

PRECONCEPTION CARE FOR HIV-INFECTED WOMEN

I. INTRODUCTION

Preconception care is patient education, evaluation, and management aimed to 1) prevent unplanned pregnancies, and 2) decrease the risk of adverse health effects for the woman, fetus, and neonate by optimizing the woman's health and knowledge before planning and conceiving a pregnancy.¹

Because many HIV-infected women report unplanned pregnancies,² all HIV-infected women of childbearing potential (from adolescence through perimenopause) should receive preconception care and counseling, regardless of pregnancy intentions. Preconception counseling provides an opportunity for clinicians to discuss the woman's current health status, ARV regimen, adherence, current and future treatment options, and strategies to either avoid an unintended pregnancy or maximize the chances of a healthy pregnancy outcome.³

II. PRINCIPLES OF PRECONCEPTION CARE FOR HIV-INFECTED WOMEN OF CHILDBEARING POTENTIAL

RECOMMENDATIONS:

Clinicians should provide preconception counseling for all women of childbearing potential during the first few visits after the diagnosis of HIV infection and at least annually thereafter (see Table 1). The patient also should receive preconception counseling after becoming involved with a new sexual partner. The counseling should include the following: (AIII)

- **Contraception**
- **Prevention of HIV/STI transmission**
- **Importance of maintaining optimal health**

Clinicians should: (AIII)

- **Be nondirective and respectful of patients' autonomy in decision-making when counseling HIV-infected women about reproductive issues**
- **Address psychosocial issues that may affect pregnancy, pregnancy outcome, and postpartum care for the infant and make referrals as necessary**
- **Document the patient's preconception counseling and, with permission from the patient, communicate that information to other providers as necessary**

When discussing preconception care, clinicians should stress the importance of optimal maternal health before conception. These discussions should be nonjudgmental, reassuring, and respectful of patients' autonomy in reproductive decision-making. The use of open-ended questions, such as, *What are your thoughts about having children now that you are HIV-infected?* may facilitate an open discussion and provide an opportunity for preconception counseling.

TABLE 1
ELEMENTS OF PRECONCEPTION CARE FOR ALL
HIV-INFECTED WOMEN OF CHILDBEARING POTENTIAL

Pre-pregnancy Considerations^a

Prevention

- Prevention of HIV sexual transmission
- Prevention of acquisition or transmission of other sexually transmitted infections (STIs)
- Prevention of re-exposure to HIV

Optimizing health/Reducing risk

- Sustained clinical and immunologic stability
- Establishing/maintaining routine gynecologic care
- Folic acid supplementation before and during pregnancy
- Smoking and alcohol cessation; drug and alcohol rehabilitation when necessary^b
- Avoidance of medications known to be harmful to the fetus (see Section III.C.)
- Administration of varicella, rubella, hepatitis A, hepatitis B, and influenza vaccines before pregnancy^c
- Prophylaxis for opportunistic infections when indicated, and management of comorbidities^d
- Maintaining good oral health prior to pregnancy

Contraception

- Routine contraception
- Emergency contraception and termination of pregnancies
- Misconceptions about HIV and contraception use
- Effect of ARV drugs on hormonal contraception (see Appendix A)

^a These issues should be discussed in the first few visits after HIV diagnosis and at least annually thereafter.

^b For opioid-dependent pregnant women, methadone maintenance treatment is effective therapy, does not adversely affect fetal or post-natal development, and is preferred to detoxification.

^c Also see [Prevention of Secondary Disease: Preventive Medicine – Immunizations](#).

^d See [Prevention of Secondary Disease: Preventive Medicine – Opportunistic Infections](#).

A. Prevention of HIV Transmission, Superinfection, and Other STIs

RECOMMENDATION:

Clinicians should emphasize to all HIV-infected women the importance of barrier protection to prevent transmission of HIV/STIs to partners and acquisition of superinfection from partners, regardless of whether the woman is pregnant or using another form of contraception. (AI)

Preconception care should include a review of safer-sex practices to prevent the sexual transmission of the following:

- HIV to a non-infected partner,
- Re-exposure to HIV (acquisition of new strains) to/from an infected partner, and
- Prevention of other STIs to/from a partner

The risk of transmission of HIV is increased in the setting of STIs. The importance of correct and consistent use of barrier protection during vaginal, rectal, or oral sex for the prevention of both HIV and STI transmission should be stressed. Patients should be informed that because condoms do not cover all exposed areas, they are more effective in preventing infections transmitted by fluids from mucosal surfaces than in preventing infections transmitted by skin-to-skin contact.

