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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What's New in the Guidelines? (Last updated July 31, 2012; last reviewed July 31, 2012)

Key changes made to update the September 14, 2011, version of the guidelines are summarized below. Throughout the revised guidelines, significant updates are highlighted and discussed. The addendum to the guidelines—**Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy**—includes updated information from the Antiretroviral Pregnancy Registry and updates on recent studies of various antiretroviral agents in human pregnancy.

Lessons from Clinical Trials of Antiretroviral Interventions to Reduce Perinatal Transmission of HIV and Table 3, Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child Transmission of HIV:

- Table 3 updated to include data on 48-week results of the Breastfeeding and Nutrition (BAN) study in Malawi.

Preconception Counseling and Care for HIV-Infected Women of Childbearing Age and Table 4, Drug Interactions Between Hormonal Contraceptives and Antiretroviral Agents:

- Table 4 updated to include data on hormonal contraceptive interactions with rilpivirine and raltegravir.
- **Reproductive Options for HIV-Concordant and Serodiscordant Couples:**
  - For serodiscordant couples who want to conceive, use of antiretroviral therapy is now recommended for the HIV-infected partner, with the strength of the recommendation differing based on the CD4-cell count of the infected partner:
    - **AI** for CD4 T-lymphocyte (CD4-cell) count ≤550 cells/mm^3, **BIII** for CD4-cell count >550 cells/mm^3). If therapy is initiated, maximal viral suppression is recommended before conception is attempted **(AIII)**.
  - Added discussion of the pre-exposure prophylaxis (PrEP) studies in heterosexual couples, with a new recommendation regarding PrEP in discordant couples who wish to conceive. Discussion includes information on counseling, laboratory testing, and monitoring of individuals on PrEP and importance of reporting uninfected women who become pregnant on PrEP to the Antiretroviral Pregnancy Registry:
    - Periconception administration of antiretroviral PrEP for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission **(CIII)**. The utility of PrEP of the uninfected partner when the infected partner is receiving antiretroviral therapy has not been studied.

Antepartum Care

- **General Principles Regarding Use of Antiretroviral Drugs During Pregnancy:**
  - Initial assessment for HIV-infected pregnant women expanded to include screening for hepatitis C virus and tuberculosis infection, as well as history of side effects or toxicities from prior antiretroviral drug regimens.
  - Additional benefit of antiretroviral drug regimens expanded to include benefits of therapy for reducing sexual transmission to discordant partners when viral suppression is maintained, with

discussion of the HPTN 052 trial results.

- **Recommendations for Use of Antiretroviral Drugs During Pregnancy and Table 5, Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy:**

  - Modified recommendations regarding categorization of various antiretroviral agents in categories of drugs that are ***preferred***, ***alternative***, or ***use in special circumstances***.

  - **Nucleoside reverse transcriptase inhibitors:**
    - Didanosine and stavudine moved from ***alternative*** NRTI category to ***use in special circumstances*** category because they have more toxicity than the preferred and alternative NRTI drugs.

  - **Protease inhibitors:**
    - Atazanavir with low-dose ritonavir boosting moved from an ***alternative*** protease inhibitor to a ***preferred*** protease inhibitor for use in antiretroviral-naive pregnant women, along with lopinavir/ritonavir, because of increased information on safety in pregnancy.

    - Darunavir moved from ***insufficient data to recommend use*** to an ***alternative*** protease inhibitor for use in antiretroviral-naive pregnant women.

  - **Integrase inhibitors:**
    - Raltegravir moved from ***insufficient data to recommend use*** to ***use in special circumstances*** for antiretroviral-naive pregnant women when preferred or alternative agents cannot be used.

- **HIV-Infected Pregnant Women Who Have Never Received Antiretroviral Drugs (Antiretroviral Naive):**

  - Increased discussion on when to initiate an antiretroviral drug regimen in pregnant women:
    - The decision as to whether to start the regimen in the first trimester or delay until 12 weeks' gestation will depend on CD4-cell count, HIV RNA levels, and maternal conditions such as nausea and vomiting **(AIII)**. Earlier initiation of a combination antiretroviral regimen may be more effective in reducing transmission, but benefits must be weighed against potential fetal effects of first-trimester drug exposure.

- **HIV-Infected Pregnant Women Who Are Currently Receiving Antiretroviral Therapy:**

  - Discussion of efavirenz use in the first trimester:
    - Because the risk of neural tube defects is restricted to the first 5 to 6 weeks of pregnancy and pregnancy is rarely recognized before 4 to 6 weeks of pregnancy, and unnecessary antiretroviral drug changes during pregnancy may be associated with loss of viral control and increased risk of perinatal transmission, efavirenz can be continued in pregnant women receiving an efavirenz-based regimen who present for antenatal care in the first trimester, provided the regimen produces virologic suppression **(CIII)**.

- **Special Situations - Failure of Viral Suppression:**

  - Use of raltegravir in late pregnancy in women with high viral loads to decrease viral load discussed but not endorsed. The efficacy and safety of this approach have not been evaluated and

only anecdotal reports are available. In the setting of a failing regimen related to nonadherence and/or resistance, there are concerns that the addition of a single agent may further increase risk of resistance and potential loss of future effectiveness with raltegravir. Until more data become available on the safety of raltegravir use in pregnancy, this approach cannot be recommended.

Special Considerations Regarding the Use of Antiretroviral Drugs by HIV-Infected Pregnant Women and Their Infants

- **Combination Antiretroviral Drug Regimens and Pregnancy Outcome:**
  - Addition of a new table—Table 7– Results of Studies Assessing Association Between Antiretroviral Regimens and Preterm Delivery—that summarizes the results of studies assessing the association between antiretroviral regimens and preterm delivery.

Intrapartum Care

- **Intrapartum Antiretroviral Therapy/Prophylaxis:**
  - Discussion of use of intravenous (IV) zidovudine during labor and maternal viral load:
    - IV zidovudine is no longer required for HIV-infected women receiving combination antiretroviral regimens who have HIV RNA <400 copies/mL near delivery **(BII)**.
    - HIV-infected women with HIV RNA ≥400 copies/mL (or unknown HIV RNA) near delivery should be administered IV zidovudine during labor, regardless of antepartum regimen or mode of delivery **(AI)**.
    - Based on pharmacokinetic data, in women with HIV RNA ≥400 copies/mL near delivery for whom zidovudine is recommended, IV would be preferred to oral administration in the United States; in situations where IV administration is not possible, oral administration can be considered.

Postpartum Care

- **Infant Antiretroviral Prophylaxis and Table 9, Recommended Neonatal Dosing for Prevention of Mother-to-Child Transmission of HIV:**
  - Table 9 revised to reflect neonatal dosing only of zidovudine (in term and preterm infants) and nevirapine in the regimen used in the NICHD-HPTN 040 study.
  - Choice of neonatal antiretroviral drug prophylaxis includes discussion of the NICHD-HPTN 040 study and concerns regarding use of lopinavir/ritonavir in neonates.
  - Addition of new pharmacokinetic data on nevirapine in preterm infants.
- **Initial Postnatal Management of the HIV-Exposed Neonate:**
  - Because of the potential for enhanced hematologic toxicity in infants receiving a zidovudine/lamivudine-containing prophylaxis regimen, a recheck of hemoglobin and neutrophil counts is recommended 4 weeks after initiation of prophylaxis **(AI)**.
  - New recommendation that health care providers should routinely inquire about premastication of foods fed to infants, instruct HIV-infected caregivers to avoid this practice, and advise on safer feeding options **(AII)**.