https://aidsinfo.nih.gov/guidelines>

DRUG/DOSAGES*	TOXICITIES	COMMENTS
PNEUMOCYSTIS PNEUMONIA		
INDICATIONS: CD4 count <200 cells/μL		
→ Can stop primary and secondary PCP prophylaxis if CD4 count increases to >200 cells/μL for 3 months.		
FIRST CHOICE		
TMP-SMX (Bactrim, Septra) 1 DS daily <i>OR</i> 1 SS daily	rash, fever, nausea, leukopenia, hepatitis	<ul style="list-style-type: none"> Prevents toxoplasmosis and bacterial infections. Use 1 DS/day if toxo IgG+.
ALTERNATIVES		
Dapsone 100 mg/day <i>OR</i> 50 mg bid	hemolysis, methemoglobinemia	<ul style="list-style-type: none"> Screening for G6-PD deficiency recommended in high-risk patients.
Pentamidine 300 mg q month aerosolized	bronchospasm/ cough (responds to bronchodilator tx)	<ul style="list-style-type: none"> Obtain screening chest x-ray for TB. Administer pentamidine by Respigard II nebulizer.
Atovaquone 1500 mg daily	rash, GI intolerance	<ul style="list-style-type: none"> Must be taken with meals for absorption.
TOXOPLASMOSIS		
INDICATION: Toxo IgG+ and CD4 count <100 cells/μL		
→ Can stop primary toxoplasmosis prophylaxis if CD4 count is >200 cells/μL for >3 months. Can stop secondary prophylaxis if CD4 count is >200 cells/μL AND asymptomatic for >6 months.		
FIRST CHOICE		
TMP-SMX (Bactrim, Septra) 1 DS daily	rash, fever, nausea, leukopenia, hepatitis	<ul style="list-style-type: none"> Repeat toxo IgG if titer was negative when CD4 count was <100 cells/μL. Monitor for anemia/leukopenia; CBC q 3–4 months
ALTERNATIVE		
Dapsone 50 mg/day plus (pyrimethamine 50 mg + leucovorin 25 mg)/week	hemolysis, anemia	<ul style="list-style-type: none"> Monitor for anemia/leukopenia; CBC q 3–4 months.
Atovaquone 1500 mg daily	rash, GI intolerance	<ul style="list-style-type: none"> Must be taken with meals for absorption.
MYCOBACTERIUM AVIUM COMPLEX (MAC)		
INDICATION: CD4 count <50 cells/μL		
→ Can stop primary prophylaxis once CD4 count >100 cells/ μL for 3 months in response to ART. Can stop secondary prophylaxis if completed ≥12 months of therapy AND no symptoms of MAC AND CD4 count >100 cells/μL for ≥6 months.		
FIRST CHOICES		
Azithromycin 1200 mg/week	nausea/vomiting	
Clarithromycin 500 mg bid	nausea/vomiting	
ALTERNATIVE		
Rifabutin Adjust dose based on concomitant ART	uveitis, arthralgias, hepatitis	<ul style="list-style-type: none"> Uveitis when given with fluconazole; creates rifampin resistance; review drug interactions.
* q = “every” bid = “twice daily”		

**APPENDIX 7. ADVANTAGES AND DISADVANTAGES OF ARV COMPONENTS
RECOMMENDED AS INITIAL ANTIRETROVIRAL THERAPY**

ARV CLASS	ARV AGENT(S)	ADVANTAGES	DISADVANTAGES
DUAL-NRTI	ABC/3TC	<ul style="list-style-type: none"> • Co-formulated with DTG as an STR. 	<ul style="list-style-type: none"> • Inferior virologic responses in patients with baseline HIV RNA $\geq 100,000$ 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.
	TAF/FTC	<ul style="list-style-type: none"> • Co-formulated with EFV, EVG/c, and RPV as an STR. • Active against HBV. • Safe in patients with eGFR ≥ 30 ml/min. 	<ul style="list-style-type: none"> • Fasting lipid levels, including LDL and HDL cholesterol and triglycerides, increased more in the TAF group than in the TDF group.
	TDF/FTC	<ul style="list-style-type: none"> • Co-formulated with EFV, EVG/c, and RPV as an STR. • Active against HBV; recommended dual-NRTI for HIV/HBV coinfecting patients. • Better virologic responses than with ABC/3TC in patients with baseline viral load $\geq 100,000$ cps/mL, when combined with ATV/r or EFV. 	<ul style="list-style-type: none"> • Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency. • Decreases BMD more than other NRTI combinations. • Osteomalacia has been reported as a consequence of proximal tubulopathy.
INSTI (continues on next page)	DTG	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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. • Insomnia, depression, and suicidal ideation (usually in patients with pre-existing psychiatric conditions). • DHHS recommendations against using dolutegravir in individuals of child-bearing potential who have plans to conceive or are not taking effective contraception, due to possible neural tube defects.

