

Preconception Counseling and Care for HIV-Infected Women of Childbearing Age (Last updated October 26, 2016; last reviewed October 26, 2016)

Panel's Recommendations

- Discuss childbearing intentions with all women of childbearing age on an ongoing basis throughout the course of their care **(AIII)**.
- Provide 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, tobacco, and other drugs of abuse; if elimination is not feasible, appropriate treatment (e.g., methadone) should be provided **(AII)**.
- All HIV-infected women contemplating pregnancy should be receiving antiretroviral therapy (ART), and have a plasma viral load below the limit of detection prior to conception **(AII)**.
- When selecting or evaluating ART for HIV-infected women of childbearing age, consider a regimen's effectiveness, a woman's hepatitis B status, teratogenic potential of the drugs in the ART regimen, and possible adverse outcomes for the mother and fetus **(AII)**.
- HIV infection does not preclude the use of any contraceptive method **(AII)**. However, drug-drug interactions between hormonal contraceptives and ART should be taken into account.

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

Overview

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 outcomes, 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 something that occurs in 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,²⁻⁸ 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.⁹⁻¹² Health care providers who routinely care for HIV-infected 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.¹³⁻¹⁶ Issues that impact pregnancy should be addressed before conception during their routine medical care for HIV disease because many HIV-infected women are aware of their HIV status before becoming pregnant. In addition to the principles outlined by the CDC Preconception Care Work Group,¹⁷ the following components of preconception counseling and care are specifically recommended for HIV-infected women. Health care providers should:

- 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.^{18,19}

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

- Counsel on safer sexual practices (including condoms) that prevent HIV transmission to sexual partners, protect women from acquiring sexually transmitted diseases, and reduce the potential to acquire resistant strains of HIV.
- Counsel on eliminating alcohol, tobacco, and other drugs of abuse or appropriately treat when elimination is not feasible.
- Counsel women contemplating pregnancy to take a daily multivitamin that contains 400 mcg of folic acid to help prevent certain birth defects.
- Educate and counsel women about risk factors for perinatal transmission of HIV, strategies to reduce those risks, potential effects of HIV or of antiretroviral (ARV) drugs given during pregnancy 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 to their infants and the availability of safe and sustainable infant feeding alternatives.
- When prescribing antiretroviral therapy (ART) to women of childbearing age, consider the regimen's effectiveness, an individual's hepatitis B (HBV) status, the potential for teratogenicity, and possible adverse outcomes for mother and fetus.²⁰⁻²²
- Use the preconception period in women who are contemplating pregnancy to modify their ART regimen to optimize virologic suppression and minimize potential adverse effects (See Table 6).
- Make a primary treatment goal for women who are on ART and who are planning a pregnancy attainment of sustained suppression of plasma viral load below the limit of detection prior to conception for the health of the woman and to decrease the risk of perinatal transmission and of sexual transmission to an uninfected partner.
- Evaluate and manage therapy-associated side effects (e.g., hyperglycemia, anemia, hepatotoxicity) that may adversely impact maternal-fetal health outcomes.
- Administer all vaccines as indicated (see <http://www.cdc.gov/vaccines/acip/committee/guidance/rec-vac-preg.html> and 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host) including against influenza, pneumococcus, hepatitis B, and tetanus. All HIV-infected women should also receive Tdap vaccination during each pregnancy.
- All women, including those with HIV infection, should receive Tdap vaccination during each pregnancy.
- Encourage sexual partners to receive counseling and HIV testing and, if infected, to seek HIV care. If partners of HIV-infected women are uninfected, counsel about the potential benefits and risks of starting oral pre-exposure prophylaxis to prevent HIV acquisition.
- Offer all women who do not desire pregnancy effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. HIV-infected women can use all available contraceptive methods, including hormonal contraception (e.g., pill, patch, ring, injection, implant) and intrauterine devices (IUDs).²³ Providers should be aware of potential interactions between ARV drugs and hormonal contraceptives that could lower contraceptive efficacy (see Table 3 below).
- Offer emergency contraception as appropriate, including emergency contraceptive pills and the copper IUD. Concerns about drug interactions between ARV drugs and emergency contraceptive pills containing estrogen and a progestin, or containing levonorgestrel only, may be similar to concerns when those formulations are used for regular contraception.²⁴ There are no data on potential interactions between ARV drugs and ulipristal acetate, a progesterone receptor modulator; however, ulipristal acetate is

predominantly metabolized by CYP3A4, so interactions can be expected.

