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Drug-Resistance Testing

Updated: September 12, 2024
Reviewed: September 12, 2024

Panel's Recommendations

For Initial Treatment of HIV

- HIV drug-resistance testing is recommended at entry into care for people with HIV to guide the selection of the initial antiretroviral (ARV) regimen **(AII).** If antiretroviral therapy (ART) is deferred, repeat testing may be considered at the time of ART initiation **(CIII).**
- The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends genotypic, rather than phenotypic, testing as the preferred resistance testing to guide therapy in ARV-naive people **(AIII).**
- In people with early (acute and recent) HIV infection, in pregnant women 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 people involves testing for mutations in the reverse transcriptase and protease genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is suspected, if the person has ever used long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis, or if the person has ever received an INSTI-based regimen for post-exposure prophylaxis, providers should ensure that genotypic resistance testing also includes the integrase gene **(AIII).**

For Antiretroviral Therapy–Experienced People

- HIV drug-resistance testing should be performed to assist the selection of active drugs when changing ARV regimens in—
  - People with virologic failure and HIV RNA levels >200 copies/mL (**AI** for >1,000 copies/mL**, AIII** for 501–1,000 copies/mL**, CIII** for confirmed HIV RNA 201–500 copies/mL). For people with confirmed HIV RNA levels >200 copies/mL but <500 copies/mL, drug-resistance testing may be unsuccessful but should still be considered.
  - People with suboptimal viral load reduction **(AII).**
- Reverse transcriptase and protease genotypic resistance testing should be performed on people with virologic failure. Integrase resistance testing should be performed on individuals who have virologic failure and have a history of prior use of an INSTI (for prevention or treatment) or are currently receiving an INSTI-based regimen **(AII).**
- For people taking a non–long-acting ARV regimen, drug-resistance testing in the setting of virologic failure should be performed while the person is still taking their ARV regimen or, if that is not possible, within 4 weeks after discontinuing their ARV regimen **(AII).** If more than 4 weeks have elapsed since the non–long-acting agents have been 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).**
- For people who previously received long-acting cabotegravir and rilpivirine (LA CAB/RPV) and present with virologic failure, resistance testing (including INSTI genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).**
- Genotypic testing is preferred over phenotypic-resistance testing to guide therapy in people with suboptimal virologic response or virologic failure while on first- or second-line regimens and in people 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 people with known or suspected complex drug-resistance mutation patterns **(BIII).**
- All prior and current drug-resistance test results, when available, should be reviewed and considered when constructing a new regimen **(AIII).**

- When the use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

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

Updated: October 25, 2018
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 = Weak* ***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

Updated: December 1, 2007
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 = Weak* ***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

Updated: September 25, 2025
Reviewed: September 25, 2025

Panel's Recommendations
• The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends antiretroviral therapy (ART) for all people with HIV to reduce morbidity and mortality **(AI)** and to prevent transmission of HIV to others **(AI).** • The Panel 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 people with HIV **(AII).** • When initiating ART, people with HIV should be counseled on the benefits, lifelong need, and importance of adherence to ART; clinicians should also identify and address barriers to care engagement and ART adherence **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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)

Updated: September 25, 2025
Reviewed: September 25, 2025

Panel's Recommendations
• All people 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. This concept may be recognized as Undetectable = Untransmittable or U=U **(AII).** • People with HIV who are starting ART should use another form of prevention with sexual partners (e.g., condoms, sexual abstinence, pre-exposure prophylaxis [PrEP] for the sexual partner who is HIV-negative) for at least the first 6 months of ART 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 transmission of HIV **(AIII).** • When the viral load is ≥200 copies/mL, at least one additional HIV prevention method (e.g., condoms, sexual abstinence, or PrEP for the HIV-negative partner) is recommended to prevent sexual HIV transmission until resuppression to <200 copies/mL is confirmed **(AIII).** • People with HIV who intend to rely on ART as 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 people with HIV on the importance of ART for their own health as well as its role in preventing sexual HIV transmission **(AIII).** • Providers should inform people with HIV 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 people with HIV who are sexually active for STIs, both for their own health and to prevent transmission of STIs to others **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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*

