



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Drug-Resistance Testing (Last updated October 25, 2018; last reviewed October 25, 2018)

Panel's Recommendations

For Antiretroviral Therapy-Naive Persons:

- HIV drug-resistance testing is recommended at entry into care for persons with HIV to guide selection of the initial antiretroviral therapy (ART) regimen **(AII)**. If therapy is deferred, repeat testing may be considered at the time of ART initiation **(CIII)**.
- Genotypic, rather than phenotypic, testing is the preferred resistance testing to guide therapy in antiretroviral (ARV)-naive patients **(AIII)**.
- In persons with acute or recent (early) HIV infection, in pregnant people with HIV, or in people who will initiate ART on the day of or soon after HIV diagnosis, ART initiation should not be delayed while awaiting resistance testing results; the regimen can be modified once results are reported **(AIII)**.
- Standard genotypic drug-resistance testing in ARV-naive persons involves testing for mutations in the reverse transcriptase (RT) and protease (PR) genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern, providers should ensure that genotypic resistance testing also includes the integrase gene **(AIII)**.

For Antiretroviral Therapy-Experienced Persons:

- HIV drug-resistance testing should be performed to assist the selection of active drugs when changing ART regimens in the following patients:
 - Persons with virologic failure and HIV RNA levels >1,000 copies/mL **(AI)**
 - Persons with HIV RNA levels >500 copies/mL but <1,000 copies/mL, drug-resistance testing may be unsuccessful but should still be considered **(BII)**
 - Persons with suboptimal viral load reduction **(AII)**
- When a person with HIV experiences virologic failure while receiving an INSTI-based regimen, genotypic testing for INSTI resistance (which may need to be ordered separately) should be performed to determine whether to include a drug from this class in subsequent regimens **(AII)**.
- Drug-resistance testing in the setting of virologic failure should be performed while the person is taking prescribed ARV drugs or, if that is not possible, within 4 weeks after discontinuing therapy **(AII)**. If more than 4 weeks have elapsed since the ARVs were discontinued, resistance testing may still provide useful information to guide therapy; however, it is important to recognize that previously selected resistance mutations can be missed due to lack of drug-selective pressure **(CIII)**.
- Genotypic testing is preferred over phenotypic resistance testing to guide therapy in persons with suboptimal virologic response or virologic failure while on first- or second-line regimens and in individuals in whom resistance mutation patterns are known or not expected to be complex **(AII)**.
- The addition of phenotypic to genotypic resistance testing is recommended for persons with known or suspected complex drug-resistance mutation patterns **(BIII)**.
- All prior and current drug-resistance test results, if available, should be considered when constructing a new regimen for a patient **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Co-Receptor Tropism Assays (Last updated October 25, 2018; last reviewed October 25, 2018)

Panel's Recommendations

- A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered (**AI**).
- Co-receptor tropism testing is recommended for patients who exhibit virologic failure on a CCR5 antagonist (**BIII**).
- A phenotypic tropism assay is preferred to determine HIV-1 co-receptor usage (**AI**).
- A genotypic tropism assay should be considered as an alternative test to predict HIV-1 co-receptor usage (**BII**).
- A proviral DNA tropism assay can be utilized for patients with undetectable HIV-1 RNA when a CCR5 antagonist is considered for use in a new regimen (e.g., as part of a regimen switch or simplification) (**BII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

HLA-B*5701 Screening (Last updated December 1, 2007; last reviewed January 10, 2011)

Panel's Recommendations

- The Panel recommends screening for HLA-B*5701 before starting patients on an abacavir (ABC)-containing regimen to reduce the risk of hypersensitivity reaction (HSR) (**AI**).
- HLA-B*5701-positive patients should not be prescribed ABC (**AI**).
- The positive status should be recorded as an ABC allergy in the patient's medical record (**AII**).
- When HLA-B*5701 screening is not readily available, it remains reasonable to initiate ABC with appropriate clinical counseling and monitoring for any signs of HSR (**CIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Initiation of Antiretroviral Therapy (Last updated December 18, 2019; last reviewed December 18, 2019)