B. Optimizing Health/Reducing Risk

RECOMMENDATION:

Clinicians should:

- **Educate all HIV-infected women of childbearing potential about the importance of maintaining optimal health (AI)**
- **Consider the possibility of pregnancy in all women of childbearing potential when prescribing medications that are known to be harmful to the fetus (AI)**
- **Obtain a comprehensive medical history, including previous pregnancies, routine laboratory tests, and perform a physical examination (see [Primary Care Approach to the HIV-Infected Patient](#)) (AI)**
- **Refer to oral health care prior to pregnancy if the patient does not routinely receive oral health care (AII)**
- **Perform mental health and substance use assessments and refer for treatment when indicated (AI)**

Treatment goals for *all* HIV-infected patients are optimization of health, clinical stability, and improved quality of life. Because of the high rate of unintended pregnancies, the benefits of optimal maternal health and pregnancy outcome should be discussed with all HIV-infected women of childbearing potential. The following should be included in the discussion: sustained clinical and immunologic stability; routine gynecologic care, including Pap test; smoking and alcohol cessation; drug and alcohol rehabilitation, when necessary; and folic acid supplementation, both before and during pregnancy.

The importance of good oral health practices should also be discussed. Poor maternal oral health, such as periodontal disease, prior to pregnancy has been shown to result in pre-term birth⁴; however, periodontal therapy during pregnancy has not been shown to reduce the rate of prematurity.⁵ Clinicians should refer HIV-infected women of childbearing potential for oral health care prior to pregnancy if the patient does not already receive routine oral health care.

C. Contraception

RECOMMENDATIONS:

Clinicians should educate all HIV-infected women of childbearing potential about the following: (AIII)

- **Contraceptive options and misconceptions about their use**
- **Interactions among ARV medications and oral contraceptive pills**
- **Potential interactions with other hormonal contraception**

Clinicians should refer women who request a form of contraception that is outside the expertise of their provider, such as IUDs, to an experienced clinician who can provide the desired contraception. (AII)

Data from the Women's Interagency HIV Study (WIHS) show that highly effective contraception is underused by HIV-infected women.⁶ Clinicians should discuss contraceptive options for both the prevention of unintended pregnancies and the spacing and timing of intended pregnancies. All HIV-infected women of childbearing potential should be counseled regarding dual-protection contraception (i.e., condom and another form of contraception); emergency contraception; misunderstandings about contraception use and HIV infection (e.g., some patients may believe that hormonal contraceptives cannot be used while taking ARV medications); and the importance of planning a pregnancy. Women who request a form of contraception that is outside the expertise of their provider, such as IUDs, should be referred to an experienced clinician who can provide the desired contraception.

Knowledge of available contraceptive options and the effect of ARV drugs on each option enables patients to make informed decisions that result in preventing pregnancy or optimal timing for pregnancy. Certain ARV medications, such as ritonavir, nelfinavir, and lopinavir/ritonavir, can alter the concentration of oral contraceptive pills, thereby reducing the efficacy of the contraceptive. See Appendix A and *Contraception for HIV-Infected Women* for more information.

D. Termination of Pregnancy

RECOMMENDATION:

Clinicians should be aware of facilities/providers offering safe pregnancy termination services in their area for pregnant HIV-infected women who wish to terminate a pregnancy. (AIII)

Some pregnant women, regardless of HIV status, may not want to carry the pregnancy to term. Clinicians should be aware of facilities/clinicians offering safe termination services in their area and refer women who request such services.

III. ELEMENTS OF PRECONCEPTION CARE FOR HIV-INFECTED WOMEN CONSIDERING PREGNANCY

RECOMMENDATION:

For HIV-infected women considering pregnancy, preconception care should include discussion of the elements in Tables 1-3.