MANAGEMENT OF PEOPLE WITH HIV AND ANTIRETROVIRAL THERAPY EXPERIENCE

Virologic Failure

Updated: September 12, 2024
Reviewed: September 12, 2024

Key Considerations and Recommendations
• Assessing and managing a person with HIV who is experiencing antiretroviral therapy (ART) failure can be complex. Expert advice can be critical and should be sought in many instances. • Evaluation of virologic failure should include an assessment of ART 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 person is taking the failing antiretroviral (ARV) regimen **(AI)** or within 4 weeks of discontinuing a non–long-acting ARV regimen **(AII).** If more than 4 weeks have elapsed since non–long-acting ARV regimens were discontinued, resistance testing still can provide useful information to guide therapy, although it may not detect previously selected resistance mutations **(CIII).** • For people who previously received long-acting (LA) cabotegravir (CAB) plus rilpivirine (RPV), or LA CAB/RPV, and present with virologic failure, resistance testing (including integrase strand transfer inhibitor [INSTI] genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).** • The goal of treatment for people with HIV 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 ARV regimen should preferably include two fully active drugs if at least one has a high resistance barrier, such as a second-generation INSTI or a boosted protease inhibitor (PI) **(AI).** • A new ARV regimen can also include a second-generation INSTI (i.e., dolutegravir [DTG]) plus a boosted PI (preferably boosted darunavir) without nucleoside reverse transcriptase inhibitors (NRTIs) if both are fully active **(AI)**. • If the above two options are not feasible, a new ARV regimen that includes at least one drug with a high resistance barrier plus two partially active NRTIs—particularly tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) with lamivudine (3TC) or emtricitabine (FTC)—can also be considered, although this is a less well-defined strategy and is based on an extrapolation of existing data. Caution with close monitoring of virologic response is advised **(BII),** as discussed below**.** • If no fully active drug with a high resistance barrier is available, every effort should be made to include three fully active drugs in the new ARV regimen **(AI).** • In general, adding a single ARV drug to a virologically failing regimen **is not recommended,** because this would rarely result in full virologic suppression and may risk the development of resistance to all drugs in the regimen **(BII).** • In some rare instances, it might not be possible to achieve maximal virologic suppression in people with HIV who are highly ART-experienced and have extensive drug resistance. In this case, ART should be continued **(AI)** with regimens that are designed to maintain CD4 counts, preserve treatment options, delay clinical progression, and minimize toxicity. • When it is not possible to construct a viable suppressive regimen for a person with multidrug-resistant HIV, the clinician should consider enrolling the person in a clinical trial of investigational agents or contacting pharmaceutical companies that may have investigational agents available. • In people with HIV and virologic failure, it is crucial to provide continuous adherence support before and after ARV regimen changes. • When switching an ARV regimen in a person with hepatitis B virus (HBV)/HIV coinfection, the person should remain on an ARV agent that is active against HBV and has a high resistance barrier to HBV (i.e., TAF, TDF,

or entecavir) to avoid HBV rebound and hepatocellular damage **(AII)** (see Hepatitis B Virus/HIV Coinfection for more information).

- 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, discontinuing or interrupting ART **is not recommended** in the setting of virologic failure **(AI).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

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*

Suboptimal CD4 Cell Recovery Despite Viral Suppression

Reviewed: September 25, 2025
Updated: September 25, 2025

Key Considerations and Recommendations
• Suboptimal CD4 T lymphocyte (CD4) cell recovery is associated with increased AIDS- and non–AIDS-related morbidity and mortality among individuals with antiretroviral therapy (ART)–mediated viral suppression. • Promptly initiating ART in people diagnosed early with HIV provides the best opportunity for maximal CD4 cell recovery. • Adding antiretroviral (ARV) drugs to a suppressive ART regimen (ART intensification) does not improve CD4 cell recovery and therefore **is not recommended** for this purpose **(AI).** • Switching ARV drugs or drug classes in people with suppressed viral load does not improve CD4 cell recovery substantially and **is not recommended** for this purpose **(AII).** • Interleukin-2 **is not recommended** to increase CD4 counts because clinical trial data demonstrated no clinical benefit **(AI).** • Other interventions to increase CD4 counts **are not recommended** outside of a clinical trial, because no current interventions have been proven to decrease morbidity or mortality during ART-mediated viral suppression **(AII).** • Efforts to decrease morbidity and mortality during ART-mediated viral suppression should focus on preventive care (e.g., opportunistic infection prophylaxis, vaccinations, cancer screening, statin therapy to reduce cardiovascular risk), addressing modifiable risk factors for chronic disease (e.g., tobacco use, alcohol and substance use, unhealthy diet, sedentary lifestyle), and optimizing management of comorbidities (e.g., hypertension, diabetes).
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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

Updated: September 12, 2024
Reviewed: September 12, 2024

Key Considerations and Recommendations
• Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance have made it possible to consider switching a person with HIV from an effective ARV regimen to an alternative ARV regimen in some situations. • The fundamental principle of ARV regimen optimization is to maintain viral suppression without jeopardizing future treatment options. • Adverse events, drug–drug or drug–food interactions, pill burden, pregnancy, cost, stigma, inconvenience from taking oral medications, or the desire to simplify a regimen may prompt regimen optimization. • It is critical to review a person's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results before selecting a new ARV regimen **(AI).** • People with HIV who have no reliable full history of drug-resistance mutations or virologic failure can likely switch to any regimen that has been shown to be highly effective in people who are ARV-naive **(AI)** or to NRTI-sparing options extensively researched in switch studies, such as dolutegravir (DTG) plus rilpivirine (RPV) **(AI)** or long-acting cabotegravir plus rilpivirine (LA CAB/RPV) **(AI).** • For regimen optimization in the setting of existing nucleoside reverse transcriptase inhibitor (NRTI) resistance, if an NRTI is to be included in the new regimen, two NRTIs (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF] plus emtricitabine [FTC] or lamivudine [3TC]) should be included, along with a fully active drug with a high resistance barrier, such as DTG **(AII),** bictegravir (BIC) **(BIII),** or boosted darunavir **(BIII).** Alternatively, as noted above, an NRTI-sparing regimen (such as DTG/RPV **[AI]** or LA CAB/RPV **[AI]**) is possible if there is no reliable evidence of prior integrase strand transfer inhibitor (INSTI) or RPV resistance**.** • Monotherapy with either a boosted protease inhibitor or an INSTI 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 chronic hepatitis B virus (HBV)/HIV coinfection, HBV-active drugs that are potent and have a high barrier to resistance (i.e., TAF, TDF, or entecavir) should be used **(AII).** 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 person with a history of resistance to two 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 = Weak* ***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*