Panel's Recommendations

- Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality (**AI**) and to prevent the transmission of HIV to others (**AI**).
- The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV (**AII**).
- When initiating ART, it is important to educate patients regarding the benefits of ART and to deploy strategies to optimize care engagement and treatment adherence (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Antiretroviral Therapy to Prevent Sexual Transmission of HIV (Treatment as Prevention) (Last updated December 18, 2019; last reviewed December 18, 2019)

Panel's Recommendations

- All persons with HIV should be informed that maintaining a plasma HIV RNA (viral load) of <200 copies/mL, including any measurable value below this threshold value, with antiretroviral therapy (ART) prevents sexual transmission of HIV to their partners. Patients may recognize this concept as Undetectable = Untransmittable or U=U (**AII**).
- Persons with HIV who are starting ART should use another form of prevention with sexual partners (e.g., condoms, pre-exposure prophylaxis [PrEP] for the HIV-negative sexual partner, sexual abstinence) for at least the first 6 months of treatment and until a viral load of <200 copies/mL has been documented (**AII**). Many experts would recommend confirming sustained suppression before assuming that there is no further risk of sexual HIV transmission (**AIII**).
- When the viral load is ≥ 200 copies/mL, additional methods are needed to prevent transmission of HIV to sexual partners until resuppression to <200 copies/mL has been confirmed (**AIII**).
- Persons with HIV who intend to rely upon ART for prevention need to maintain high levels of ART adherence (**AIII**). They should be informed that transmission is possible during periods of poor adherence or treatment interruption (**AIII**).
- At each visit for HIV care, clinicians should assess adherence to ART and counsel patients regarding the importance of ART to their own health as well as its role in preventing sexual HIV transmission (**AIII**).
- Providers should inform patients that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other sexually transmitted infections (STIs) (**AII**).
- Providers should also routinely screen all sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations and Recommendations

- An antiretroviral (ARV) regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) administered in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (also known as a booster; the two drugs used for this purpose are cobicistat and ritonavir).
- Data also support the use of the two-drug regimen, dolutegravir plus lamivudine, for initial treatment.
- Before initiating antiretroviral therapy (ART) in a person of childbearing potential, a pregnancy test should be performed (**AIII**). Before prescribing ART to a person of childbearing potential, please refer to Table 6b for information about safety of different INSTI-based regimens taken around the time of conception.
- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies the following regimens as *Recommended Initial Regimens for Most People with HIV* (in alphabetical order):
 - Bictegravir/tenofovir alafenamide/emtricitabine (**AI**)
 - Dolutegravir/abacavir/lamivudine—**only** for individuals who are HLA-B*5701 negative and without chronic hepatitis B virus (HBV) coinfection (**AI**)
 - Dolutegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide or tenofovir disoproxil fumarate)^a (**AI**)
 - Dolutegravir/lamivudine (**AI**)—except for individuals with HIV RNA >500,000 copies/mL, HBV co-infection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
 - Raltegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF])^a (**BI** for TDF, **BII** for TAF)
- To address individual patient characteristics and needs, the Panel also provides a list of *Recommended Initial Regimens in Certain Clinical Situations* (Table 6a).
- Given the many 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, dosing frequency, drug-drug interaction potential, resistance test results, comorbid conditions, access, and cost. Table 7 provides guidance on choosing an ARV regimen based on selected clinical case scenarios. Table 9 highlights the advantages and disadvantages of different components in a regimen.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

^a TAF and TDF are two forms of tenofovir that are approved by the Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Management of the Treatment-Experienced Patient

Virologic Failure (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations and Recommendations

