



## **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living 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 October 17, 2017; last reviewed October 17, 2017)

### Panel's Recommendations

- Antiretroviral therapy (ART) is recommended for all individuals with HIV, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection (AI).
- ART is also recommended for individuals with HIV to prevent HIV transmission (AI).
- When initiating ART, it is important to educate patients regarding the benefits and considerations of ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.

**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 October 25, 2018; last reviewed October 25, 2018)

### Panel's 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).
- A pregnancy test should be performed for those of childbearing potential prior to the initiation of antiretroviral therapy (AIII).
- 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<sup>a</sup>—only for patients who are HLA-B\*5701 negative (AI)
    - Dolutegravir (DTG) plus tenofovir<sup>b</sup>/emtricitabine<sup>a</sup> (AI)
    - Raltegravir plus tenofovir<sup>b</sup>/emtricitabine<sup>a</sup> (BI for tenofovir disoproxil fumarate, BII for tenofovir alafenamide)
  - Preliminary data have raised concerns about an increased risk of neural tube defects in infants born to people who were receiving DTG at the time of conception. Before prescribing DTG or another INSTI, please refer to Table 6b for specific recommendations on initiating these drugs as part of initial therapy.
- 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

<sup>a</sup> Lamivudine may substitute for emtricitabine or vice versa.

<sup>b</sup> Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (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 October 25, 2018; last reviewed October 25, 2018)

### Panel's 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 ARVs 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 on the basis of the patient's ART history and his or her 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 designed to minimize toxicity, preserve CD4 cell 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.
- Preliminary data suggest that there is an increased risk of neural tube defects in infants born to individuals who were receiving dolutegravir (DTG) at the time of conception. In patients with virologic failure who are of childbearing potential, pregnancy testing should be performed before starting DTG (**AIII**).
- For patients who are pregnant and within 12 weeks post-conception, or those who are of childbearing potential and who are not using effective contraception or who are contemplating pregnancy, the following factors should be considered:
  - If an alternative active ARV option to DTG exists, DTG should not be prescribed (**AII**).
  - If no alternatives exist, providers and individuals of childbearing potential should discuss the possible association between neural tube defects and DTG use during conception, and 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 careful consideration of 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 cell 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 October 25, 2018; last reviewed October 25, 2018)**

**Panel's Recommendations**

- Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance make it possible to consider switching an effective regimen to an alternative regimen in some situations.
- The fundamental principle of regimen switching is to maintain viral suppression without jeopardizing future treatment options **(AI)**.
- 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)**.
- Adverse events, drug-drug or drug-food interactions, pill burden, pregnancy, cost, or the desire to simplify a regimen may prompt a regimen switch. Within-class and between-class switches can usually maintain viral suppression, provided that there is no viral resistance to the ARV agents in the new 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 switching 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. Discontinuation of HBV drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage.
- Consultation with an HIV specialist should be considered when planning a regimen switch for a patient with a history of resistance to one or more drug classes **(BIII)**.
- 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

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# Considerations for Antiretroviral Use in Special Patient Populations