Immune Activation and Inflammation Among People With HIV Receiving Antiretroviral Therapy

Updated: September 25, 2025
Reviewed: September 25, 2025

Key Considerations and Recommendations
• HIV-related immune activation and systemic inflammation, despite viral suppression with antiretroviral therapy, are associated with increased risk for cardiovascular disease and metabolic complications, as well as a broad spectrum of comorbidities. • Switching or adding antiretroviral (ARV) drugs solely to reduce immune activation or inflammation **is not recommended,** except in a clinical trial **(AII).** • The use of immunomodulatory or anti-inflammatory therapy to reduce HIV-related immune activation or inflammation **is not recommended,** except in a clinical trial **(AII).** • Routine monitoring of markers of immune activation or inflammation (e.g. high-sensitivity C-reactive protein [CRP] or interleukin-6 [IL-6]) to inform the clinical management of HIV **is not recommended (BII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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*

Cardiovascular Complications in People With HIV

Updated: September 25, 2025
Reviewed: September 25, 2025

Key Considerations and Recommendations
Antiretroviral Management • All people with HIV should maintain viral suppression with continuous antiretroviral therapy (ART) to reduce the risk of atherosclerotic cardiovascular disease (ASCVD) **(AII).** • Due to concerns regarding an increased risk of cardiovascular events, alternative antiretroviral (ARV) medications should be considered in place of abacavir and lopinavir/ritonavir in people with higher underlying ASCVD risk or known ASCVD **(AII).** **ASCVD Risk Stratification** • For people with HIV aged 40–75 years, 10-year ASCVD risk score should be calculated using the Pooled Cohort Equations (or PCE) at least annually to inform management, including whenever lipids are measured or in certain clinical scenarios that may affect ASCVD risk* **(BIII)** (see Atherosclerotic Cardiovascular Disease Risk Scores in the text). • Lipid screening should be performed in people with HIV **(AIII),** with the following suggested frequency: (1) at entry into care or at the time of ART initiation, (2) 3–6 months after ART initiation once viral suppression is achieved, (3) annually for those aged ≥40 years or receiving statin therapy, (4) every 1–3 years for those aged <40 years **and** not on statin therapy, and (5) with changes in cardiovascular disease (CVD) risk factors (see text for additional details on monitoring). • There is insufficient evidence to support the use of inflammatory biomarkers for ASCVD risk stratification among people with HIV. • When compared to the general population, women with HIV have both a greater increase in relative risk of ASCVD and a greater underprediction of ASCVD by risk scores than men with HIV. For women with HIV, it is critical to ensure optimal ASCVD risk factor modification regardless of ASCVD risk score, implement ASCVD prevention strategies, and perform diagnostic evaluation if they present with possible cardiac symptoms. **ASCVD Prevention and Risk Factor Management** • Statin therapy is recommended for all people with HIV aged 40–75 years and in additional clinical scenarios for other age groups to reduce the risk of ASCVD and major adverse cardiovascular events. See Statin Therapy in People With HIV for recommendations on statin use. • The use of immunomodulatory therapy to reduce HIV-associated ASCVD risk **is not recommended** except in a clinical trial **(AII).** • Some drugs prescribed to prevent or treat CVD may have clinically significant interactions with certain ARV drugs. Before initiating or changing ARV drugs or concomitant medications, clinicians should carefully assess for potential interactions **(AIII).** • All people with HIV should be counselled about ways to reduce CVD risk through behavioral modifications such as healthy diet, weight control, regular exercise, smoking cessation, and limiting alcohol consumption. • Optimal management of comorbidities (e.g., hypertension, diabetes, obesity) remains important to further reduce CVD risk among people with HIV.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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-related CVD risk enhancing factors include prolonged duration of HIV infection, delayed antiretroviral therapy initiation, long periods of HIV viremia and/or treatment nonadherence, low current or nadir CD4 T lymphocyte cell count (e.g., <350 cells/mm^3), exposure to some older antiretroviral drugs associated with cardiometabolic toxicity, and/or coinfection with hepatitis C virus.

