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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Preconception Counseling and Care for HIV-Infected Women of Childbearing Age (Last updated July 31, 2012; last reviewed July 31, 2012)

Overview

Panel's Recommendations
• Discuss childbearing intentions with all women of childbearing age on an ongoing basis throughout the course of their care **(AIII)**. • Include information about effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy **(AI)**. • During preconception counseling, include information on safer sexual practices and elimination of alcohol, illicit drugs, and smoking, which are important for the health of all women as well as for fetal/infant health, should pregnancy occur **(AII)**. • When evaluating HIV-infected women, include assessment of HIV disease status and need for antiretroviral therapy (ART) for their own health **(AII)**. • Choose an ART regimen for HIV-infected women of childbearing age based on consideration of effectiveness for treatment of maternal disease, hepatitis B virus disease status, teratogenic potential of the drugs in the regimen should pregnancy occur, and possible adverse outcomes for mother and fetus **(AII)**.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional* ***Rating of Evidence:*** *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*

The Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists, and other national organizations recommend offering all women of childbearing age comprehensive family planning and the opportunity to receive preconception counseling and care as a component of routine primary medical care. The purpose of preconception care is to improve the health of each woman before conception by identifying risk factors for adverse maternal or fetal outcome, providing education and counseling targeted to patients' individual needs, and treating or stabilizing medical conditions to optimize maternal and fetal outcomes.[1] Preconception care is not a single clinical visit but, rather, a process of ongoing care and interventions integrated into primary care to address the needs of women during the different stages of reproductive life. Because more than half of all pregnancies in the United States are unintended[2-5] it is important that comprehensive family planning and preconception care be integrated into routine health visits. Providers should initiate and document a nonjudgmental conversation with all women of reproductive age concerning their reproductive desires because women may be reluctant to bring this up themselves.[6, 7] HIV care providers who routinely care for women of reproductive age play an important role in promoting preconception health and informed reproductive decisions.

The fundamental principles of preconception counseling and care are outlined in the CDC Preconception Care Work Group's *Recommendations to Improve Preconception Health and Health Care*. In addition to the general components of preconception counseling and care that are appropriate for all women of reproductive age, HIV-infected women have specific needs that should be addressed.[8, 9] Because many women infected with HIV are aware of their HIV status before becoming pregnant, issues that impact pregnancy can be addressed before conception during their routine medical care for HIV disease. In addition to the principles outlined by the CDC Preconception Care Work Group[10], the following components of preconception

counseling and care are specifically recommended for HIV-infected women. Health care providers should:

a. Discuss reproductive options; actively assess women's pregnancy intentions on an ongoing basis throughout the course of care; and, when appropriate, make referrals to experts in HIV and women's health, including experts in reproductive endocrinology and infertility when necessary.[11, 12]
b. Offer all women effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. Providers should be aware of potential interactions between antiretroviral (ARV) drugs and hormonal contraceptives that could lower contraceptive efficacy (see Table 4).
c. Counsel on safe sexual practices that prevent HIV transmission to sexual partners, protect women from acquiring sexually transmitted diseases, and reduce the potential to acquire more virulent or resistant strains of HIV.
d. Counsel on eliminating alcohol, illicit drug use, and cigarette smoking.
e. Educate and counsel women about risk factors for perinatal transmission of HIV, strategies to reduce those risks, potential effects of HIV or of ARV drugs given either for treatment or solely for prevention of mother-to-child transmission (MTCT) on pregnancy course and outcomes, and the recommendation that HIV-infected women in the United States not breastfeed because of the risk of transmission of HIV and the availability of safe and sustainable infant feeding alternatives.
f. When prescribing antiretroviral therapy (ART) to women of childbearing age, consider the regimen's effectiveness for treatment of HIV, an individual's hepatitis B disease status, the drugs' potential for teratogenicity should pregnancy occur, and possible adverse outcomes for mother and fetus.[13-15]
g. Use the preconception period in women who are contemplating pregnancy to adjust ARV regimens to exclude efavirenz or other drugs with teratogenic potential.
h. Make a primary treatment goal for women who are on ART for their own health and who want to get pregnant the attainment of a stable, maximally suppressed maternal viral load prior to conception to decrease the risk of MTCT.
i. Evaluate and appropriately manage therapy-associated side effects such as hyperglycemia, anemia, and hepatotoxicity that may adversely impact maternal-fetal health outcomes.
j. Evaluate the need for appropriate prophylaxis or treatment for opportunistic infections, including safety, tolerability, and potential toxicity of specific agents when used in pregnancy.
k. Administer medical immunizations for influenza, pneumococcal or hepatitis A and B vaccines, and other vaccines as indicated (see http://www.cdc.gov/vaccines/recs/acip/rec-vac-preg.htm and http://www.cdc.gov/vaccines/recs/acip/downloads/preg-principles05-01-08.pdf).
l. Encourage sexual partners to receive HIV testing and, if infected, to seek counseling and appropriate HIV care.

