What's New in the Guidelines

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These guidelines were updated by the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) based on key new clinical evidence on the use of antiretroviral therapy (ART) for the treatment of people with HIV.

New Section Added to the Guidelines

Transplantation in People With HIV

This new section has been added to provide guidance on ART management in people with HIV who are candidates or recipients of solid organ and hematopoietic cell transplants. The Panel emphasizes the importance of maintaining HIV viral suppression before and after a transplant. The addition of immunosuppressive therapy and prophylaxis against opportunistic infections to ART increases pill burden and the potential for drug–drug interactions and adverse effects. Because of the complexities of medical management, the Panel recommends that people with HIV who require transplantation be managed by a multidisciplinary team before, during, and after transplant **(AIII).**

Key Revisions to the Guidelines

What to Start: Initial Combination Antiretroviral Regimens for People With HIV

Several changes have been made to the Panel's recommendations for initial ART regimens for people with HIV. The regimens recommended by the Panel as initial ART for people with HIV include those that have demonstrated clinical efficacy, have a high barrier to resistance, are well tolerated, and can be given as once-daily therapy. The Panel made the following changes to the recommended initial ART regimens:

- Dolutegravir (DTG)/abacavir/lamivudine (3TC) has been changed from one of the Recommended Initial Regimens for Most People With HIV (Table 6a) to a regimen recommended as part of Other Initial Antiretroviral Regimens for Certain Clinical Scenarios (Table 6b) due to the need for HLA-B*5701 testing before initiating therapy, the potential increase in the risk of cardiovascular events, and the availability of other options for initial therapy.
- Several antiretroviral (ARV) regimens are no longer recommended as initial therapy due to higher pill burdens, more adverse effects, or a lower barrier to resistance than other ART regimens recommended by the Panel. These regimens include the following:
    - Elvitegravir/cobicistat and raltegravir-based regimens
    - Boosted atazanavir-based regimens
    - Efavirenz-based regimens
    - Rilpivirine (RPV)/tenofovir disoproxil fumarate/emtricitabine (FTC) regimens

Virologic Failure

Updates made to the Virologic Failure section include the following:

- For people who experience virologic failure while on their first ARV regimen of a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus two nucleoside reverse transcriptase inhibitors (NRTIs), a salvage regimen of DTG plus boosted darunavir can be used **(AI)**. This recommendation is based on data from the D^2EFT trial, a large randomized controlled trial comparing this regimen to a regimen of DTG plus two NRTIs.
- Some people with HIV cannot reach or maintain viral suppression on oral ART despite intensive adherence support. A complete regimen of long-acting injectable cabotegravir and rilpivirine (LA CAB/RPV) has been used in this population with some success, although long-term efficacy data are limited. Based on very limited data, the Panel 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, who have no evidence of resistance to CAB or RPV, and with shared decision-making between providers and people with HIV **(CIII).** The Panel notes that people with HIV and their providers must be aware of the significant risk of developing resistance to NNRTIs, and particularly integrase strand transfer inhibitors (INSTIs) if virologic failure occurs on LA CAB/RPV. Such resistance may limit future treatment options and may also lead to HIV transmission.

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression

Updates made to the Optimizing Antiretroviral Therapy in the Setting of Viral Suppression section include the following:

- Because more people with HIV are switched to regimens that do not include NRTIs or only include 3TC, the Panel has expanded the guidance to emphasize the importance of keeping regimens that contain hepatitis B virus (HBV)–active drugs for people with HBV/HIV coinfection. For people with no known history of HBV infection, the Panel noted the need to screen for HBV before initiating NRTI-sparing (or limited) regimens.
- The discussion of LA CAB/RPV as a switch strategy with data from additional clinical trials and information on the use of this regimen in people who have challenges with adherence to oral ART.
- The Panel expanded on the discussion of clinical trial data on switch strategies in people with limited or extensive drug resistance.

HIV and the Older Person

Updates made to the HIV and the Older Person section include the following:

- A new subsection on HIV and Immunologic Aging.
- Expanded discussions on non-AIDS complications among older people with HIV.
- A discussion on atherosclerotic cardiovascular disease in older people with HIV and the recent recommendation for the use of statins in people with HIV (see Statin Therapy in People With HIV).

Substance Use Disorders and HIV

Updates made to the Substance Use Disorders and HIV section include the following:

- A new subsection on Substance Use and Unstable Housing that includes discussion of the impact of unstable housing on the HIV care continuum and adherence to ART.