## Acute and Recent (Early) HIV Infection (Last updated October 25, 2018; last reviewed October 25, 2018)

### Panel's Recommendations

- Antiretroviral therapy (ART) is recommended for all individuals with HIV-1 infection (AI), including those with early<sup>a</sup> HIV-1 infection.
- Once initiated, the goal of ART is to suppress plasma HIV-1 RNA to undetectable levels (AIII). Testing for plasma HIV-1 RNA levels, CD4 T lymphocyte cell counts, and toxicity monitoring should be performed as recommended for patients with chronic HIV-1 infection (AII).
- Genotypic drug resistance testing should be performed before initiation of ART to guide the selection of the regimen (AII).
- ART can be initiated before drug resistance test results are available. Either boosted darunavir (DRV) or dolutegravir (DTG) with emtricitabine (FTC) plus either tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) are recommended regimens in this setting (AIII). The rationales and precautions for these regimens are discussed below.
- A DRV-based regimen is a good option for people with early HIV-1 infection, because resistance to pharmacokinetically enhanced protease inhibitors (PIs) emerges slowly and clinically significant transmitted resistance to PIs is uncommon.
- A DTG-based regimen is also a reasonable option; however, data regarding transmission of integrase strand transfer inhibitor (INSTI)-resistant HIV and the efficacy of DTG regimens in early HIV infection are more limited (AIII).
- Preliminary data from Botswana suggested that infants born to women who were receiving dolutegravir (DTG) at the time of conception have an increased risk of neural tube defects. Until more information are available, DTG should not be prescribed for individuals:
  - Who are pregnant and within 12 weeks post-conception;
  - Who are of childbearing potential, who are sexually active, and who are not using effective contraception; or
  - Who are contemplating pregnancy.
- When results of drug resistance testing are available, the treatment regimen can be modified if warranted (AII). In patients without transmitted drug-resistant virus, therapy should be initiated with one of the combination regimens that is recommended for patients with chronic HIV-1 infection (see [What to Start](#)) (AIII).
- Patients starting ART should be willing and able to commit to life-long treatment and should understand the importance of adherence (AIII). Patients may choose to postpone ART, and providers, on a case-by-case basis, may recommend that patients defer therapy because of clinical or psychosocial factors.

**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

<sup>a</sup> Early infection represents either acute or recent infection.



## Adolescents and Young Adults with HIV (Last updated October 25, 2018; last reviewed October 25, 2018)

### Key Summary and Panel's 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. Thus, 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**).
- Preliminary data from Botswana suggested that infants born to women who were receiving dolutegravir (DTG) at the time of conception have an increased risk of neural tube defects. Until more information is available, DTG should not be prescribed for adolescents:
  - Who are pregnant and within 12 weeks post-conception;
  - Who are of childbearing potential, are sexually active, and who are not using effective contraception; or
  - Who are contemplating pregnancy.
- The adolescent sexual maturity rating (SMR) can be helpful to guide regimen selection for initiation of or changes in ART as recommended by either these Adult and Adolescent Antiretroviral Guidelines or the [Pediatric Guidelines](#). These Adult and Adolescent 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

## Women with HIV (Last updated October 25, 2018; last reviewed October 25, 2018)

### Panel's 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 sex 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 to prevent unplanned pregnancy is recommended (AIII). Switching to an ARV drug without 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 (NTD) in infants born to women who were receiving dolutegravir (DTG) at the time of conception. Until more information is available, DTG is not recommended for use in individuals who are pregnant and within 12 weeks post-conception and those who are contemplating pregnancy, unless there are no alternative options (AII).
- Providers should discuss the potential risks and benefits of DTG with individuals of childbearing potential and provide appropriate counseling so that the individual can make an informed decision. For those who are sexually active and not using effective contraception, choosing an alternative to DTG is recommended. For those who are using effective contraception, use of a DTG-based regimen is reasonable after discussing the risks and benefits with the individual.
- Individuals who become pregnant and present for antenatal care at 12 weeks post-conception or later may initiate or continue DTG-based regimens (CIII).
- In a patient with multidrug-resistant HIV who has no alternatives to DTG, the decision of whether to use DTG should be made after careful consideration of 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