*Appendix 7, Advantage/Disadvantages of ARV Components, page 1 of 4
(See [KEY TO ACRONYMS](#) on last page of Appendix.)*

ARV CLASS	ARV AGENT(S)	ADVANTAGES	DISADVANTAGES
INSTI (continued from previous page)	EVG/c	<ul style="list-style-type: none"> • Co-formulated as an STR with TDF/FTC or TAF/FTC. • Once-daily dosing. • Compared with ATV/r, causes smaller increases in total and LDL cholesterol. 	<ul style="list-style-type: none"> • 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 • Insomnia, depression, and suicidal ideation (usually in patients with pre-existing psychiatric conditions) • Food requirement. • Emerging data on cobicistat-containing regimens suggest decreased drug levels occur during pregnancy, with an associated risk of loss of virologic suppression. Cobicistat-containing regimens should therefore not be initiated in treatment-naïve pregnant women. Consider switching ART if an HIV-infected woman becomes pregnant.
	BIC	<ul style="list-style-type: none"> • Co-formulated as an STR with TAF/FTC. • Once-daily dosing. • Higher barrier to resistance than EVG or RAL. • No food requirement • BIC is not a CYP3A4 inducer or inhibitor. 	<ul style="list-style-type: none"> • 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. • CYP3A4 and UGT substrate; potential for drug interactions. • BIC is an inhibitor of the drug transporters OAT2 and MATE1; dofetilide is contraindicated.
	RAL	<ul style="list-style-type: none"> • Compared to other INSTIs, has longest post-marketing experience. • Once- or twice-daily dosing. • No food requirement. • No CYP3A4 interactions. 	<ul style="list-style-type: none"> • 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. • Insomnia, depression and suicidal ideation (usually in patients with pre-existing psychiatric conditions) • UGT substrate; potential for drug interactions.

Appendix 7, Advantage/Disadvantages of ARV Components, page 2 of 4
(See [KEY TO ACRONYMS](#) on last page of Appendix.)

ARV CLASS	ARV AGENT(S)	ADVANTAGES	DISADVANTAGES
NNRTI	EFV	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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 • QTc interval prolongation • 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	<ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> - Fewer CNS adverse effects. - Fewer lipid effects. - Fewer rashes. 	<ul style="list-style-type: none"> • 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. • QTc interval prolongation; Consider alternative when taking medications known to increase the risk of torsades de pointes.
PI (continues on next page)	ATV/c or ATV/r	<ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • 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. • COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. • Emerging data on cobicistat-containing suggest decreased drug levels during pregnancy and an associated risk of loss of virologic. Cobicistat-containing regimens should therefore not be initiated in treatment-naïve pregnant women. Consider switching ART if an HIV-infected woman becomes pregnant.

Appendix 7, Advantage/Disadvantages of ARV Components, page 3 of 4
(See [KEY TO ACRONYMS](#) on last page of Appendix.)

ARV CLASS	ARV AGENT(S)	ADVANTAGES	DISADVANTAGES
PI (continued from previous page)	DRV/c or DRV/r	<ul style="list-style-type: none"> Higher genetic barrier to resistance than NNRTIs, EVG, and RAL. PI resistance at the time of treatment failure uncommon with pharmacokinetically-boosted PIs. 	<ul style="list-style-type: none"> Skin rash. Food requirement. GI adverse effects. Potential for drug interactions with CYP3A4 inhibitors and substrates. COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. Emerging data on cobicistat-containing regimens suggest decreased drug levels occur during pregnancy, with an associated risk of loss of virologic suppression. Cobicistat-containing regimens should therefore not be initiated in treatment-naïve pregnant women. Consider switching ART if an HIV-infected woman becomes pregnant.
	LPV/r	<ul style="list-style-type: none"> Only RTV co-formulated PI. No food requirement. 	<ul style="list-style-type: none"> 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; **BIC** = Bictegravir; **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; **TAF/FTC** = tenofovir alafenamide/emtricitabine; **TDF/FTC** = tenofovir disoproxil fumarate/emtricitabine

APPENDIX 8. 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 <u>NO</u> RENAL DOSAGE ADJUSTMENT			
Abacavir	600 mg qd <i>OR</i> 300 mg bid	No dosage adjustment necessary	<i>Child-Pugh Class A:</i> • 200 mg PO BID (use oral solution) <i>Child-Pugh Class B or C:</i> • Contraindicated
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 <i>OR</i> 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
TAF+FTC (Descovy®)	1 tablet qd	CrCl <30/HD: → Not recommended	No dosage adjustment necessary
Zidovudine	300 mg bid	CrCl <15/HD: 100 mg tid <i>OR</i> 300 mg qd	No dosage adjustment necessary
NNRTI REQUIRING NO RENAL DOSAGE ADJUSTMENT			
Efavirenz	600mg qd	No dosage adjustment necessary	Use with caution in patients with hepatic impairment.
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	<i>Child-Pugh Class B or C:</i> → Contraindicated
* q = “every”; qd = once daily; bid = twice daily; tid = three times a day			
<i>Appendix 8, Dosing of ARV Drugs with CKD and Hepatic Impairment, page 1 of 2</i>			

ARV	USUAL DAILY DOSE*	DOSING IN RENAL INSUFFICIENCY/ HEMODIALYSIS (HD)*	DOSING IN HEPATIC IMPAIRMENT
PIs REQUIRING NO RENAL DOSAGE ADJUSTMENT			
Darunavir	800 mg qd <i>OR</i> 600 mg bid, if DRV mutation	No dosage adjustment necessary	Severe hepatic impairment: → Not recommended
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 <i>OR</i> 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
Genvoya®	1 tablet qd	→ Not recommended for use in patients with CrCl <30 mL/min.	Not recommended in severe hepatic insufficiency
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 8, Dosing of ARV Drugs with CKD and Hepatic Impairment, page 2 of 2			