- An expanded discussion on considerations when using LA CAB/RPV in people with HIV and substance use disorder.
- A new subsection that includes a discussion on xylazine, an adulterant that may be added to opioids, such as fentanyl. The Panel notes that xylazine is a cytochrome P450 (CYP) 3A4 substrate; thus, its half-life may be prolonged in the presence of CYP3A4 inhibitors, such as ritonavir or cobicistat, further increasing the risk of overdose.

Transgender People With HIV

Updates made to the Transgender People With HIV section include the following:

- An update on the epidemiology of transgender people with HIV based on recent data from national surveys and Centers for Disease Control and Prevention (CDC) surveillance reports.
- An expanded discussion on barriers that transgender adults and adolescents with HIV may face in accessing care and maintaining HIV suppression.
- A new table that lists the most commonly used gender-affirming hormone therapies (GAHT).
- Updates to the drug–drug interaction table for interactions between GAHT and ARV drugs to include newer ARV drugs used in clinical practice.
- The Panel expanded discussion on cardiovascular disease risk in transgender people with HIV who use GAHT.

Hepatitis B Virus/HIV Coinfection

Updates made to the Hepatitis B Virus/HIV Coinfection section include the following:

- The Panel no longer recommends pegylated interferon as a therapy for the treatment of HBV in people with HIV **(AIII).** Pegylated interferon should only be considered in rare cases and with consultation with an expert in HBV**.**
- The Panel noted that approximately 4% of people with HBV/HIV coinfection are also found to have hepatitis D virus (HDV) in serologic testing. Because HBV/HDV coinfection is associated with serious liver complications, experts recommend screening for HDV in people with HBV/HIV coinfection.
- The Panel emphasizes that for people with HBV/HIV coinfection who are planning to switch to an NRTI-sparing regimen, ARV drugs that are active against HIV should be continued **(AII)** or another anti-HBV drug (i.e., entecavir) should be initiated **(AII).**
- Due to increased interest in switching people to NRTI-sparing or NRTI-limiting ARV regimens, this section stresses the importance of screening for HBV before switching to NRTI-sparing or NRTI-limiting regimens in people who are not known to have HBV infection. The Panel recommends vaccination for those found to be nonimmune to HBV and provides guidance for monitoring and managing people with prior exposure to HBV.

Tuberculosis/HIV Coinfection

Updates made to the Tuberculosis/HIV Coinfection section include the following:

- The Panel previously did not recommend the use of a DTG-based regimen for people with HIV who use a once-daily isoniazid plus rifapentine regimen for the treatment of latent tuberculosis infection. Based on data from a recently published pharmacokinetics (PK) study, the Panel now recommends that—
    - For a person with virologic suppression while on a once-daily DTG 50 mg regimen, the DTG dose should be increased to 50 mg twice daily throughout the course of once-daily isoniazid plus rifapentine for 1 month (1HP), continuing DTG twice daily for 14 days after 1HP completion before switching back to once-daily DTG dosing **(AII).**
- The subsection on Drug Interaction Considerations has been updated to indicate that rifamycins are not recommended for use with the long-acting injectable drugs CAB, RPV, or lenacapavir.

Adherence to the Continuum of Care Section

Updates made to the Adherence to the Continuum of Care section include the following:

- The section emphasizes that addressing social determinants of health is essential for enhancing adherence throughout the HIV continuum of care.
- A new subsection has been added to discuss the importance of guiding individuals with HIV through transitions between different health care systems to ensure continuity of care.
- The subsection on the use of LA CAB/RPV in people with viremia and ongoing challenges to oral ART adherence or retention in care has been expanded to incorporate recommendations from the Virologic Failure section of the guidelines.

Drug–Drug Interactions

Tables 24a through 24g have been updated with new PK data on interactions between ARV drugs and other drugs, including drugs that were approved by the U.S. Food and Drug Administration in the past 3 years and that may have interactions with ARV drugs.

Other Updates

Minor updates have been made to the following sections of the guidelines:

- Drug-Resistance Testing
- Early (Acute and Recent) HIV Infection
- Women With HIV
- Cost Considerations and Antiretroviral Therapy
- Appendix B, Table 12

Sections Removed From the Guidelines

- Antiretroviral Components or Regimens Not Recommended as Initial Therapy
- What Not to Use