## HIV-2 Infection (Last updated April 8, 2015; last reviewed April 8, 2015)

### Summary of HIV-2 Infection

- Compared to HIV-1 infection, the clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma HIV-2 RNA levels, and lower mortality; however, progression to AIDS does occur.
- There have been no randomized trials addressing the question of when to start antiretroviral therapy (ART) or the choice of initial or second-line therapy for HIV-2 infection; thus, the optimal treatment strategy has not been defined.
- Although the optimal CD4 T lymphocyte (CD4) cell count threshold for initiating ART in HIV-2 infection is unknown, therapy should be started before there is clinical progression.
- HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors and to enfuvirtide; thus, these drugs should not be included in an antiretroviral regimen for a patient living with HIV-2 infection.
- Pending more definitive data on outcomes in an ART-naive patient who has HIV-2 mono-infection or HIV-1/HIV-2 dual infection and requires treatment, an initial antiretroviral therapy regimen for these patients should include two nucleoside reverse transcriptase inhibitors plus an HIV-2 active boosted protease inhibitor or integrase strand transfer inhibitors.
- A few laboratories now offer quantitative plasma HIV-2 RNA testing for clinical care (see section text).
- Monitoring of HIV-2 RNA levels, CD4 cell counts, and clinical improvements can be used to assess treatment response, as is recommended for HIV-1 infection.
- Resistance-associated viral mutations to nucleoside reverse transcriptase inhibitors, protease inhibitors, and/or integrase strand transfer inhibitors may develop in patients with HIV-2 while on therapy. However, no validated HIV-2 genotypic or phenotypic antiretroviral resistance assays are available for clinical use.
- In the event of virologic, immunologic, or clinical failure, second-line treatment should be instituted in consultation with an expert in HIV-2 management.

## HIV and the Older Patient (Last updated January 28, 2016; last reviewed January 28, 2016)

### Key Considerations When Caring for Older Patients With HIV

- Antiretroviral therapy (ART) is recommended for all patients regardless of CD4 T lymphocyte cell count (**AI**). ART is especially important for older patients because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART.
- Adverse drug events from ART and concomitant drugs may occur more frequently in older patients living with HIV than in younger patients with HIV. Therefore, the bone, kidney, metabolic, cardiovascular, and liver health of older patients should be monitored closely.
- Polypharmacy is common in older patients 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.
- HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older patients with HIV with complex comorbidities.
- Early diagnosis of HIV and counseling to prevent secondary transmission of HIV remains an important aspect of the care of the older patient 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

# 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 October 25, 2018; last reviewed October 25, 2018)

### 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 13).
- All patients with HCV/HIV coinfection should be evaluated for HCV therapy, which includes having their liver fibrosis stage assessed to inform the length of their therapy and 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 IgG). 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, persons with HCV/HIV coinfection and active HBV infection (HBsAg positive) 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

## Tuberculosis/HIV Coinfection (Last updated July 14, 2016; last reviewed July 14, 2016)

### Panel's Recommendations

- Selection of a tuberculosis (TB)-preventive treatment for individuals living with HIV and coinfecting with 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 (**AII**).
  - Only efavirenz (EFV)- or raltegravir (RAL)-based regimens (in combination with either abacavir/lamivudine [ABC/3TC] or tenofovir disoproxil fumarate/emtricitabine [TDF/FTC]) can be used with once-weekly isoniazid plus rifapentine (**AIII**).
  - If rifampin or rifabutin is used to treat LTBI, clinicians should review [Tables 18a through 18e](#) to assess the potential for interactions among different antiretroviral (ARV) drugs and the rifamycins (**BIII**).
- All patients with both HIV and active TB who are not on ART should be started on ART as described below:
  - **In patients with CD4 counts <50 cells/mm<sup>3</sup>:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment (**AI**).
  - **In patients with CD4 counts ≥50 cells/mm<sup>3</sup>:** Initiate ART within 8 weeks of starting TB treatment (**AIII**).
  - **In all pregnant women with HIV:** Initiate ART as early as feasible, for treatment of maternal HIV infection and to prevent mother-to-child transmission (MTCT) of HIV (**AIII**).
  - **In patients with tuberculous meningitis:** Caution should be exercised when initiating ART early, as high rates of adverse events and deaths have been reported in a randomized trial (**AI**).
- Rifamycins are critical components of TB treatment regimens and should be included for patients with both HIV and active TB, unless precluded because of TB resistance or toxicity. However, rifamycins have a considerable potential for drug-drug interactions. Clinicians should review [Tables 18a through 18e](#) to assess the potential for interactions among different ARV drugs and the rifamycins (**BIII**).

**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>).