TABLE 2 ELEMENTS OF PRECONCEPTION CARE COUNSELING FOR HIV-INFECTED WOMEN CONSIDERING PREGNANCY
<p>Pregnancy Considerations</p> <p>Planning and Timing of Pregnancy</p> <ul style="list-style-type: none"> • Optimization of woman’s current health status • Partner’s health status • Social support before, during, and after pregnancy from partner, family, and/or friends <p>Effect of HIV on Pregnancy</p> <ul style="list-style-type: none"> • Importance of adherence to therapy • Effect of HIV viral load on MTCT <p>Effect of HIV-Related Drugs on Pregnancy</p> <ul style="list-style-type: none"> • Drugs to avoid/use with caution (see Table 3) <p>Reproductive Options^a</p> <ul style="list-style-type: none"> • Knowledge of available reproductive options and the facilities offering reproductive services • Risk of transmitting HIV infection to a serodiscordant partner, or risk of re-exposure to a seroconcordant partner during conception attempts <p>Effect of Pregnancy on HIV</p> <ul style="list-style-type: none"> • No evidence that pregnancy changes the course of HIV in infected women <p>Routine Prenatal Care</p> <ul style="list-style-type: none"> • Optimizing health, including smoking and alcohol cessation, and drug and alcohol rehabilitation when necessary^b • Early identification of pregnancy • Early collaboration with experienced HIV provider • Early routine prenatal care <p>Perinatal HIV Transmission</p> <ul style="list-style-type: none"> • Risk of perinatal HIV transmission • ARV prophylaxis for mother and infant • Mode of delivery • Avoidance of breastfeeding • ARV prophylaxis for HIV-exposed infants and follow-up pediatric care <p>Guardianship Issues</p> <ul style="list-style-type: none"> • Possible guardianship considerations
<p>^a Studies on pre-exposure prophylaxis (PrEP) are currently underway. Until more data are available, a recommendation cannot be made.</p> <p>^b For opioid-dependent pregnant women, methadone maintenance treatment is effective, does not adversely affect fetal or post-natal development, and is preferred to detoxification.</p>

A. Planning and Timing of Pregnancy

The best time for an HIV-infected woman to become pregnant is when her viral load is undetectable (<50 copies/mL). If viral load suppression is not achievable, the woman's health should be optimized before conception and maximal suppression with a stable viral load should be the goal (see Section III. F. *Routine Prenatal Care*).

Ideally, pregnancy should occur at a time when the woman has social support from her partner, family, and/or friends. A strong social support network may improve adherence to ARV prophylactic regimens,^{7,8} reduce the stigma of being infected, and decrease stress after the baby is born.⁹

B. Effect of HIV on Pregnancy

A clear association between HIV infection and poor pregnancy outcome has not been demonstrated.¹⁰ However, an elevated (>1000 copies/mL) maternal plasma viral load level significantly increases the risk for MTCT.

C. Medications Commonly Prescribed in HIV-Infected Pregnant Women

RECOMMENDATIONS:

Clinicians should: (All)

- **Conduct a medication history at each visit that includes all prescription and over-the-counter medications, recreational drugs, and herbal/alternative therapies (see [HIV Drug-Drug Interactions](#))**
- **Review current medication prescribing information, including package inserts and the antiretroviral pregnancy registry, before prescribing any medication**
- **Consider the possibility for pregnancy in all women of childbearing potential when prescribing medications that are known to be harmful to the fetus. Selection of drugs for the ARV regimen should be guided by available data.**
- **Involve the patient when planning her treatment regimen**
- **Discuss the safety of ARV use during pregnancy**

Clinicians should advise HIV-infected women considering pregnancy, or likely to become pregnant, about the following HIV-related medications: (All)

- **Contraindicated medications**
 - **Efavirenz and all combination pills containing efavirenz are contraindicated during the first trimester of pregnancy; an alternative regimen should be used**
 - **Ribavirin (patients and/or partners being treated for HCV)**
- **If a woman is receiving efavirenz and pregnancy is discovered during the second or third trimester, an alternative regimen should be offered, but the efavirenz-containing regimen can be continued if the benefits outweigh the risks**
- **Efavirenz should be avoided in women of childbearing potential who are not using effective contraception if other treatment options are available**
- **Stavudine/didanosine in combination should be avoided and only used when no other combinations are feasible (see *Management of HIV-infected Pregnant Women Including Prevention of Perinatal Transmission* for more information)**
- **Pegylated interferon (used in combination with ribavirin for the treatment of HCV)**

Preconception care includes the discussion of potential harmful effects of ARV agents and regimens to both the woman and the fetus, especially during the first trimester (see Table 3). Clinicians should address concerns and possible misconceptions about any medication effects, particularly ARVs. Women should be involved in making decisions regarding the treatment regimen and whether to continue or modify their current ARV regimen to minimize pregnancy-related nausea and first trimester fetal exposure to potentially harmful drugs.

When other effective agents are available, efavirenz should not be prescribed to women of childbearing potential who are not using effective contraception. Treatment with efavirenz should be avoided during the first trimester because of the risk of neural tube defects in the infant.¹¹ For women receiving efavirenz or an efavirenz-containing regimen whose pregnancy is discovered in the second or third trimester, the ARV regimen should be reviewed and an alternate regimen offered. However, if HIV is fully suppressed, the current regimen is well tolerated, and other regimens have not been successful, the benefits of continuing the efavirenz-containing regimen may outweigh the risks.