- Optimize the woman's health prior to conception (e.g., ensure appropriate folate intake, test for sexually transmitted infections and treat as indicated, consider the teratogenic potential of **all** prescribed medications, consider the option of switching to safer medications).

A World Health Organization expert group reviewed all available evidence regarding hormonal contraception and HIV transmission to an uninfected partner and recommended that women living with HIV continue to use all existing hormonal contraceptive methods without restriction.²⁵ However, drug-drug interactions between hormonal contraceptives and ART should be taken into account (see [Table 3](#)).

Data on drug interactions between ARV agents and hormonal contraceptives primarily come from drug labels and limited studies.^{24,26-41} Newer data provide some understanding as to the magnitude of changes in contraceptive drug levels that may reduce contraceptive efficacy. In a study of 570 HIV-infected women in Swaziland using Jadelle implants, none of the women on nevirapine or lopinavir/ritonavir-based regimens (n = 208 and 13, respectively) became pregnant, whereas 15 women on efavirenz (n = 121; 12.4%) became pregnant.³⁷ Scarsi et al reported on 3 groups of HIV-infected Ugandan women (not on ART [17 women], nevirapine-based ART [20 women], and efavirenz-based ART [20 women]) who had levonorgestrel implants placed, and had levonorgestrel pharmacokinetic (PK) levels assessed at 1, 4, 12, 36, and 48 weeks post insertion. The geometric mean ratio of efavirenz in ART-naive patients was 0.53 at 36 weeks and 0.43 at 48 weeks. Three pregnancies (3/20, 15%) occurred in the efavirenz group between weeks 36 and 48, whereas no pregnancies occurred in the ART-naive or nevirapine groups.⁴¹ Hormonal contraceptives can be used with ART in women without other contraindications. Additional or alternative methods of contraception may be recommended when drug interactions are known. For women using ritonavir-boosted protease inhibitors who are on combination hormonal contraceptives (e.g., pills, patches, rings) or progestin-only pills, use of an alternative or additional method of contraception **can be considered since the area under the curve of hormones may be decreased (see Table 3)**. Implants generally can be used, but providers can consider use of an alternative method or recommend the additional use of a reliable barrier method **with efavirenz-based regimens**.^{37,42,43} Depot medroxyprogesterone acetate (DMPA) can be used without restriction because of its relatively higher dose and limited studies that have shown no significant interaction between DMPA and ARV drugs.^{27,29,39,44}

Because no high-quality, definitive studies exist on pregnancy rates among women on different hormonal contraceptives and ARV drugs, the dosing recommendations in Table 3 are based on consensus expert opinion. Whenever possible, the recommendations are based on available data regarding PK interactions between ARV drugs and combined hormonal methods, DMPA, and etonogestrel implants. The smallest decreases in PK for which an alternative method was recommended were 14% in norethindrone (with darunavir/ritonavir) and 19% in ethinyl estradiol (with atazanavir/ritonavir). For women using atazanavir without ritonavir boosting (ethinyl estradiol increase 48%, norethindrone increase 110%), the Panel recommends use of oral contraceptives containing ≤ 30 μg ethinyl estradiol. The Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission did not recommend any change in ethinyl estradiol dose for etravirine (ethinyl estradiol increase 22%), rilpivirine (ethinyl estradiol increase 14%), or indinavir (ethinyl estradiol increase 25%, norethindrone increase 26%).