- Assessing and managing a patient who is experiencing failure of antiretroviral therapy (ART) is complex. Expert advice is critical and should be sought.
- Evaluation of virologic failure should include an assessment of adherence, drug-drug and drug-food interactions, drug tolerability, HIV RNA level and CD4 T lymphocyte (CD4) cell count trends over time, ART history, and prior and current drug-resistance test results.
- Drug-resistance testing should be performed while the patient is taking the failing antiretroviral (ARV) regimen (**AI**) or within 4 weeks of treatment discontinuation (**AII**). Even if more than 4 weeks have elapsed since ARV drugs were discontinued, resistance testing can still provide useful information to guide therapy, although it may not detect previously selected resistance mutations (**CIII**).
- The goal of treatment for ART-experienced patients with drug resistance who are experiencing virologic failure is to establish virologic suppression (i.e., HIV RNA levels below the lower limits of detection of currently used assays) (**AI**).
- A new regimen should include at least two, and preferably three, fully active agents (**AI**). A fully active agent is one that is expected to have uncompromised activity based on the patient's ART history and current and past drug-resistance test results. A fully active agent may also have a novel mechanism of action.
- In general, adding a single ARV agent to a virologically failing regimen **is not recommended**, because this may risk the development of resistance to all drugs in the regimen (**BII**).
- For some highly ART-experienced patients with extensive drug resistance, maximal virologic suppression may not be possible. In this case, ART should be continued (**AI**) with regimens that are designed to minimize toxicity, preserve CD4 counts, and delay clinical progression.
- It is crucial to provide continuous adherence support to all patients before and after regimen changes due to virologic failure.
- **Data from an observational study in Botswana suggest that there is** an increased risk of neural tube defects (NTDs) in infants born to individuals who were receiving dolutegravir (DTG) at the time of conception; however, the risk of these defects is still low. In patients with virologic failure who are of childbearing potential and who are not using effective contraception or who are contemplating pregnancy, the following factors should be considered:
 - Clinicians should review **Table 6b** for information to consider when choosing to initiate or continue an integrase strand transfer inhibitor.
 - If there is an active ARV agent that can be used in place of DTG, DTG should not be prescribed (**AII**).
 - If no alternatives exist, providers and patients should discuss the possible risk of NTDs and weigh that risk against the risks of persistent viremia in the patient and HIV transmission to the fetus if pregnancy occurs while the patient is not on effective ART. The decision of whether to initiate or continue DTG should be made after carefully considering these risks.
- When it is not possible to construct a viable suppressive regimen for a patient with multidrug-resistant HIV, the clinician should consider enrolling the patient in a clinical trial of investigational agents or contacting pharmaceutical companies that may have investigational agents available.
- When switching an ARV regimen in a patient with hepatitis B virus (HBV)/HIV coinfection, ARV drugs that are active against HBV should be continued as part of the new regimen. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage.
- Discontinuing or briefly interrupting therapy may lead to a rapid increase in HIV RNA, a decrease in CD4 count, and an increase in the risk of clinical progression. Therefore, this strategy **is not recommended** in the setting of virologic failure (**AI**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Poor CD4 Cell Recovery and Persistent Inflammation Despite Viral Suppression (Last updated April 8, 2015; last reviewed April 8, 2015)

Panel's Recommendations

- Morbidity and mortality from several AIDS and non-AIDS conditions are increased in individuals with HIV despite antiretroviral therapy (ART)-mediated viral suppression, and are predicted by persistently low CD4 T lymphocyte (CD4) cell counts and/or persistent immune activation.
- ART intensification by adding antiretroviral (ARV) drugs to a suppressive ART regimen does not consistently improve CD4 cell recovery or reduce immune activation and is not recommended (**AI**).
- In individuals with viral suppression, switching ARV drug classes does not consistently improve CD4 cell recovery or reduce immune activation and is not recommended (**BIII**).
- No interventions designed to increase CD4 cell counts and/or decrease immune activation are recommended at this time (in particular, interleukin-2 **is not recommended [AI]**) because no intervention has been proven to decrease morbidity or mortality during ART-mediated viral suppression.
- Monitoring markers of immune activation and inflammation **is not recommended** because no immunologically targeted intervention has proven to improve the health of individuals with abnormally high biomarker levels, and many markers that predict morbidity and mortality fluctuate widely in individuals (**AII**).
- Because there are no proven interventions to improve CD4 cell recovery and/or inflammation, efforts should focus on addressing modifiable risk factors for chronic disease (e.g., encouraging smoking cessation, a healthy diet, and exercise; treating hypertension and hyperlipidemia) (**AII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations and Panel's Recommendations

- Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance make it possible to consider switching a person with HIV from an effective regimen to an alternative regimen in some situations.
- The fundamental principle of regimen optimization is to maintain viral suppression without jeopardizing future treatment options.
- Adverse events, drug-drug or drug-food interactions, pill burden, pregnancy, cost, or the desire to simplify a regimen may prompt a regimen switch.
- It is critical to review a patient's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results, before selecting a new antiretroviral therapy regimen **(AI)**.
- Monotherapy with either a boosted protease inhibitor or an integrase strand transfer inhibitor has been associated with unacceptable rates of virologic failure and the development of resistance; therefore, monotherapy as a switch strategy **is not recommended (AI)**.
- When switching an ARV regimen in a person with hepatitis B virus (HBV)/HIV coinfection, ARV drugs that are active against HBV infection should be continued **(AII)**. Using 3TC or FTC as the only drug in a regimen with HBV activity **is not recommended (AII)**, as HBV resistance to these drugs can emerge. Discontinuation of HBV drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage.
- Consultation with an HIV specialist is recommended when planning a regimen switch for a patient with a history of resistance to one or more drug classes **(AIII)**.
- Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Considerations for Antiretroviral Use in Special Patient Populations

Acute and Recent (Early) HIV Infection (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations and Recommendations

- Antiretroviral therapy (ART) is recommended for all individuals with HIV, including those with early^a HIV infection (AI). ART should be initiated as soon as possible after HIV diagnosis (AII).
- The goal of ART is to suppress plasma HIV RNA to undetectable levels (AI) and to prevent transmission of HIV (AI). Testing for plasma HIV RNA levels, CD4 T lymphocyte cell counts, and toxicity monitoring should be performed as recommended for persons with chronic HIV infection (AII).
- A sample for genotypic testing should be sent before initiation of ART (AIII). ART can be initiated before drug resistance testing and HLA-B*5701 test results are available. In this setting, one of the following ART regimens is recommended (AIII):
 - Bictegravir (BIC)/tenofovir alafenamide (TAF)/emtricitabine (FTC)
 - Dolutegravir (DTG) with (TAF or tenofovir disoproxil fumarate [TDF])^b plus (FTC or lamivudine [3TC])
 - Boosted darunavir (DRV) with (TAF or TDF)^b plus (FTC or 3TC)
- Pregnancy testing should be performed in individuals of childbearing potential before initiation of ART (AIII).
- Data from an observational study in Botswana suggest there may be an increased risk of neural tube defects in infants born to individuals who were receiving DTG at the time of conception. Before initiating an integrase strand transfer inhibitor-based regimen in a person of childbearing potential, clinicians should review Table 6b for information to consider when choosing an ART regimen.
- As there are no safety data for BIC use around the time of conception, an approach similar to that outlined for DTG should be considered for BIC-containing ART (AIII).
- When the results of drug resistance and HLA-B*5701 testing are available, the treatment regimen can be modified if needed (AII).
- Providers should inform individuals starting ART of the importance of adherence to achieve and maintain viral suppression (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

^a Early infection represents either acute or recent infection.

^b TAF and TDF are two forms of tenofovir that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

Adolescents and Young Adults with HIV (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations and Recommendations

