



**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

The *Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women and Interventions to Reduce Perinatal HIV Transmission in the United States* guidelines are published in an electronic format that can be updated as relevant changes in prevention and treatment recommendations occur. The Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission is committed to timely changes in this document because so many health care providers, patients, and policy experts rely on this source for vital clinical information.

Major revisions within the last 12 months are as follows:

### October 26, 2016

The Perinatal Guidelines text, appendices, and references were updated to include new data and publications where relevant. Throughout the Perinatal Guidelines, content was revised to refer to expedited HIV testing, preferably using fourth-generation antigen/antibody expedited HIV tests, in accordance with current Centers for Disease Control and Prevention (CDC) recommendations. Major changes are summarized below and all changes are highlighted throughout the guidelines.

#### 1. Preconception Counseling and Care for HIV-Infected Women of Childbearing Age

- [Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives](#) was updated and expanded to include new data and additional content (e.g., contraceptive effects on antiretroviral therapy [ART] and HIV, clinical studies, justification/evidence for recommendations). More details can be found in CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2016, <http://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6503.pdf>.
- Counseling about the potential benefits and risks of starting oral pre-exposure prophylaxis to prevent HIV acquisition was added to the guidance for preconception care of women living with HIV who have uninfected partners.

#### 2. General Principles Regarding Use of Antiretroviral Drugs during Pregnancy

- The Panel now recommends that ART should be initiated as early in pregnancy as possible.
- The Panel added a recommendation that providers should initiate patient counseling during pregnancy about key intrapartum and postpartum considerations, including mode of delivery, maternal lifelong HIV therapy, postpartum contraception, infant feeding, infant antiretroviral (ARV) prophylaxis and timing of infant diagnostic testing and neonatal circumcision.
- The initial assessment of pregnant women with HIV infection was updated to include intimate partner violence-related screening and supportive care and referral of sexual partners for HIV testing and ARV prophylaxis.

#### 3. Teratogenicity

- The Panel now recommends that—based on the preponderance of studies indicating no difference in rates of birth defects for first-trimester compared with later ARV exposures—women can be counseled that ART during pregnancy generally does not increase the risk of birth defects.
- In the past, efavirenz use was not recommended before 8 weeks' gestational age, because of concerns regarding potential teratogenicity. Although this caution remains in the package insert, review of available data has been reassuring that risks of neural tube defects after first trimester efavirenz exposure are not greater than those in the general population. As a result, the current Perinatal Guidelines do not include the restriction on efavirenz use before 8 weeks' gestation, consistent with both the British HIV Association and World Health Organization guidelines for use of ARV drugs in pregnancy. Importantly, women who become pregnant on suppressive efavirenz-containing regimens

should continue their current regimens.

#### **4. Combination Antiretroviral Drug Regimens and Pregnancy Outcome**

- This section was updated to include new studies, and content was reorganized and presented as a summary with new subsections that discuss the potential mechanism of preterm birth associated with ART and the evidence for additional other pregnancy outcomes potentially associated with ART (i.e., low birth weight, small for gestational age, and stillbirth).

#### **5. Recommendations for Use of Antiretroviral Drugs during Pregnancy**

- Although in general, the same regimens recommended for treatment of non-pregnant adults should be used in pregnant women, the Panel has added “if appropriate drug exposure is achieved during pregnancy” to other considerations (e.g., adverse effects for women, fetuses, or infants that outweigh benefits).
- The Panel recommends that in most cases, women who present for obstetric care on fully suppressive ARV regimens should continue their current regimens unless the regimen includes didanosine, stavudine, or full-dose ritonavir.

#### **6. Table 6: What to Start: Initial Combination Regimens for Antiretroviral Naive-Pregnant Women was updated with new recommendations for initial therapy.**

- Zidovudine/lamivudine was changed from a Preferred to an Alternative dual nucleoside reverse transcriptase inhibitor (NRTI) combination for ARV-naive women, because it requires twice-daily dosing and is associated with higher rates of mild-to-moderate adverse effects than Preferred NRTI combinations.
- The Panel has removed efavirenz from the Preferred agents list; it is now classified as Alternative. The change was principally related to the association of efavirenz with neurological adverse effects. However, the Panel recommends that women who become pregnant on suppressive efavirenz-containing regimens should continue their current regimens and notes that efavirenz may be suitable for women who desire a once-daily fixed-dose combination regimen and who tolerate efavirenz without adverse effect.
- Safety and PK data about the use of tenofovir alafenamide in pregnancy are insufficient to recommend this medication for use in initial regimens for ARV-naive women.

#### **7. Table 8: Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy and Appendix B: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy**

- These sections were updated with new data for cobicistat, darunavir, efavirenz, elvitegravir, enfuvirtide, lopinavir, maraviroc, raltegravir, zidovudine. A new section was added for tenofovir alafenamide (TAF), an oral product of tenofovir, based on FDA approval of 3 fixed-dose combination products that contain TAF. No data are currently available about the use of TAF in pregnancy.

#### **8. HIV-Infected Pregnant Women Who Have Never Received Antiretroviral Drugs (Antiretroviral Naive)**

- The section was updated in accordance with changes in Recommendations for Use of Antiretroviral Drugs in Pregnancy (see [Table 6: What to Start: Initial Combination Regimens for Antiretroviral Naive-Pregnant Women](#)).
- The section now includes a statement that zidovudine monotherapy during pregnancy is no longer recommended because of the clear health benefit of ART to the mother and for the prevention of perinatal transmission of HIV.