Ribavirin is an absolute contraindication during pregnancy. Because many HIV-infected individuals are co-infected with hepatitis C, the possibility of pregnancy in women receiving ribavirin needs to be considered. Because ribavirin is a nucleoside analogue that may potentially impact fetal DNA, it should only be administered after a negative pregnancy test. If a woman or her partner is receiving ribavirin, dual contraception should be used for the duration of ribavirin therapy and for 6 months after the cessation of ribavirin therapy. A monthly pregnancy test should be performed during ribavirin therapy and for 6 months after the cessation of ribavirin therapy.

Amprenavir oral solution, which is no longer available because of the availability of fosamprenavir, contained a high level of excipient propylene glycol and was therefore contraindicated during pregnancy. Although fosamprenavir oral solution contains a lesser amount of propylene glycol, at this time there is insufficient data to recommend its use during pregnancy.

TABLE 3
HIV-RELATED MEDICATIONS TO AVOID OR
USE WITH CAUTION DURING PREGNANCY

Medication^{a,b}	Concern/Recommendation
Efavirenz (EFV) FDA Pregnancy Category D	<ul style="list-style-type: none"> • EFV is contraindicated during the first trimester due to teratogenicity. Significant congenital CNS abnormalities have been seen in animal primates and in humans • Do not give to women of childbearing potential if other treatment options are available. If pregnancy is discovered during the second or third trimester, an alternative regimen should be offered but EFV can be continued if the benefits outweigh the risks
Stavudine/Didanosine (d4T/ddI) FDA Pregnancy Categories Stavudine – Category C Didanosine – Category B	<ul style="list-style-type: none"> • Should be avoided during pregnancy. If no alternative combinations are feasible, use with caution. • Fatal lactic acidosis in pregnant or postpartum women has been reported • Several less severe cases of pancreatitis with or without lactic acidosis and hepatic failure have also been reported in pregnant women • Monitor hepatic and renal function monthly if pregnancy occurs while taking stavudine/didanosine
Ribavirin (non-ARV agent) FDA Pregnancy Category X	<ul style="list-style-type: none"> • Ribavirin is an absolute contraindication during pregnancy • Effective contraception should be used during ribavirin therapy and for 6 months after cessation of therapy • Fetal abnormalities demonstrated in animal and human studies • Its function as a nucleoside analogue may impact fetal DNA
Pegylated interferon (non-ARV agent) FDA Pregnancy Category C	<ul style="list-style-type: none"> • Abortifacient effects in rhesus monkeys • Birth defects and fetal death with combination ribavirin therapy

Adapted from Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy. Updated May 24, 2010. Also available at: http://aidsinfo.nih.gov/contentfiles/PerinatalGLSafetyTox_Sup.pdf

^a Hydroxyurea is no longer recommended as part of an ARV regimen for the management of HIV infection and should be avoided during pregnancy.

^b Amprenavir oral solution contained a high level of excipient propylene glycol and was therefore contraindicated during pregnancy. It is no longer available because of the availability of fosamprenavir oral solution, which contains a lesser amount of propylene glycol; however, at this time there is insufficient data to recommend fosamprenavir use during pregnancy.

Because many pregnancies are unplanned, clinicians should carefully consider the potential for pregnancy in all women of childbearing potential when prescribing all [medications](#) that are known to be harmful to the fetus. Current package insert prescribing information and the [antiretroviral pregnancy registry](#) should be consulted before selecting medications. For more information about drugs to avoid during pregnancy, see *Management of HIV-Infected Pregnant Women Including Prevention of Perinatal Transmission*.

D. Reproductive Options

RECOMMENDATIONS:

Clinicians should: (AIII)

- **Develop a list of resources for reproductive options for HIV-infected women/couples**
- **Facilitate prompt referrals to clinical venues offering assisted reproductive services for couples who wish to use these services**
- **Educate HIV-infected women and HIV-serodiscordant and -seroconcordant couples about available reproductive options to help them choose the most appropriate method for them**

HIV-infected women have the same reproductive desires as non-HIV-infected women: some want to have children and some do not. For HIV-infected women who want children, weighing the desire to have children against the risks of partner-to-partner transmission or re-exposure to HIV and MTCT presents a challenge to both the woman and her clinician. Discussing reproductive options available to HIV-serodiscordant and -seroconcordant couples may help couples make more informed choices to reduce sexual transmission and to improve pregnancy outcome.