Note: All recommendations in the following table are based on consensus expert opinion. More details can be found in the CDC's [U.S. Medical Eligibility Criteria for Contraceptive Use](#), 2016.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 1 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/Clinical Comment for COC/P/R	Dosing Recommendation/Clinical Comment POPs	Dosing Recommendation/Clinical Comment for DMPA ^a	Dosing Recommendation/Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
NNRTIs							
EFV	<p>COC:</p> <ul style="list-style-type: none"> No effect on EE concentrations ↓ active metabolites of norgestimate LN AUC ↓ 83%; norelgestromin AUC ↓ 64%³⁰ Etonogestrel (in COC) C24 ↓ 61%³⁶ <p>DMPA:</p> <ul style="list-style-type: none"> No effect on DMPA levels^{27,29} <p>Etonogestrel Implant:</p> <ul style="list-style-type: none"> Etonogestrel AUC ↓ 63%⁴⁵ <p>LN Implant:</p> <ul style="list-style-type: none"> LN AUC ↓ 47%⁴¹ <ul style="list-style-type: none"> LN (emergency contraception) AUC ↓ 58%²⁴ <p>Changes in ARV Levels and/or Effects on HIV:</p> <p>COC:</p> <ul style="list-style-type: none"> No effect on EFV concentrations³⁰ EFV C12 ↓ 22%; was under therapeutic threshold in 3/16 subjects³⁶ <p>DMPA:</p> <ul style="list-style-type: none"> No effect on HIV disease progression^{27,46,47} No effect on EFV concentrations²⁷ <p>LN Implant:</p> <ul style="list-style-type: none"> No effect on HIV disease progression⁴¹ 	<p>COC:</p> <ul style="list-style-type: none"> Pregnancy rates no difference⁴⁸ Pregnancy rate higher (13%) in women using COCs and EFV than COCs alone^{43,49} Progesterone >3 (a surrogate for ovulation) in 3/16⁵⁰ No ovulations³⁰ <p>DMPA:</p> <ul style="list-style-type: none"> No increase in pregnancy^{27,43,47,48} Low progesterone^{27,29,47} <p>Etonogestrel Implant:</p> <ul style="list-style-type: none"> Pregnancy rate higher with EFV compared with no ART, but still lower than other hormonal methods⁴³ Presumptive ovulation in 5%⁴⁵ <p>LN Implant:</p> <ul style="list-style-type: none"> 12% pregnancy rate³⁷ 15% pregnancy rate⁴¹ Pregnancy rate higher with EFV compared with no ART, but still lower than other hormonal methods⁴³ No increase in pregnancy rate⁴⁸ 	Consider an alternative method or a reliable method of barrier contraception in addition to this method.	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	<p>For COCs, some studies suggest higher pregnancy rate and ovulation and decreased progestin levels. EFV may decrease, but clinical significance unclear.</p> <p>For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. Also no effect on HIV disease progression or EFV levels.</p> <p>For implants, some studies suggest higher pregnancy rate and decreased hormone levels.</p>