## 9. HIV-Infected Pregnant Women Who Are Currently Receiving Antiretroviral Drugs

- HIV-infected women may present for prenatal care on ART regimens that include ARV drugs that lack significant experience in pregnancy, with limited data on pharmacokinetics and safety. Providers are encouraged to consult with an HIV perinatal specialist before considering altering a regimen that is achieving full viral suppression and is well tolerated.
- Providers should make every effort to report all ART exposures in pregnant women to the [Antiretroviral Pregnancy Registry](#), because little is known about the use of newly approved drugs in pregnancy.

## 10. Antiretroviral Drug Resistance and Resistance Testing in Pregnancy

- Previous versions of the Perinatal Guidelines have provided guidance for situations in which women stop their ART regimen postpartum. However, the Panel strongly recommends that ART regimens, once initiated, not be discontinued. If a woman desires to discontinue ART after delivery, a consultation with an HIV specialist is strongly recommended.

## 11. Lack of Viral Suppression

- Suppression of HIV RNA to undetectable levels should be achieved as rapidly as possible in pregnancy; both HIV-RNA level and timing of ART initiation have been independently associated with perinatal transmission.
- In the setting of acute HIV infection in pregnancy the rate of viral decline following ART initiation may be significantly slower than among those with chronic HIV infection, after adjustment for baseline CD4 count; strategies to accelerate viral decline may be considered, in consultation with HIV treatment experts.

## 12. Special Populations: HIV/Hepatitis B Virus Coinfection

- Because all pregnant women newly diagnosed with HIV should begin ART as soon as possible, they should also be screened as soon as possible for hepatitis B virus (HBV) because ART in HIV/HBV-coinfected pregnant women should include tenofovir disoproxil fumarate plus lamivudine or emtricitabine.
- Women should be counseled on the importance of continuing anti-HBV medications indefinitely, both during and after pregnancy.

## 13. HIV-2 Infection and Pregnancy

- Pregnant women with HIV-1 and HIV-2 coinfection should be treated as per guidelines for HIV-1 mono-infection, but using ARV drugs to which HIV-2 is sensitive.
- A regimen with two NRTIs and an integrase strand transfer inhibitor was added to the prophylactic regimens recommended for all HIV-2-infected pregnant women.
- No randomized clinical trials have been performed to address when to start treatment or what is the optimal treatment for HIV-2 mono-infection.

## 14. Pregnancy in Women with Perinatal HIV Infection

- The management of prenatal care and general principles of ART and HIV management do not differ between pregnant women who were perinatally infected and those who acquired HIV infection postnatally. With appropriate ART, prenatal management and when optimal viral suppression is attained, the risk of perinatal transmission does not appear to be increased in women who acquired HIV perinatally.
- Optimal ART regimens should be selected on the basis of resistance testing, prior ART history, and minimization of pill burden just as the same guiding principles are used for heavily ART-experienced adults.

- The benefits from drugs with limited experience for use in pregnancy may be needed due to extensive resistance. Consultation with experts in HIV and pregnancy is recommended.

### 15. Intrapartum Antiretroviral Therapy/Prophylaxis Care

- The recommendations for testing women who present in labor with unknown HIV status were updated to reflect current CDC testing algorithms.
- The Panel added a bulleted recommendation to emphasize that women testing HIV positive on initial screening during labor should not breastfeed until HIV infection has been ruled out.

### 16. Transmission and Mode of Delivery

- In women on ART with HIV RNA  $\leq 1,000$  copies/ml, duration of ruptured membranes is not associated with an increased risk of perinatal transmission, and vaginal delivery is recommended.

### 17. Other Intrapartum Management Considerations

- Artificial rupture of membranes (ROM) performed in the setting of ART and virologic suppression is not associated with increased risk of perinatal transmission and can be performed for standard obstetric indications.

### 18. Postpartum Care

- The Panel added a recommendation that women with a positive rapid HIV antibody test during labor should not breastfeed unless a confirmatory HIV test is negative.

### 19. Infant Antiretroviral Prophylaxis

- The Panel recommends a 4-week zidovudine prophylaxis regimen for full-term infants when the mother has received a standard combination ART regimen during pregnancy with sustained viral suppression.
- The Panel recommends a 6-week course of combination ARV prophylaxis regimen for all infants at higher risk of HIV transmission including those born to mothers who have received no antepartum or intrapartum ARV drugs, intrapartum ARV drugs only, or who have received combination ARV drugs and do not have sustained viral suppression. The Panel was unable to reach clear consensus on the specific ARV prophylaxis regimen in these infants, but options are listed in an update of [Table 7. Neonatal Dosing for Prevention of Perinatal Transmission of HIV.](#)

## June 7, 2016

1. [Appendix B: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy and Table 8: Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy](#) were revised to incorporate new data and publications, where available, Food and Drug Administration drug label changes, and new fixed dose combination formulations. Updates were made to the following drug sections: Atazanavir, Dolutegravir, Emtricitabine, Fosamprenavir, Indinavir, Lamivudine, Nelfinavir, Nevirapine, Rilpivirine, Ritonavir, Saquinavir, Stavudine, Tenofovir, and Tipranavir. There were no major changes related to management of these drugs during pregnancy.

## April 29, 2016

1. [Appendix B: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy and Table 8: Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy](#) were revised.
  - a. The [Abacavir](#), [Etravirine](#) and [Didanosine](#) sections were updated to include new data and publications,

including Food and Drug Administration label updates.

- b. The Amprenavir, Delavirdine, and Zalcitabine sections were removed from the guidelines as they are no longer available in the United States. Additional information on these drugs can be found in the *Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women and Interventions to Reduce Perinatal HIV Transmission in the United States* [archives](#).