Weight Gain in People With Treated HIV

Updated: September 25, 2025
Reviewed: September 25, 2025

Panel's Recommendations and Key Considerations
• All people with HIV should receive antiretroviral therapy (ART) to reduce morbidity and mortality **(AI)** and to prevent transmission of HIV to others **(AI).** • Weight gain after ART initiation is common. ART initiation should not be delayed because of concerns for weight gain **(AIII),** and ART should not be interrupted or discontinued because of weight gain **(AIII).** • ART selection, whether for initiation or switch, should be based on optimization of virologic suppression. Specific antiretrovirals should not be selected to prevent or reduce weight gain **(AII),** as available evidence suggests this strategy is ineffective. • Providers should include weight monitoring in conjunction with counseling on strategies for weight control as part of comprehensive care for people with HIV.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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 POPULATIONS

Adolescents and Young Adults with HIV

Updated: June 3, 2021
Reviewed: June 3, 2021

Key Considerations and Recommendations
• Adolescents and young adults (AYA) with HIV largely belong to two distinct groups: those who acquired HIV in the first decade of life and who may be heavily antiretroviral therapy (ART)–experienced (early-acquired HIV); and those who acquired HIV in or after the second decade of life who may be mostly ART-naive. • ART is recommended for **all** AYA with HIV **(AI)** to reduce HIV-related morbidity, mortality, and transmission. • For AYA with HIV who are at risk for poor clinical outcomes, it is critically important to assess the behavioral and psychosocial context, and their ability to adhere to ART. Efforts should be made to provide youth-friendly support and infrastructure to reduce barriers to adherence and maximize success in achieving sustained viral suppression **(AIII).** • Pediatric and adolescent care providers should prepare AYA with HIV for the transition into adult care settings. Adult providers should be knowledgeable about this unique patient population and the challenges that frequently accompany the transition into the adult care setting. Consulting and collaborating with pediatric and adolescent HIV care providers is critical to ensure the successful transition of AYA with HIV to adult providers and continued engagement in care **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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*

Early (Acute and Recent) HIV Infection

Updated: September 12, 2024
Reviewed: September 12, 2024

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all people with HIV, including those with early[a] HIV infection **(AI).** ART should be initiated as soon as possible after HIV diagnosis **(AII).** • The goals of ART are to suppress plasma HIV RNA to undetectable levels **(AI),** prevent transmission of HIV **(AI),** and preserve immune function **(AIII).** Monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and antiretroviral (ARV) drug-related adverse effects should be done as recommended for people with chronic HIV infection **(AII).** • A blood sample for genotypic resistance testing should be sent to the laboratory before initiating ART **(AIII).** o Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes **(AIII)** for all people with early HIV**.** o Genotype testing for integrase strand transfer inhibitor (INSTI) resistance should be performed for those who acquire HIV during or after the use of long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP), if transmitted integrase stand transfer inhibitor (INSTI) resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for post-exposure prophylaxis (PEP) **(AIII).** • ART can be initiated before drug-resistance test results are available. o For those without a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended[b] **(AIII):** ▪ Bictegravir (BIC)/tenofovir alafenamide (TAF)/emtricitabine (FTC) ▪ Dolutegravir (DTG) with (TAF or tenofovir disoproxil fumarate [TDF])[c] plus (FTC or lamivudine [3TC]) o For those with a history of CAB-LA use as PrEP, genotype testing before starting ART should include screening for INSTI-resistance mutations **(AIII).** ▪ A regimen of cobicistat- (COBI)[d] or ritonavir-boosted darunavir (DRV) with (TAF or TDF)[b] plus (FTC or 3TC) is recommended while awaiting the results of the genotype testing **(AIII).** ▪ Use of an empiric INSTI-containing regimen **is not recommended** unless genotype testing shows no evidence of INSTI resistance **(AIII).** This is because INSTI resistance may be present in those who acquire HIV during and possibly after the use of CAB-LA as PrEP. • In people with HIV RNA levels ≥200 copies/mL and who are taking PrEP, immediate initiation of an effective HIV treatment regimen is recommended while awaiting confirmation of HIV diagnosis **(AIII).** • Pregnancy testing should be performed in women of childbearing potential before initiating ART **(AIII).** • When the results of drug-resistance tests are available, the treatment regimen can be modified if needed **(AII).** • Providers should inform individuals starting ART of the importance of adherence in achieving and maintaining viral suppression **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed non-randomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

[a] Early infection represents either acute or recent (≤6 months) infection.

[b] Because of the low rates of transmitted INSTI resistance in the United States at present, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started while awaiting the results of the INSTI genotype.