- Adolescents living with HIV largely belong to two distinct groups—those who acquired HIV in infancy and are heavily antiretroviral therapy (ART)-experienced, and those who acquired HIV more recently during their teens.
- ART is recommended for all individuals with HIV (**AI**) to reduce morbidity and mortality and to prevent HIV transmission. Therefore, ART is also recommended for ART-naive adolescents.
- Before initiation of therapy, adolescents' readiness and ability to adhere to therapy within their psychosocial context need to be carefully considered as part of therapeutic decision making (**AIII**).
- Once ART is initiated, appropriate support is essential to reduce potential barriers to adherence and maximize the likelihood of achieving sustained viral suppression (**AII**).
- Data from an observational study in Botswana suggest that there may be an increased risk of neural tube defects in infants born to individuals who were receiving dolutegravir at the time of conception. Before initiating an integrase strand transfer inhibitor-based regimen in an adolescent of childbearing potential, clinicians should review [Table 6b](#) for information to consider when choosing an ART regimen.
- The adolescent sexual maturity rating (SMR) can help guide regimen selection when initiating or changing an ART regimen as recommended by either the Adult and Adolescent Antiretroviral Guidelines or the [Pediatric Antiretroviral Guidelines](#). The Adult and Adolescent Antiretroviral Guidelines are more appropriate for postpubertal adolescents (i.e., those with SMRs of 4 or 5) (**AIII**).
- Pediatric and adolescent care providers should prepare adolescents for the transition into adult care settings. Adult providers should be sensitive to the challenges associated with such transitions, consulting and collaborating with adolescent HIV care providers to ensure adolescents' successful transition and continued engagement in care (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

HIV-2 Infection (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations and Recommendations

- The clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma viral loads, and lower mortality rate than HIV-1 infection. However, progression to AIDS and death will occur in the majority of individuals without treatment.
- No randomized controlled trials have addressed when a person with HIV-2 should start antiretroviral therapy (ART) or which regimens are most effective for initial or second-line ART when treating HIV-2; thus, the optimal treatment strategy is not well defined.
- Existing data on the treatment of HIV-2, and extrapolation from data on the treatment of HIV-1, suggest that ART should be started at or soon after HIV-2 diagnosis to prevent disease progression and transmission of HIV-2 to others (**AIII**).
- Quantitative plasma HIV-2 RNA viral load testing for clinical care is available and should be performed before initiation of ART (**AIII**).
- HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors and to enfuvirtide; therefore, these drugs **should not be included** in ART regimens for HIV-2 infection (**AII**).
- Patients with hepatitis B virus (HBV)/HIV-2 coinfection should be prescribed ART regimens that contain drugs with activity against both HIV-2 and HBV (**AIII**).
- Initial ART regimens for ART-naive patients who have HIV-2 mono-infection or HIV-1/HIV-2 coinfection should include an integrase strand transfer inhibitor (INSTI) plus two nucleoside reverse transcriptase inhibitors (NRTIs) (**AII**). An alternative regimen is a boosted protease inhibitor (PI) that is active against HIV-2 (darunavir or lopinavir) plus two NRTIs (**BII**).
- HIV-2 RNA, CD4 T lymphocyte (CD4) cell counts, and clinical status should be used to assess treatment response (**AIII**). Unlike persons with HIV-1, persons with HIV-2 should continue to undergo periodic CD4 count testing even if their viral loads are persistently suppressed, because disease progression can occur despite an undetectable viral load.
- Resistance-associated viral mutations to INSTIs, PIs, or NRTIs may develop in persons with HIV-2 while they are on ART. However, no validated HIV-2 genotypic or phenotypic antiretroviral resistance assays are approved for clinical use.
- In the event of virologic, immunologic, or clinical failure, a new ART regimen should be constructed in consultation with an expert in HIV-2 management.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

HIV and the Older Person (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations When Caring for Older Persons With HIV

- Antiretroviral therapy (ART) is recommended for all people with HIV regardless of CD4 T lymphocyte cell count **(AI)**. ART is especially important for older individuals because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART.
- Given that the burden of aging-related diseases is significantly higher among persons with HIV than in the general population, additional medical and social services may be required to effectively manage both HIV and comorbid conditions.
- Adverse drug events from ART and concomitant drugs may occur more frequently in older persons with HIV than in younger individuals with HIV. Therefore, the bone, kidney, metabolic, cardiovascular, cognitive, and liver health of older individuals with HIV should be monitored closely.
- Polypharmacy is common in older persons with HIV; therefore, there is a greater risk of drug-drug interactions between antiretroviral drugs and concomitant medications. Potential for drug-drug interactions should be assessed regularly, especially when starting or switching ART and concomitant medications.
- The decline in neurocognitive function with aging is faster in people with HIV than in people without HIV. HIV-associated neurocognitive disorder (HAND) is associated with reduced adherence to therapy and poorer health outcomes including increased risk of death. For persons with progressively worsening symptoms of HAND, referral to a neurologist for evaluation and management or a neuropsychologist for formal neurocognitive testing may be warranted **(BIII)**.
- Mental health disorders are a growing concern in aging people with HIV. A heightened risk of mood disorders including anxiety and depression has been observed in this population. Screening for depression and management of mental health issues are critical in caring for persons with HIV.
- HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older persons with HIV and complex comorbidities.
- Early diagnosis of HIV and counseling to prevent secondary transmission of HIV remains an important aspect of the care of older people with HIV