Many new assisted reproductive technologies are available for HIV-infected and serodiscordant couples, such as sperm washing and intrauterine insemination. These technologies may provide safer but not risk-free opportunities for planning a pregnancy for serodiscordant couples.¹²⁻¹⁵ The availability of these reproductive services are generally restricted to for-profit clinical venues. The utility of these technologies in HIV-infected couples should be discussed, including the varying success rates and costs. Success rates are not the same for each method. The costs of assisted reproductive technologies are expensive and are not covered or only partially covered by Medicaid (see *Assisted Reproduction for HIV-infected Women* for further information). Clinicians should be aware of available assisted reproduction services in New York State and nationwide to provide referral for HIV-infected couples seeking assisted reproduction. Area university research settings or high-volume HIV service clinics may be able to provide useful information about assisted reproduction.

PrEP

The use of pre-exposure prophylaxis (PrEP) has been shown to be effective in animal models; however, there are not enough available data on the effectiveness of PrEP in humans. Human clinical trials to assess the effectiveness of PrEP in serodiscordant couples are currently ongoing.¹⁶ Until more data are available, a recommendation cannot be made for the use of PrEP.

E. Effect of Pregnancy on HIV

Studies have not shown an association between pregnancy and disease progression of HIV infection. One study followed 331 women with known dates of seroconversion for 5½ years, during which time 69 women became pregnant. There were no differences in disease progression and morbidity between those who became pregnant and those who did not.¹⁷

F. Routine Prenatal Care

RECOMMENDATION:

Clinicians should educate HIV-infected women of childbearing potential about the importance of:

- **Optimal maternal health, including sustained clinical and immunologic stability and appropriate prophylaxis for opportunistic infections if indicated, before and during pregnancy (AI)**
- **Obtaining routine prenatal care early in pregnancy and the need to maintain regular obstetrical visits (AII)**

Coordination of care between clinicians can provide improved maternal and infant health outcomes. The primary care clinician, HIV treatment specialist, and obstetrical provider with expertise in HIV infection should collaborate to provide optimal patient care. If additional services are required, such as mental health or neonatal care, the primary care clinician should integrate and coordinate those services as well.

The benefits of optimal maternal health, including clinical and immunologic stability, on pregnancy outcome should be stressed to HIV-infected women of childbearing potential before and during pregnancy. Routine prenatal topics to incorporate into preconception counseling are the same as those discussed with non-HIV-infected women, such as the following:

- Importance of early identification of pregnancy
- Folic acid supplementation
- Smoking cessation;
- Avoidance of alcohol and drugs and the specific effects of alcohol and illicit drugs on the developing fetus
- Exercise
- Good nutrition
- Regular prenatal care

In addition, early collaboration with an experienced HIV provider will help ensure optimal benefits from ART if treatment is initiated.

Many resources have been developed for reviewing routine prenatal care topics in the general population, including the following:

- The March of Dimes: [Preconception Health & Healthcare](http://www.marchofdimes.com/professionals/preconception.asp), available at: <http://www.marchofdimes.com/professionals/preconception.asp>
- Centers for Disease Control and Prevention: [Recommendations to Improve Preconception Health and Health Care – United States](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5506a1.htm), available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr5506a1.htm
- Centers for Disease Control and Prevention: [Preconception Care Resources](http://www.cdc.gov/ncbddd/preconception/links.htm), available at: www.cdc.gov/ncbddd/preconception/links.htm

G. Perinatal HIV Transmission

RECOMMENDATIONS:

Clinicians should discuss the benefits of using combination ART for the prevention of MTCT with all pregnant women who are HIV infected. (AI)

Clinicians should recommend that pregnant women with viral loads >1000 copies/mL initiate combination ART. For women with viral loads <1000 copies/mL, the three-part ZDV regimen should be initiated, and combination ART should be offered. (AI)

Clinicians should educate patients about current approaches to reducing the risk of perinatal transmission of HIV. (AI)

The provider should discuss current HIV treatment recommendations with HIV-infected women of childbearing potential who are considering having children, including the following:

- Use of ART to both optimize maternal health and prevent MTCT
- Factors influencing transmission, including mode of delivery, duration of membrane rupture, maternal plasma viral load and CD4 count, maternal co-infections, invasive obstetrical procedures, breastfeeding
- Newborn management and ARV prophylaxis for HIV-exposed infants

For more guidance on the care of HIV-infected pregnant women including labor and delivery issues, see *Management of HIV-Infected Pregnant Women Including Prevention of Perinatal HIV Transmission*.