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

[d] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

HIV-2 Infection

Updated: December 06, 2023
Reviewed: December 06, 2023

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, without treatment, the majority of individuals with HIV-2 will progress to AIDS and death. • 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 initiating ART **(AIII).** • For ART-naive patients who have HIV-2 mono-infection or HIV-1/HIV-2 coinfection, antiretroviral (ARV) regimens should include an integrase strand transfer inhibitor (INSTI) plus two nucleoside reverse transcriptase inhibitors (NRTIs) **(AII).** A recommended alternative regimen is a boosted protease inhibitor (PI) that is active against HIV-2 (darunavir or lopinavir) plus two NRTIs **(BII).** • HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs); therefore, NNRTI-based regimens, including long-acting injectable rilpivirine (given with the INSTI cabotegravir), **are not recommended** for treatment of HIV-2 **(AIII).** • Patients with hepatitis B virus (HBV)/HIV-2 coinfection should be prescribed ART that contains drugs with activity against both HIV-2 and HBV **(AIII).** • HIV-2 RNA, CD4 T lymphocyte (CD4) cell counts, and clinical status should be used to assess treatment response **(AII).** Unlike people with HIV-1, people with HIV-2 should continue to undergo periodic CD4 testing even if their viral loads are persistently suppressed, because disease progression can occur despite an undetectable viral load **(AIII).** • Resistance-associated viral mutations to INSTIs, PIs, or NRTIs may develop in people 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 ARV regimen should be constructed in consultation with an expert in HIV-2 management. • *In vitro* studies demonstrate that HIV-2 is intrinsically resistant to the fusion inhibitor enfuvirtide, and limited data also show that HIV-2 is intrinsically resistant to fostemsavir); therefore, these drugs **are not recommended** for treatment of people with HIV-2 **(AIII).** • For patients with multidrug-resistant virus, ibalizumab and lenacapavir demonstrate *in vitro* potency against HIV-2 and may be considered **(BIII).**
***Rating of Recommendations**: A = Strong; B = Moderate; C = Weak* ***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

Updated: September 12, 2024
Reviewed: September 12, 2024

Key Considerations and Recommendations When Caring for Older People With HIV
• Diagnosis of HIV at a later stage of disease is more common among older people. Early diagnosis and treatment of HIV and counseling to prevent secondary HIV transmission remain important in the clinical care of older people with HIV. • Antiretroviral therapy (ART) is recommended for all people with HIV **(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. • Compared to people without HIV, people with HIV have a twofold higher risk of developing atherosclerotic cardiovascular disease (ASCVD), and their age at incident ASCVD diagnosis is about a decade younger. In addition to current American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety Guidelines, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends initiating at least a moderate-intensity statin in people with HIV aged 40 to 75 years who have 10-year ASCVD risk estimates of 5% to <20% **(AI).** See Statin Therapy in People With HIV for the Panel's additional recommendations on the use of statin therapy as primary prevention for people with HIV. • Polypharmacy is common in older people with HIV, and all drugs, supplements, and herbal treatments should be assessed regularly for appropriateness, potential for adverse effects, proper dosing, and drug interactions **(AIII).** • Potential for drug–drug interactions between antiretroviral drugs and concomitant medications (including statins, supplements, and herbal medicines) should be assessed regularly, especially before a new ART regimen or concomitant medication is started. In this context, it is also important to inquire and counsel about the use of non-daily medications, including long-acting injectables and as-needed medications. • Adverse drug events from ART and concomitant drugs may occur more frequently in older people 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. • HIV infection is associated with immunologic aging and systemic inflammation, which may contribute to the development of comorbidities across multiple organ systems as well as aging phenotypes like frailty. HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older people with HIV, including adhering to treatment and prevention guidelines for different medical comorbidities. • Age-related decline in neurocognitive function is faster in people with HIV compared to those without. Cognitive impairment in people with HIV—with manifestations including problems with memory, attention, and executive function—is associated with reduced adherence to therapy and poorer health outcomes, including increased risk of death. For people with progressive cognitive impairment, referral to a specialist (e.g., neurologist, neuropsychologist, geriatrician) for evaluation, testing, and management may be warranted **(BIII).** • Mental health disorders, including an increased risk of anxiety and depression, are a concern among aging people with HIV. Screening for depression and management of mental health issues are important when caring for older people with HIV. • Given that the burden of aging-related diseases is significantly higher among people with HIV than in the general population, additional medical and social services may be required to effectively manage both HIV and comorbid conditions.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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

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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 (listed in alphabetical order): alcohol, benzodiazepines, cannabinoids, club drugs, opioids, stimulants (cocaine and methamphetamines), and tobacco. • Health care providers should be nonjudgmental when addressing substance use with people with HIV **(AIII).** • People with HIV and SUDs should be screened for additional mental health disorders **(AII).** • People with HIV and SUDs should be offered evidence-based pharmacotherapy (e.g., opioid agonist therapy, tobacco cessation treatment, alcohol use disorder treatment; see Table 15 below) as part of comprehensive HIV care in clinical settings **(AI).** • Ongoing substance use is not a contraindication to antiretroviral therapy (ART). People who use substances can achieve and maintain viral suppression with ART. • Substance use may increase the likelihood of HIV transmission risk behaviors, the potential for drug–drug interactions, and the risk or severity of substance-associated adverse events (e.g., increased hepatotoxicity or an increased risk of overdose). • Selection of antiretroviral (ARV) regimens for individuals who practice unhealthy substance and alcohol use should take into account potential adherence barriers, comorbidities that 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 **(AII).** • For people with SUDs, ARV regimens with once-daily formulations (ideally as a single-tablet regimen), high barriers to resistance, low hepatotoxicity, and low potential for drug–drug interactions are preferred **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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*