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 2 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA ^a	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
ETR	EE AUC ↑ 22% ⁵¹ <u>NE:</u> • No significant effect ⁵¹	<u>COC:</u> • No ovulations ⁵¹	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, one study found no ovulations and no significant change in progestin levels. No evidence on POCs.
NVP	EE AUC ↓ 29%; ⁵² EE AUC no change ⁵³ NE AUC ↓ 18% ⁵² Etonogestrel (in COC) AUC decreased 22% ³⁶ <u>DMPA:</u> • No significant change ²⁷ <u>LN Implant:</u> • LN AUC ↑ 35% ⁴¹ <u>Changes in ARV Levels and/or Effects on HIV</u> <u>COC:</u> • NVP no significant effect ^{50,52,54} <u>DMPA:</u> • No effect on HIV disease progression ^{27,46,47,55} <u>LN Implant:</u> • No effect on HIV disease progression ^{41,56}	<u>COC:</u> • No increase in pregnancy rate ^{43,48,49,57,58} • No ovulations ^{50,53,58} <u>DMPA:</u> • No increase in pregnancy rate ^{43,47,48,57} • No ovulations ²⁷ <u>Etonogestrel Implant:</u> • No increase in pregnancy rate ⁴³ <u>LN Implant:</u> • No increase in pregnancy rate ^{37,41,43,48,56}	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, evidence does not show effects on pregnancy rate or ovulations and demonstrated small decrease in progestin levels. Also no effect on NVP levels. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. Also no effect on HIV disease progression. For implants, evidence does not show effects on pregnancy rate or HIV disease progression.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 3 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA ^a	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
RPV	EE AUC ↑ 14% ³⁵ NE: • No significant change ³⁵ <u>Changes in ARV Levels and/or Effects on HIV</u> COC: • No change in RPV levels compared to historical controls ³⁵	<u>COC:</u> • No change in progesterone ³⁵	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, evidence does not show effects on ovulation or progestin levels. Also no change in RPV levels. No evidence on POCs.
RTV-Boosted PIs							
ATV/r	EE AUC ↓ 16% ⁵⁹ Norgestimate AUC ↑ 85% ⁵⁹ <u>POP:</u> • NE AUC ↑ 50% ⁶⁰		Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, increase in progestin levels but only one study. For POPs, increase in progestin levels but only 1 study. RTV inhibits CYP3A4 which may increase contraceptive hormone levels. However, some PI/r cause decreases in progestin levels, so there are theoretical concerns about contraceptive effectiveness.
DRV/r	EE AUC ↓ 44% ⁶¹ NE AUC ↓ 14% ⁶¹		Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, small decrease in progestin levels. No evidence on POCs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 4 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA ^a	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
FPV/r	EE AUC ↓ 37% ⁶² NE AUC ↓ 34% ⁶² FPV/r level: no change ⁶²		Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, decrease in progestin levels. No evidence on POCs.
LPV/r	EE AUC ↓ 55% ²⁸ NE AUC ↓ 17% <u>Patch:</u> • EE AUC ↓ 45% ²⁶ • Norelgestromin AUC ↑ 83% ²⁶ <u>DMPA:</u> • DMPA AUC ↑ 46% ³⁹ <u>Etonogestrel Implant:</u> • Etonogestrel AUC ↑ 52% ⁴⁵ <u>Changes in ARV Levels and/or Effects on HIV</u> <u>Patch:</u> • LPV/r level ↓ 19% ²⁶ <u>DMPA:</u> • No effect on HIV disease progression ³⁹ • LPV/r no change ³⁹	<u>COC:</u> • Increase pregnancy rate, but CIs overlap ⁴³ <u>Patch:</u> • No ovulations ²⁶ <u>DMPA:</u> • No pregnancies, no ovulations ³⁹ • Increased pregnancy rate, but CIs overlap ⁴³ <u>Etonogestrel Implant:</u> • No increase in pregnancy rate ⁴³ <u>LN Implant:</u> • No increase in pregnancy rate ^{37,43}	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, nonsignificant increase in pregnancy rate. Small decrease in progestin level. For patch, no ovulations and progestin levels increase. For DMPA, evidence shows no effect on pregnancy rate or ovulations and progestin levels increased. For implants, evidence shows no effect on pregnancy rate and progestin levels increased.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 5 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA ^a	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
SQV/r	<p>↓ EE⁶³</p> <p><u>Changes in ARV Levels and/or Effects on HIV:</u></p> <p><u>COC:</u></p> <ul style="list-style-type: none"> • SQV/r no change⁶⁴ 		Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	<p>No information on progestin levels for CHCs or POCs.</p> <p>RTV inhibits CYP3A4 which may increase contraceptive hormone levels. However, some PI/r cause decreases in progestin levels, so there are theoretical concerns about contraceptive effectiveness.</p>
TPV/r	<p>Ethinyl estradiol AUC ↓ 48%⁶⁵</p> <p><u>Norethindrone:</u></p> <ul style="list-style-type: none"> • No significant change⁶⁵ <p><u>Changes in ARV Levels and/or Effects on HIV</u></p> <ul style="list-style-type: none"> • TPV no change⁶⁵ 		Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	<p>For COCs, no significant change in progestin levels but only from product label.</p> <p>No evidence on POCs.</p> <p>RTV inhibits CYP3A4 which may increase contraceptive hormone levels. However, some PI/r cause decreases in progestin levels, so there are theoretical concerns about contraceptive effectiveness.</p>