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Substance Use Disorders and HIV (Last updated July 10, 2019; last reviewed July 10, 2019)

Key Considerations and Recommendations

- Substance use disorders (SUDs) are prevalent among people with HIV and contribute to poor health outcomes; therefore, screening for SUDs should be a routine part of clinical care **(AII)**.
- The most commonly used substances among people with HIV include alcohol, benzodiazepines, cannabinoids, club drugs, opioids, stimulants (cocaine and methamphetamines), and tobacco.
- Health care providers should be nonjudgmental when addressing substance use with their patients **(AIII)**.
- Persons with HIV and SUDs should be screened for additional mental health disorders **(AII)**.
- Persons with HIV and SUDs should be offered evidenced-based pharmacotherapy (e.g., opioid agonist therapy, tobacco cessation treatment, alcohol use disorder treatment; see [Table 13](#)) as part of comprehensive HIV care in HIV clinical settings **(AI)**.
- Ongoing substance use is not a contraindication to antiretroviral therapy (ART) **(AI)**. Persons who use substances can achieve and maintain viral suppression with ART.
- Substance use may increase the likelihood of risk-taking behaviors (e.g., risky sexual behaviors), the potential for drug-drug interactions, and the risk or severity of substance-associated toxicities (e.g., increased hepatotoxicity or an increased risk of overdose).
- Selection of ART regimens for individuals who practice unhealthy substance and alcohol use should take potential adherence barriers, comorbidities which could impact care (e.g., advanced liver disease from alcohol or hepatitis viruses), potential drug-drug interactions, and possible adverse events associated with the medications into account **(AII)**.
- ART regimens with once-daily dosing of single-tablet regimens, high barriers to resistance, low hepatotoxicity, and low potential for drug-drug interactions are preferred **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Transgender People with HIV (Last updated December 18, 2019; last reviewed December 18, 2019)

Panel's Recommendations

- Antiretroviral therapy (ART) is recommended for all transgender people with HIV to improve their health and to reduce the risk of HIV transmission to sexual partners **(AI)**.
- HIV care services should be provided within a gender-affirmative care model to reduce potential barriers to ART adherence and to maximize the likelihood of achieving sustained viral suppression **(AII)**.
- Prior to ART initiation, a pregnancy test should be performed for transgender individuals of childbearing potential **(AIII)**.
- Some antiretroviral drugs may have pharmacokinetic interactions with gender-affirming hormone therapy. Clinical effects and hormone levels should be routinely monitored with appropriate titrations of estradiol, testosterone, or androgen blockers, as needed **(AIII)**.
- Gender-affirming hormone therapies are associated with hyperlipidemia, elevated cardiovascular risk, and osteopenia; therefore, clinicians should choose an ART regimen that will not increase the risk of these adverse effects **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Women with HIV (Last updated December 18, 2019; last reviewed December 18, 2019)