Transplantation in People With HIV

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Panel's Recommendations and Key Considerations
• People with HIV who are eligible for solid organ transplant (SOT) or hematopoietic cell transplant (HCT) should have equitable access to transplant **(AII).** • People with HIV should be managed by a multidisciplinary team before, during, and after transplant **(AIII).** • Transplant candidates with HIV should be up-to-date on their vaccination schedule **(AIII).**
Antiretroviral Drug Considerations Before Transplant

• In preparation for transplant, HIV providers should review the transplant candidate's antiretroviral (ARV) history, efficacy of the current ARV regimen, prior HIV drug resistance results, ARV adherence, and the potential for drug–drug interactions **(AIII).**
• All ARV regimen changes should be guided by ARV history, along with current and prior HIV drug resistance testing results **(AIII).**
• If switching to an alternative ARV regimen is necessary, changes should be completed several weeks before the transplant whenever possible to minimize drug–drug interactions in the post-transplant period and to assure tolerability and efficacy of the new regimen before transplant **(BIII).**
• Tenofovir alafenamide (TAF) is preferred over tenofovir disoproxil fumarate (TDF) in transplant candidates and recipients due to the lower risk of affecting renal function and bone mineral density **(AII).**
• To avoid significant drug–drug interactions between ARV drugs and anticipated immunosuppressive therapies, chemotherapies (for HCT), and prophylactic regimens for opportunistic infections, the following should be considered:
  • Unboosted second-generation oral integrase strand transfer inhibitor (INSTI)–based regimens (i.e., with bictegravir or dolutegravir) are preferred in most people with HIV needing transplant **(AII).**
  • In general, potent cytochrome P450 (CYP) 3A4 inhibitors—including pharmacokinetic boosters, such as ritonavir (RTV) or cobicistat (COBI), and protease inhibitor (PI)-containing regimens—should be avoided **(AII).**
  • In general, non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as nevirapine (NVP), efavirenz (EFV), and etravirine (ETR), which are CYP3A4 inducers, should be avoided **(AII).**

Maintenance of Viral Suppression
• HIV viral suppression should be maintained before and after transplant **(AIII).*** • HIV providers with appropriate expertise should design alternative ARV regimen(s) that are likely to achieve viral suppression if post-transplant regimen changes are necessary **(AIII).**
Immediately Post-Transplant
• Immediately post-transplant, renal or hepatic function may fluctuate; close monitoring of these organ functions is recommended to ensure appropriate dosing of ARV drugs and other concomitant medications to avoid potential drug toxicities **(AIII).** • Interruption of antiretroviral therapy (ART) post-transplant should be avoided **(AIII).** • If interruption is necessary, all components of an oral ART regimen should be stopped simultaneously to avoid exposure to an incomplete regimen. The period of interruption should be kept to a minimal duration **(AIII).** • If a person cannot swallow pills, providers should consider using oral liquid formulation if available; alternatively, some pills can be crushed or dissolved for administration orally or via an enteral tube **(AIII).**

Post-Transplant

- Therapeutic drug monitoring for immunosuppressive drugs should be performed to guide dosing adjustments, especially before, during, and after the start or switch of ARV drugs that may interact with immunosuppressive drugs **(AII).**
- The burden of medication increases significantly post-transplant. Providers should continue to evaluate for potential drug–drug interactions and overlapping toxicities with the addition of new medications **(AIII).**
  - When feasible, providers should consider consolidating ART using fixed-dose combination tablets and/or single-tablet regimens to minimize pill burden and bolster adherence **(AIII).**

Hepatitis B Virus or Hepatitis C Virus Coinfection

- All donors and recipients should be screened for hepatitis B virus (HBV) and hepatitis C virus (HCV) with a serological and/or nucleic acid amplification test, according to transplant guidelines **(AIII).**
- Transplant candidates and recipients who are nonimmune to HBV (as measured by HBV surface antibody [HBsAb]) should be vaccinated, ideally before transplant **(AIII).**
- HBV serology should be monitored after transplant for loss of HBsAb in order to guide the need for revaccination per professional society and transplant center guidelines **(AIII).**
- Transplant recipients with active HBV infection should be treated with ARV regimens with anti-HBV activity before transplant and indefinitely after transplant **(AIII).** Use of nucleos(t)ide reverse transcriptase inhibitors (NRTIs) with activities against both HIV and HBV is strongly recommended unless contraindicated or not tolerated **(AIII).**
- For management of recipients with HIV without HBV who receive an organ from a donor with markers of HBV infection, see guidance in the HBV-Positive and HCV-Positive Donors section below and follow appropriate institutional protocols.
- All transplant candidates and/or recipients with HCV infection should be treated with direct-acting antivirals against HCV **(AII).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

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*

* In some cases, it may be necessary to interrupt ART due to intolerance of or inability to administer ARV drugs pre-transplant, such as in end-stage liver disease or when enteral access is limited. In these situations, the HIV provider should design a regimen that will result in viral suppression after transplant and resume therapy as soon as feasible.