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 6 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA ^a	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
PIs without RTV							
ATV	COC: EE AUC ↑ 48% ⁶⁶ NE AUC ↑ 110% ⁶⁶		Can consider an alternative method based on safety concerns (i.e., increased estrogen).	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, increased concentrations of estrogen and progestin, but only data available are from the product label. No evidence on POCs.
ATV/ COBI	Progestin and estrogen effects unknown ⁶⁷ COBI may increase steroid hormone (E/P) as COBI is a strong 3A4 inhibitor (inhibition could lead to ↑ concentrations of E and possibly P)		Can consider an alternative method based on safety concerns.	Can consider an alternative method based on safety concerns.	Can consider an alternative method based on safety concerns.	Can consider an alternative method based on safety concerns.	No evidence on POCs or COCs.
DRV/ COBI	Progestin and estrogen effects unknown ⁶⁸ COBI may increase steroid hormone (E/P) as COBI is a strong 3A4 inhibitor (inhibition could lead to ↑ concentrations of E and possibly P)		Can consider an alternative method based on safety concerns.	Can consider an alternative method based on safety concerns.	Can consider an alternative method based on safety concerns.	Can consider an alternative method based on safety concerns.	No evidence on POCs or COCs.
FPV	COC: APV: • EE AUC no change, C _{min} ↑ 32% • NE AUC ↑ 18%, C _{min} ↑ 45% ⁶² FPV with EE/Norethindrone: • ↓ APV (AUC 22%, C _{min} 20%) ⁶²		Use alternative contraceptive method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Use of fosamprenavir alone with ethinyl estradiol/norethindrone may lead to loss of virologic response. No evidence on POCs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 7 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/Clinical Comment for COC/P/R	Dosing Recommendation/Clinical Comment for POPs	Dosing Recommendation/Clinical Comment for DMPA ^a	Dosing Recommendation/Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
IDV	<p>COC:</p> <ul style="list-style-type: none"> • EE AUC ↑ 22% • NE AUC ↑ 26%⁶⁹ 	<p>COCs:</p> <ul style="list-style-type: none"> • No pregnancies among women taking IDV and COCs⁴⁹ 	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	<p>For COCs, small increases in EE and progestin, and one clinical study did not suggest any efficacy concerns.</p> <p>No evidence on POCs.</p>
NFV	<p>COC:</p> <ul style="list-style-type: none"> • EE AUC ↓ 47%; NE AUC ↓ 18%⁷⁰ <p>DMPA: No change²⁷</p> <p>NFV: AUC ↓ 18%</p>	<p>COCs:</p> <ul style="list-style-type: none"> • One small study suggested that women using COCs and NFV may have had higher pregnancy rates than those using COCs alone⁴⁹ <p>DMPA:</p> <ul style="list-style-type: none"> • No pregnancies, no ovulations^{27,47} • CD4 count/HIV RNA: no change^{27,47} 	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	<p>For COCs, small decrease in progestin and decrease in estrogen; one small clinical study suggests possible higher pregnancy rate with COC and NVP use.</p> <p>DMPA, PK, and clinical data demonstrate no change. However, NFV AUC slightly decreased.</p> <p>No evidence on POPs or implants.</p>
CCR5 Antagonist							
MVC	<p>COC:</p> <ul style="list-style-type: none"> • No significant effect on EE or LN⁷¹ 		No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	<p>For COCs, no change in EE or progestin. No clinical data.</p> <p>No evidence on POCs.</p>

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 8 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment for POPs	Dosing Recommendation/ Clinical Comment for DMPA ^a	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/Evidence for Recommendation
Integrase Inhibitors							
RAL	COC: • EE no change • Norgestimate AUC ↑ 14% ⁷²		No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, no change in EE and small increase in progestin. No clinical data. No evidence on POCs.
DTG	COC: • No significant effect on norgestimate or EE • DTG AUC no change ⁴⁰		No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	COCs, no change in EE or progestin. No clinical data No evidence on POCs.
EVG/ COBI	EVG/COBI/FTC/TDF COC: • Norgestimate AUC ↑ 126% EE AUC ↓ 25%		No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	When administered as the 4-drug regimen EVG/COBI/FTC/TDF, increases in P and small decrease in E was observed. No clinical data. No evidence on POCs.

^a Because the hormonal levels achieved with DMPA are substantially higher than are required for contraception, any small reduction in hormonal level due to ARVs is unlikely to reduce contraceptive effectiveness.

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; AUC = area under the curve; CHC = combination hormonal contraceptives; C_{min} = minimum plasma concentration; COBI = cobicistat; DMPA = depot medroxyprogesterone acetate; COC/P/R = combined oral contraceptives/patch/ring; DRV/r = darunavir/ritonavir; DTG = dolutegravir; e = estrogen; EE = ethinyl estradiol; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = IDV = indinavir; LN = levonorgestrel; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NVP = nevirapine; P = progestin; PI = protease inhibitor; PI/r = ritonavir boosted-protease inhibitor; POP = progesterone-only oral contraceptive pills; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV/r = saquinavir/ritonavir; TPV/r = tipranavir/ritonavir

Source: 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. Tables 15a, 15b, and 15d. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>. Accessed July 27, 2016.

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