Table 4: Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 1 of 2)

Data on drug interactions between antiretroviral (ARV) agents and hormonal contraceptives primarily come from drug labels and the clinical implications have not been well studied. The magnitude of changes in contraceptive drug levels that may reduce contraceptive efficacy or increase contraceptive-associated adverse effects is unknown. Hormonal contraceptives can be used with antiretroviral therapy (ART) in women without other contraindications. Additional or alternative methods of contraception may be recommended when drug interactions are known.

Antiretroviral Drug	Effect on Drug Levels	Dosing Recommendation/ Clinical Comment
Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)		
Efavirenz (EFV)	Oral ethinyl estradiol/norgestimate: No effect on ethinyl estradiol concentrations; ↓ active metabolites of norgestimate (levonorgestrel AUC ↓83%; norelgestromin AUC ↓64%)	A reliable method of barrier contraception must be used in addition to hormonal contraceptives. Efavirenz had no effect on ethinyl estradiol concentrations, but progestin levels (norelgestromin and levonorgestrel) were markedly decreased. No effect of ethinyl estradiol/norgestimate on efavirenz plasma concentrations was observed.
	Implant: ↓ etonogestrel	A reliable method of barrier contraception must be used in addition to hormonal contraceptives. The interaction between etonogestrel and efavirenz has not been studied. Decreased exposure of etonogestrel may be expected. In postmarketing reports, contraceptive failure with etonogestrel has been noted in efavirenz-exposed patients.
	Levonorgestrel AUC ↓58%	Effectiveness of emergency postcoital contraception may be diminished.
Etravirine (ETR)	Ethinyl estradiol AUC ↑22% Norethindrone: no significant effect	No dosage adjustment needed.
Nevirapine (NVP)	Ethinyl estradiol AUC ↓20% Norethindrone AUC ↓19%	Additional methods recommended; alternative methods can be considered.
	DMPA: no significant change	No dosage adjustment needed.
Rilpivirine (RPV)	Ethinyl estradiol AUC ↑14% Norethindrone: no significant change	No dose adjustment needed.
Ritonavir (RTV)-boosted Protease Inhibitor (PI)		
Atazanavir/ritonavir (ATV/r)	↓ Ethinyl estradiol ↑ Norgestimate	Oral contraceptive should contain ≥35 mcg ethinyl estradiol. Oral contraceptives containing progestins other than norethindrone or norgestimate have not been studied.

Table 4: Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 2 of 2)

Antiretroviral Drug	Effect on Drug Levels	Dosing Recommendation/ Clinical Comment
Darunavir/ritonavir (DRV/r)	Ethinyl estradiol AUC ↓44% Norethindrone AUC ↓14%	Additional methods recommended; alternative methods can be considered.
Fosamprenavir/ritonavir (FPV/r)	Ethinyl estradiol AUC ↓37% Norethindrone AUC ↓34%	Alternative methods of nonhormonal contraception are recommended.
Lopinavir/ritonavir (LPV/r)	Ethinyl estradiol AUC ↓42% Norethindrone AUC ↓17%	Additional methods recommended; alternative methods can be considered.
Saquinavir/ritonavir (SQV/r)	↓Ethinyl estradiol	Additional methods recommended; alternative methods can be considered.
Tipranavir/ritonavir (TPV/r)	Ethinyl estradiol AUC ↓48% Norethindrone: no significant change	Additional methods recommended; alternative methods can be considered.
PI without RTV		
Atazanavir (ATV)	Ethinyl estradiol AUC ↑48% Norethindrone AUC ↑110%	Oral contraceptive should contain ≤30 mcg of ethinyl estradiol or use alternative method. Oral contraceptives containing <25 mcg ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.
Fosamprenavir (FPV)	Amprenavir: ↑ Ethinyl estradiol and ↑ norethindrone Fosamprenavir with ethinyl estradiol/norethindrone: ↓ Amprenavir (AUC 22%, C_{min} 20%)	Use alternative method. Use of fosamprenavir alone with ethinyl estradiol/norethindrone may lead to loss of virologic response.
Indinavir (IDV)	Ethinyl estradiol AUC ↑25% Norethindrone AUC ↑26%	No dose adjustment needed.
Nelfinavir (NFV)	Ethinyl estradiol AUC ↓47% Norethindrone AUC ↓18%	Additional methods recommended; alternative methods may be considered.
CCR5 Antagonist		
Maraviroc (MVC)	No significant effect on ethinyl estradiol or levonorgestrel	No dose adjustment needed.
Integrase Inhibitor		
Raltegravir (RAL)	No significant effect	No dose adjustment needed.

Key to Abbreviations: AUC = area under the curve, C_{min} = minimum plasma concentration, DMPA = depot medroxyprogesterone acetate

Table 4 derived from: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Tables 15a, 15b, and 15d. Accessed June 7, 2012.

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