Key Considerations and Recommendations

- Antiretroviral therapy (ART) is recommended for all persons living with HIV to improve their health and to reduce the risk of HIV transmission to sexual partners without HIV **(AI)**.
- When prescribing antiretroviral (ARV) drugs, clinicians should take into account that some ARV drugs have significant pharmacokinetic (PK) interactions with hormonal contraceptives; an alternative or additional effective contraceptive method is recommended to prevent unplanned pregnancy **(AIII)**. Switching to an ARV drug that does not have interactions with hormonal contraceptives may also be considered **(BIII)**.
- A pregnancy test should be performed for those of childbearing potential prior to initiation of ART **(AIII)**.
- Preliminary data suggest there may be an increased risk of neural tube defects (NTDs) (0.9%) in infants born to women who were receiving dolutegravir (DTG) at the time of conception. Updated results have shown that the prevalence of NTDs in infants who were exposed to DTG at the time of conception is lower (0.3%) than reported in the preliminary data, but still higher than in infants born to women who received ART that did not include DTG (0.1%).
- Providers should discuss the potential risks and benefits of using DTG with individuals of childbearing potential and provide appropriate counseling so that individuals can make informed decisions.
- Before initiating an integrase strand transfer inhibitor-based regimen in a person of childbearing potential, clinicians should review [Table 6b](#) for information to consider when choosing an ART regimen.
- In a patient with multidrug-resistant HIV who has no alternatives to DTG, the decision of whether to use DTG should be made after carefully considering the risk of NTDs in the infant if pregnancy occurs while a patient is taking DTG, and the risks of persistent viremia in the patient and potential HIV transmission to the fetus if pregnancy occurs while the patient is not on effective ART.
- During pregnancy, an additional goal of ART is to maintain a viral load below the limit of detection throughout pregnancy to reduce the risk of transmission to the fetus and newborn **(AI)**.
- When selecting an ARV combination regimen for a pregnant woman, clinicians should consider the available safety, efficacy, and PK data on use during pregnancy for each agent. The risks and benefits of ARV use during pregnancy should be discussed with all individuals of childbearing potential **(AIII)** and clinicians should consult the most current [Perinatal Guidelines](#) when designing a regimen **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B/HIV Virus Coinfection (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations

- Before initiation of antiretroviral therapy (ART), all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication (**AIII**).
- Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) have activity against both HIV and HBV, an ART regimen for patients with both HIV and HBV should include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen (**AI**).
- If TDF or TAF cannot safely be used, the alternative recommended HBV therapy is entecavir in addition to a fully suppressive ARV regimen (**BI**). Entecavir has activity against HIV; its use for HBV treatment without ART in patients with dual infection may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to patients with HBV/HIV-coinfection (**AII**). Peginterferon alfa monotherapy may also be considered in certain patients (**CII**).
- Other HBV treatment regimens, including adefovir alone or in combination with 3TC or FTC and telbivudine, **are not recommended** for patients with HBV/HIV coinfection (**CII**).
- Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against stopping these medications and be carefully monitored during interruptions in HBV treatment (**AII**).
- If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression (**AIII**).
- HBV reactivation has been observed in persons with HBV infection during interferon-free HCV treatment. For that reason, all patients initiating HCV therapy should be tested for HBV. Persons with HCV/HIV coinfection and active HBV infection (determined by a positive HBsAg test) should receive ART that includes two agents with anti-HBV activity prior to initiating HCV therapy (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Hepatitis C Virus/HIV Coinfection (Last updated December 18, 2019; last reviewed December 18, 2019)

Panel's Recommendations

- All people with HIV should be screened for hepatitis C virus (HCV) infection (**AIII**). Patients at high risk of HCV infection should be screened annually and whenever incident HCV infection is suspected (**AIII**).
- Antiretroviral therapy (ART) may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most persons with HCV/HIV coinfection, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury. Therefore, ART should be initiated in all patients with HCV/HIV coinfection, regardless of CD4 T lymphocyte cell count (**AI**).
- Initial ART regimens that are recommended for most patients with HCV/HIV coinfection are the same as those recommended for individuals without HCV infection. However, when treatment for both HIV and HCV is indicated, the ART and HCV treatment regimens should be selected with special consideration for potential drug-drug interactions and overlapping toxicities (**AIII**) (see discussion in the text below and in [Table 15](#)).
- All patients with HCV/HIV coinfection should be evaluated for HCV therapy, which includes assessing their liver fibrosis stage to guide the duration of therapy and predict subsequent risk of hepatocellular carcinoma and liver disease complications (**AIII**).
- 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 or Immunoglobulin G). Persons who are not immune to HBV infection (HBsAb negative) should receive anti-HBV vaccination (**AIII**).
- HBV reactivation has been observed in persons with HBV infection during HCV treatment with direct-acting antivirals (DAAs). Accordingly, before initiating HCV therapy, persons with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes two agents with anti-HBV activity (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Key Considerations and Recommendations