Women With HIV

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Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all people 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 for women with HIV, clinicians should consider that some ARV drugs have significant pharmacokinetic (PK) interactions with hormonal contraceptives **(AII)** and hormone replacement therapy **(BIII).** Consult Tables 24a, 24b, 24d, 24e, 24f, and 24g for detailed recommendations and a summary of available data when selecting ARV and hormone combination therapy **(AIII).** • Clinicians should discuss with women the possibility of weight gain after initiating or changing ART. Some women in general, and Black women in particular, experience greater weight gain with ART over time than men. Concerns for weight gain should not be a reason for deferring ART. • A pregnancy test should be performed for women of childbearing potential before initiation of ART **(AIII).** • When selecting or evaluating an ARV regimen for women with HIV of childbearing potential, clinicians should consider the regimen's effectiveness, the woman's hepatitis B status, the teratogenic potential of the drugs in the ARV regimen, and the possible adverse outcomes for the mother and the fetus if the woman becomes pregnant while receiving the regimen **(AII).** • During pregnancy, an additional goal of ART is to maintain a viral load below the limit of detection throughout pregnancy in order to reduce the risk of HIV transmission to the fetus and newborn **(AI).** • When selecting an ARV regimen for a pregnant woman, clinicians should consider the available safety, efficacy, and PK data on the use of each agent during pregnancy. The risks and benefits of ARV use during pregnancy should be discussed with all pregnant women **(AIII),** and clinicians should consult the Perinatal Guidelines when designing a regimen **(AIII).** • Achieving and maintaining viral suppression with ART while breastfeeding does not completely eliminate HIV transmission risk but does reduce it to less than 1% **(AI).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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 PEOPLE WITH COINFECTIONS

Hepatitis B Virus/HIV Coinfection

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Panel's Recommendations
• Hepatitis A, B, and C virus serologies should be performed for all people with HIV **(AIII).** • Before initiating or switching antiretroviral therapy (ART), all people 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 tenofovir alafenamide (TAF), tenofovir disoproxil fumarate (TDF), emtricitabine (FTC), and lamivudine (3TC) are active against both HIV and HBV, an antiretroviral (ARV) regimen for people 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 ARV regimen **(AI).** • In people with HBV/HIV coinfection, using 3TC or FTC as the only drug in a regimen with HBV activity **is not recommended (AII),** because HBV resistance to these drugs can emerge. • If TAF or TDF cannot be safely used, or if there is a desire to use a tenofovir-sparing ART regimen, entecavir should be used as the alternative HBV therapy **(BI).** Entecavir has weak activity against HIV. Using entecavir for HBV treatment without ART may result in 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 people with HBV/HIV coinfection **(AII).** • Adefovir **(AI)** or pegylated interferon alfa **(AIII) are not recommended** for people with HBV/HIV coinfection. • In people with HBV/HIV coinfection, the discontinuation of agents with anti-HBV activity may cause serious hepatocellular injury resulting from HBV reactivation hepatitis; people with HBV/HIV coinfection should be advised against stopping these medications and should be carefully monitored during interruptions of HBV-active treatment **(AII).** • When switching or modifying an ARV regimen in a person with HBV/HIV coinfection, including switching to long-acting injectables, ARV drugs that are active against HBV should be continued **(AII)** or specific anti-HBV drugs, such as entecavir, should be initiated **(AII).** • HBV reactivation has been reported in people with HIV and prior exposure to HBV (positive hepatitis B core antibody, negative HBsAg) when HBV-active agents are withdrawn as part of an ART regimen. Regardless of hepatitis B surface antibody level, people with HIV and prior HBV exposure are at low risk for reactivation and the associated hepatitis, which can result in serious hepatocellular injury. A monitoring strategy is considered a safe and effective way to assess HBV reactivation in low-risk people **(BIII).** • HBV reactivation has been observed in people with HBV/hepatitis C virus (HCV) coinfection while receiving interferon-free HCV treatment. For this reason, all people initiating HCV therapy should be tested for HBV. People 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 before initiating HCV therapy **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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

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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 patients 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 antiretroviral (ARV) regimens that are recommended for most patients with HCV/HIV coinfection are the same as those recommended for people with HIV who do not have HCV infection. However, when treatment for both HIV and HCV is indicated, the ARV 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 18). • 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 to predict subsequent risk of hepatocellular carcinoma and liver disease complications **(AIII).** • Patients 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 hepatitis B 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 people with HBV infection during HCV treatment with direct-acting antivirals. Accordingly, before initiating HCV therapy, patients 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 = Weak* ***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

