



**Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States**

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### General Principles Regarding Use of Antiretroviral Drugs During Pregnancy

Panel's Recommendations
<ul style="list-style-type: none"><li>Initial evaluation of HIV-infected pregnant women should include assessment of HIV disease status and recommendations regarding initiation of combination antiretroviral therapy (cART) or the need for any modification if currently receiving cART (AIII). The National Perinatal HIV Hotline (888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.</li><li>All pregnant HIV-infected women should receive cART to prevent perinatal transmission regardless of plasma HIV RNA copy number or CD4 T lymphocyte count (AI). The goal of cART is to maintain a viral load below the limit of detection throughout pregnancy.</li><li>Combined antepartum, intrapartum, and infant antiretroviral prophylaxis is recommended because antiretroviral drugs reduce perinatal transmission by several mechanisms, including lowering maternal antepartum viral load and providing infant pre- and post-exposure prophylaxis (AI).</li><li>The known benefits and potential risks of all medication use, including antiretroviral use, during pregnancy should be discussed with all HIV-infected women (AIII).</li><li>The importance of adherence to antiretroviral regimens should be emphasized in patient counseling (AII).</li><li>Antiretroviral drug-resistance studies should be performed before starting or modifying ARV drug regimens in women whose HIV RNA levels are above the threshold for resistance testing (i.e., &gt;500 to 1,000 copies/mL) (see <a href="#">Antiretroviral Drug Resistance and Resistance Testing in Pregnancy</a>) (AIII). In pregnant women not already receiving cART, consideration should be given to initiating cART before results of drug-resistance testing are available because earlier viral suppression has been associated with lower risk of transmission. If cART is initiated before results are available, the regimen should be modified, if necessary, based on resistance assay results (BIII).</li><li>Coordination of services among prenatal care providers, primary care and HIV specialty care providers, and when appropriate, mental health and drug abuse treatment services, and public assistance programs, is essential to ensure that infected women adhere to their antiretroviral drug regimens (AIII).</li></ul>
<p><b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Optional</p> <p><b>Rating of Evidence:</b> I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion</p>

In addition to the standard antenatal assessments for all pregnant women, the initial evaluation of those who are HIV infected should include assessment of HIV disease status and recommendations for HIV-related medical care. This initial assessment should include the following:

- Review of prior HIV-related illnesses and past CD4 T lymphocyte (CD4) cell counts and plasma HIV RNA levels;
- Current CD4 cell count;
- Current plasma HIV RNA level;
- Assessment of the need for prophylaxis against opportunistic infections such as *Pneumocystis jirovecii* pneumonia and *Mycobacterium avium* complex (see [Adult and Adolescent Opportunistic Infections Guidelines](#));
- Screening for hepatitis A virus (HAV), hepatitis C virus and tuberculosis in addition to standard screening for hepatitis B virus (HBV) infection;
- Assessment of the need for immunizations per guidelines from the American College of Obstetricians and Gynecologists, the Centers for Disease Control and Prevention (CDC), and the Infectious Diseases Society of America with particular attention to HAV, HBV, influenza, pneumococcus, and Tdap immunizations;<sup>1,2</sup>
- Complete blood cell count and renal and liver function testing;

- HLA-B\*5701 testing if abacavir use is anticipated (see [Table 7](#));
- History of prior and current antiretroviral (ARV) drug use, including prior ARV use for prevention of perinatal transmission or treatment of HIV and history of adherence problems;
- Results of prior and current HIV ARV drug-resistance studies;
- History of adverse effects or toxicities from prior ARV regimens; and
- Assessment of supportive care needs such as mental health services, substance abuse treatment, and smoking cessation.

### ***The National Perinatal HIV Hotline***

The National Perinatal HIV Hotline (888-448-8765) is a federally funded service providing free clinical consultation to providers caring for HIV-infected women and their infants.