- Selection of tuberculosis (TB)-preventive treatment for individuals with HIV and latent tuberculosis infection (LTBI) should be based on the individual's antiretroviral therapy (ART) regimen as noted below:
 - Any ART regimen can be used when isoniazid alone is used for LTBI treatment (AIII).
 - Efavirenz 600 mg once daily or raltegravir 400 mg twice daily-based regimens (in combination with either abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine) can be used without dose adjustment with once-weekly isoniazid plus rifapentine (AII).
 - If rifampin or rifapentine is used to treat LTBI, clinicians should review Tables 21a through 21e to assess the potential for drug-drug interactions among different antiretroviral (ARV) drugs and the rifamycins (AIII).
- All patients with HIV and active TB who are not on ART should be started on ART as described below:
 - **CD4 T lymphocyte (CD4) cell counts <50 cells/mm³**: Initiate ART as soon as possible, but within 2 weeks of starting TB treatment (AI).
 - **CD4 counts ≥50 cells/mm³**: Initiate ART within 8 weeks of starting TB treatment (AI).
 - **During pregnancy, regardless of CD4 count**: Initiate ART as early as feasible, for treatment of the person with HIV and to prevent HIV transmission to the infant (AIII).
 - **With tuberculous meningitis**: When initiating ART early, patients should be closely monitored as high rates of adverse events and deaths have been reported in a randomized trial (AI).
- For patients with active TB who are receiving ART, the ARV regimen should be assessed with particular attention to potential drug-drug interactions between ARVs and TB drugs. The ARV regimen may need to be modified to permit use of the optimal TB treatment regimen (see Tables 21a through 21e for dosing recommendations).
- Rifamycin antibiotics (rifabutin, rifampin, and rifapentine), are critical components of TB treatment regimens and should be included in regimens for patients with both HIV and active TB, unless precluded because of TB resistance or toxicity. However, rifamycin antibiotics have a considerable potential for drug-drug interactions. Clinicians should review Tables 21a through 21e to assess the potential for interactions among different ARV drugs and the rifamycins (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Limitations to Treatment Safety and Efficacy

Adherence to the Continuum of Care (Last reviewed October 17, 2017)

Key Summary of Adherence to the Continuum of Care

- Linkage-to-care and adherence to both antiretroviral therapy (ART) and clinic appointments should be regularly assessed.
- An individual's barriers to adherence to ART and appointments should be assessed before initiation of ART and regularly thereafter.
- Patients with ART adherence problems should be placed on regimens with high genetic barriers to resistance, such as dolutegravir (DTG) or boosted darunavir (DRV). Side effects, out-of-pocket costs, convenience, and patient preferences also need to be considered.
- Patients having difficulties with adherence to appointments or ART should be approached in a constructive, collaborative, nonjudgmental, and problem-solving manner.
- The approach to improved adherence should be tailored to each person's needs (or barriers to care). Approaches could include, but are not limited to:
 - Changing ART to simplify dosing or reduce side effects
 - Finding resources to assist with treatment costs to maintain uninterrupted access to both ART and appointments
 - Allowing flexible appointment scheduling
 - Assisting with transportation, or
 - Linking patients to counseling to overcome stigma, substance use, or depression.
- Multidisciplinary approaches to find solutions to ART and appointment adherence problems are often necessary, including collaboration with social work and case management (to the extent available). The clinician's role is to help the patient understand the importance of adherence to the continuum of care and reveal barriers to adherence, and link the patient to resources to overcome those barriers.
- A summary of best practice interventions to improve linkage, retention, and adherence can be found at a Centers for Disease Control and Prevention compendium (<https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html>).