H. Guardianship Issues

RECOMMENDATION:

Clinicians should discuss possible guardianship issues in a caring and supportive manner with HIV-infected women who express a desire to have children. (AIII)

Life expectancy and quality of life have been improved for most HIV-infected persons since the advent of combination ART, but HIV-infected women should still address and plan for the possibility of their children surviving without them. A supportive environment from both family and clinician can be positive reinforcement for an HIV-infected woman once she has decided to have children, especially if guardianship becomes an issue.

The New York State Department of Health AIDS Institute offers supportive and legal services through the [Families in Transition Initiative](#), which assists families affected by HIV/AIDS in planning for the care and custody of children during the illness and after the death of a parent. For more information about the Initiative, contact the Family and Youth Services Section, Bureau of HIV Ambulatory Care Services, at 518-473-8427.

Another AIDS Institute support service, [Family-Centered HIV Health Care Services Initiative](#), helps fund community-based programs in New York City to provide assistance and supportive services to women living with HIV and their families. More information about this service can be obtained by calling 518-473-3435.

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APPENDIX A

Updated January 2010

TABLE 1 INTERACTIONS BETWEEN ETHINYL ESTRADIOL AND ARVs AND OTHER DRUGS		
<i>Antiretrovirals</i>		
ARV	Effect on EE	Recommendation
<i>NNRTIs</i>		
Efavirenz (EFV)	↑ EE 37%	Consider using alternative form of contraception. Use lowest dose of hormonal contraception and monitor for adverse contraceptive reactions. Consider an alternative ARV in patients not adherent to an oral contraceptive regimen
Etravirine (ETR)	↑ EE AUC 22% ↓ Norethindrone AUC 5%	No dose adjustment needed
Nevirapine (NVP)	↓ EE ~ 20% ↓ Norethindrone	Consider using alternative or additional forms of contraception
<i>PIs</i>		
Atazanavir (ATV)	↑ EE AUC 48% ↑ Norethindrone AUC 110%	<ul style="list-style-type: none"> • Co-administered with ATV without RTV, OC should contain no more than 30 mcg EE. May ↑ progesterone exposure substantially
Atazanavir/ritonavir (ATV/r)	↓ EE AUC 19% ↑ Norethindrone metabolite by 85%	<ul style="list-style-type: none"> • Co-administered with ATV/r, OC should contain at least 35 mcg EE • If other OCs are used, use alternative method of nonhormonal contraceptive
Darunavir/r (DRV/r)	↓ EE AUC 44% ↓ Norethindrone AUC 14%	Consider using alternative or additional forms of contraception.
Fosamprenavir (FPV)	↑ EE and Norethindrone levels APV levels ↓ 20%	Do not co-administer. Consider using alternative form of contraception
Indinavir (IDV)	↑ Norethindrone 26% ↑ EE 25%	No dosage adjustment necessary
Lopinavir/ritonavir (LPV/r)	↓ EE 42% ↓ Norethindrone AUC 17%	Consider using alternative or additional forms of contraception
Nelfinavir (NFV)	↓ EE 47% ↓ Norethindrone 18%	Consider using alternative or additional forms of contraception
Ritonavir (RTV)	↓ EE 40%	Consider using alternative or additional forms of contraception
Saquinavir/r (SQV/r)	↓ EE	Consider using alternative or additional forms of contraception

Tipranavir/r (TPV/r)	↓ EE 48% No change in norethindrone AUC	Consider using alternative or additional forms of contraception
CCR5 blocker		
Maraviroc (MVC)	No significant change in EE or levonorgestrel	Use standard dose
Other Drugs		
Drug	Effect on EE	Recommendation
Barbiturates	↓ EE	Consider using alternative or additional forms of contraception
Rifampin, rifabutin, griseofulvin, phenytoin, ethotoin, mephenytoin, phenobarbital, primidone, carbamazepine, ethosuximide	↓ EE	Avoid co-administration or use alternative or additional forms of contraception with close monitoring. Use highest dose of hormonal contraception
Ciprofloxacin (fluoroquinolones), penicillins, and cephalosporins	EE may be decreased	Use additional forms of contraception with close monitoring
<p>CHC, combined hormonal contraception; OC, oral contraceptive. <i>Note:</i> Medroxyprogesterone acetate can be safely co-administered with EFV, NVP, NFV without dose adjustments.</p>		