### ***Mechanism of Action of Antiretrovirals in Prevention of Perinatal Transmission***

ARV drugs for prevention of perinatal transmission of HIV are recommended for all pregnant women, regardless of CD4 cell counts and HIV RNA levels. ARV drugs can reduce perinatal transmission through a number of mechanisms. Antenatal drug administration decreases maternal viral load in blood and genital secretions. Although the risk of perinatal transmission in women with undetectable plasma HIV RNA levels appears to be extremely low, it has been reported even among women on combination antiretroviral therapy (cART).<sup>3-5</sup> Low-level cervicovaginal HIV RNA and DNA shedding has been detected even in women treated with cART who have undetectable plasma viral load.<sup>6-8</sup> Penetration of ARV drugs into the female genital tract has been shown to vary between drugs.<sup>9-11</sup> Another mechanism of protection is infant pre-exposure prophylaxis achieved by administering ARV drugs that cross the placenta and produce adequate systemic drug levels in the fetus. Infant post-exposure prophylaxis is achieved by administering drugs after birth, providing protection from cell-free or cell-associated virus that may have entered the fetal/infant systemic circulation during labor and delivery. The importance of the pre- and post-exposure components of prophylaxis in reducing perinatal transmission is demonstrated by the reduced efficacy of interventions that involve administration of ARVs only during labor and/or to the newborns.<sup>12-18</sup> Therefore, combined antepartum ARV prophylaxis, intrapartum **continuation of current regimen with intravenous zidovudine added if the plasma viral load is >1,000 copies/mL**, and infant ARV prophylaxis are recommended to prevent perinatal transmission of HIV.

### ***General Principles of Drug Selection***

In general, guidelines for the use of cART for the benefit of maternal health during pregnancy are the same as for women who are not pregnant, with some modifications based on concerns about specific drugs and limited experience during pregnancy with newer drugs.

The known benefits and known and unknown risks of ARV drug use during pregnancy should be considered and discussed with women (see [Table 7](#) and [Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy](#)). Potential risks of these drugs should be placed into perspective by reviewing the substantial benefits of ARV drugs for maternal health and in reducing the risk of transmission of HIV to infants. Counseling of pregnant women about ARV use should be **directive but** non-coercive, and providers should help them make informed decisions regarding use of ARV drugs.

Discussions with women about initiation of cART drug regimens should include information about:

- Maternal risk of disease progression and the benefits and risks of initiation of therapy for maternal health;
- Benefit of cART for preventing perinatal transmission of HIV;<sup>4</sup>
- Benefits of therapy for reducing sexual transmission to discordant partners when viral suppression is maintained;<sup>19</sup>

- The need for strict adherence to the prescribed drug regimen to avoid resistance;
- Potential adverse effects of ARV drugs for mothers, fetuses, and infants, including potential interactions with other medications the women may already be receiving;
- The limited long-term outcome data for women with higher CD4 cell counts who choose to stop cART after delivery rather than continuing therapy; and
- The limited long-term outcome data for infants after *in utero* drug exposure.

Transplacental passage of ARVs is an important mechanism of infant pre-exposure prophylaxis. Thus, when selecting an ARV regimen for a pregnant woman, at least one nucleoside/nucleotide reverse transcriptase inhibitor agent with high placental transfer should be included as a component of the cART regimen (see [Table 7](#)).<sup>20-23</sup>

In women with plasma HIV RNA levels above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL), ARV drug-resistance studies should be performed before starting cART. As with non-pregnant, HIV-infected adults, cART may be initiated before genotype results are available under certain circumstances. Starting cART pending genotype results is particularly relevant after the first trimester because taking cART for 24 weeks or more has been associated with reduced transmission rates compared to a shorter duration of cART. If cART is initiated before results are available the regimen should be modified, if necessary, based on resistance assay<sup>24</sup> (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)). Counseling should emphasize the importance of adherence to the ARV drug regimen to minimize the development of resistance.

Support services, mental health services, smoking cessation, and drug abuse treatment may be required, depending on a woman's individual circumstances. Coordination of services among prenatal care providers, primary care and HIV specialty care providers, mental health and drug abuse treatment services, and public assistance programs is essential to ensure that infected women adhere to their ARV drug regimens.

All HIV-infected pregnant women should be started on cART during pregnancy to minimize the risk of transmission. Providers should work with women to develop long-range plans regarding continuity of medical care. Considerations regarding postpartum continuation of cART for maternal therapeutic indications are the same as for non-pregnant individuals.

Medical care of HIV-infected pregnant women requires coordination and communication between HIV specialists and obstetric providers. General counseling should include current knowledge about risk factors for perinatal transmission. Risk of perinatal transmission of HIV has been associated with potentially modifiable factors, including cigarette smoking, illicit drug use, genital tract infections, and unprotected sexual intercourse with multiple partners during pregnancy.<sup>25-29</sup> Besides improving maternal health, cessation of cigarette smoking and drug use, treatment of genital tract infections, and use of condoms with sexual intercourse during pregnancy may reduce risk of perinatal transmission. In addition, the CDC and American Academy of Pediatrics recommend that HIV-infected women in the United States (including those receiving cART) refrain from breastfeeding to avoid postnatal transmission of HIV to their infants through breast milk,<sup>30,31</sup> and avoid pre-mastication of food for their infants, a potential risk factor for transmission.<sup>32</sup>

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