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Key Considerations and Recommendations
• Treatment for latent tuberculosis infection (LTBI) in people with HIV should take into consideration the individual's antiretroviral (ARV) regimen as noted below. o General recommendations for **once-weekly** isoniazid plus rifapentine for 3 months (3HP) and **once-daily** isoniazid plus rifapentine for 1 month (1HP): ▪ These regimens **are not recommended** for people who require twice-daily dolutegravir (DTG) therapy (e.g., those with certain integrase strand transfer inhibitor [INSTI]–associated resistance substitutions or clinically suspected INSTI resistance) **(AIII).** ▪ Tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) **(AIII),** tenofovir alafenamide (TAF)/FTC **(BIII),** or abacavir (ABC)/lamivudine (3TC) **(BIII)** can be used as the nucleoside reverse transcriptase inhibitor (NRTI) backbone. Rifapentine may lower concentrations of TAF. If used, monitor for virologic response. o For 3HP ▪ Efavirenz (EFV) 600 mg once daily or raltegravir 400 mg twice daily can be used **(AII).** ▪ DTG 50 mg once daily may be used for those in whom once-daily DTG is appropriate **(BII).** o For 1HP ▪ EFV 600 mg once daily can be used without dose adjustment **(AI).** ▪ For a person with virologic suppression while on a DTG 50 mg once-daily regimen, the DTG dose should be increased to 50 mg twice daily throughout the course of 1HP, continuing DTG 50 mg twice daily for 14 days after 1HP completion before switching back to once-daily DTG dosing **(AII).** o With daily isoniazid alone for 6 or 9 months, any ARV regimen can be used **(AIII).** o If rifampin is used to treat LTBI, clinicians should review Tables 24a through 24g to assess the potential for drug–drug interactions between rifampin and different ARV drugs **(AII).** • All people with HIV and active tuberculosis (TB) who are not on antiretroviral therapy (ART) should be started on ART **(AI)** as described below. o **CD4 T lymphocyte (CD4) cell counts <50 cells/mm^3:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment **(AI).** o **CD4 counts ≥50 cells/mm^3:** Initiate ART within 2 to 8 weeks of starting TB treatment **(AI).** o **During pregnancy, regardless of CD4 count:** Initiate ART as early as feasible for treatment of the person with HIV and prevention of HIV transmission to the infant **(AIII).** o **With TB meningitis:** Initiate ART after TB meningitis is under control and after at least 2 weeks of anti-TB treatment to reduce the risk of life-threatening inflammation in a closed space as a result of immune reconstitution **(AIII).** • For people 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. Rifamycin antibiotics (rifabutin, rifampin, and rifapentine), in particular, have considerable potential for drug–drug interactions. The ARV regimen may need to be modified to permit use of the optimal TB treatment regimen (see Tables 24a through 24g for drug interaction data and dosing recommendations) **(AII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***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

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Key Considerations and Recommendations
• Linkage to HIV care and adherence to both antiretroviral therapy (ART) and clinic appointments should be regularly assessed. • An individual's barriers to ART and clinic appointment adherence should be assessed before or shortly after the initiation of ART and regularly thereafter. • Rapid access to ART is one of the pillars of the United States' plan to end the HIV epidemic; therefore, delays in access to ART should be addressed and treatment initiated as soon as possible. • People with HIV having ART adherence problems should be placed on regimens with high genetic barriers to resistance, such as dolutegravir, bictegravir, or boosted darunavir. Side effects, out-of-pocket costs, convenience, and individual preferences should also be considered. • People with HIV having difficulties with adherence to appointments or ART should be provided additional adherence support using a constructive, collaborative, nonjudgmental, and problem-solving approach. • The approach taken to improve adherence should be tailored to each person's needs and barriers to care. Approaches could include, but are not limited to— o Changing ART to simplify dosing or to reduce side effects o Allowing flexible appointment scheduling o Finding resources to assist with treatment costs to maintain uninterrupted access to both ART and appointments o Linkage to resources to assist with unmet social and economic needs, such as transportation, food, housing, and other support services o Linkage to services to overcome stigma, substance use, or mental illness • A multidisciplinary approach—including collaborations with nursing, pharmacy, social work, and case management (to the extent available—is often necessary to identify solutions to ART and appointment adherence. The clinician's role is to help people with HIV understand the importance of adherence to the continuum of care, identify the barriers to adherence and address those that are within their purview, and link them to resources to overcome other barriers. • Single-tablet ART regimens are generally recommended when clinically appropriate, but high-quality evidence to definitively recommend them is lacking and shared decision-making between clinicians and people with HIV is essential **(BIII).** • At this time, evidence does not support the use of financial incentives to engage people with HIV in ongoing routine care. • Methods to estimate adherence based on drug levels measured in plasma, dried blood spots, urine, and hair samples are available. Measuring adherence with these methods has not been shown in randomized studies to improve outcomes. However, these methods should be used in a collaborative manner to avoid an adversarial relationship between the provider and people with HIV. • Because delayed administration of long-acting cabotegravir plus rilpivirine (LA CAB/RPV) may lead to the emergence of drug resistance, LA CAB/RPV is not generally recommended as a complete regimen in people with viremia due to suboptimal adherence to ART, or in people who have ongoing challenges with retention in HIV care. However, based on very limited data, the Panel for the Use of Antiretroviral Agents in Adults and

Adolescents With HIV recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, and who have no evidence of resistance to rilpivirine RPV or CAB and, with shared decision-making between providers and people with HIV **(CIII).** See Virologic Failure for a more detailed discussion.

- A summary of best practice interventions to improve linkage, retention, and adherence can be found in the Centers for Disease Control and Prevention's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention.

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

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*