Preconception Counseling and Care for Women of Childbearing Age Living with HIV (Last updated December 7, 2018; last reviewed December 7, 2018)

Panel's Recommendations
• Discuss reproductive desires 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 unplanned pregnancy **(AI)**.
• During preconception counseling, provide information on safe sex and encourage the elimination of alcohol, tobacco, and other drugs of abuse; if elimination is not feasible, clinicians should provide appropriate treatment (e.g., methadone or buprenorphine) or counsel patients on how to manage health risks (e.g., use of syringe services program) **(AII)**.
• All women living with HIV who are 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 women of childbearing age living with HIV, 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; however, drug-drug interactions between hormonal contraceptives and ART should be considered **(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*

Overview

The Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists (ACOG), 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 tailored 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; rather, it is a process of ongoing care and interventions integrated into primary care to address the needs of women during the different stages of reproductive life. It is important that comprehensive family planning and preconception care be integrated into routine health visits, because almost half of all pregnancies in the United States are unplanned.[2-10] 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.[11-14] Health care providers who routinely care for women of reproductive age who are living with HIV play an important role in promoting preconception health and informed reproductive decisions. However, even among providers who offer primary care to women living with HIV, the delivery of comprehensive reproductive counseling often falls short of the current guidelines.[15]

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, women living with HIV have specific needs that should be addressed.[16-19] 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.[11,20]
- The primary treatment goal for women who are on ART and planning a pregnancy should be sustained suppression of plasma viral load (below the limit of) detection prior to conception. This is important for the

health of the woman and to decrease the risk of both perinatal transmission and sexual transmission to a partner without HIV (see Reproductive Options).

- Counsel women on safer sex practices (including condoms and ART) that prevent HIV transmission to sexual partners, protect women from acquiring sexually transmitted infections, and reduce the risk of acquiring resistant strains of HIV (see Reproductive Options).
- Encourage sexual partners to receive HIV counseling and testing so that they can seek HIV care if they have HIV or seek advice about oral pre-exposure prophylaxis (PrEP) and other measures to prevent HIV acquisition if they do not have HIV.
- Counsel women on eliminating the use of alcohol, tobacco, and other drugs of abuse. Appropriately treat (e.g., with methadone or buprenorphine) and manage (e.g., provide access to syringe services program) the use of these drugs 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. Women who are at higher risk of having a child with neural tube defects than the baseline population are candidates for higher (1 to 4 mg) dose folic acid supplementation.
- 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 women living with HIV 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 virus (HBV) status, the potential for teratogenicity, and possible adverse outcomes for mother and fetus.[21-23]
- Provide counseling about the potential risk of neural tube defects when dolutegravir is taken during conception to patients who are currently receiving dolutegravir as part of their ARV regimen or who wish to be started on dolutegravir, see Interim Recommendations about the Use of Dolutegravir at the Time of Conception and During Pregnancy in Teratogenicity and Recommendations for the Use of Antiretroviral Drugs During Pregnancy.
- Use the preconception period to modify the ART regimen of women who are contemplating pregnancy to optimize virologic suppression and minimize potential adverse effects, see Recommendations for Use of Antiretroviral Drugs in Pregnancy and Table 7.
- Recognize that women with perinatally acquired HIV may have special needs[24] (see Women with Perinatal HIV Infection).
- 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 Guidance for Vaccine Recommendations for Pregnant and Breastfeeding Women and 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host) including vaccines for influenza, pneumococcus, HBV, and tetanus. All women, including those with HIV, should receive Tdap vaccination during each pregnancy.
- Offer all women who do not currently desire pregnancy effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. Women living with HIV can use all available contraceptive methods, including hormonal contraception (e.g., pill, patch, ring, injection, implant) and

intrauterine devices (IUDs).[25] 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 (see The ACOG Practice Bulletin on Emergency Contraception). 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.[26] There are no data on potential interactions between ARV drugs and ulipristal acetate, a progesterone receptor modulator; however, ulipristal acetate is predominantly metabolized by cytochrome P450 (CYP) 3A4, so interactions may be expected (see the HIV Drug Interaction Checker).
- Optimize the woman's health prior to conception (e.g., ensure appropriate folate intake, test for **all** sexually transmitted infections and treat as indicated, consider the teratogenic potential of **all** prescribed medications, and consider switching to safer medications).

Drug-Drug Interactions Between Hormonal Contraceptives and Antiretroviral Therapy

Data on drug interactions between ARV agents and hormonal contraceptives primarily come from drug labels and limited studies.[26-42] The contraceptive effectiveness of the levonorgestrel IUD (Mirena) is largely through local (i.e., intrauterine) release of levonorgestrel, not through systemic absorption. The CDC's U.S. Medical Eligibility Criteria for Contraceptive Use list the levonorgestrel IUD (Mirena) as category 1 (no restrictions) in drug interactions with all ARVs in women who already have an IUD and category 1/2 (benefits outweigh risk) for those initiating use of an IUD.

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 (PI/r) who are also on combination hormonal contraceptives (e.g., pills, patches, rings) or progestin-only pills, use of an alternative or additional method of contraception may be considered, since the AUC of hormones may be decreased in some PI/r (i.e., darunavir/ritonavir [DRV/r], fosamprenavir/ritonavir, and lopinavir/ritonavir [LPV/r]) but not in others (see Table 3). Depot medroxyprogesterone acetate (DMPA) can be used without restriction because of its relatively higher dose than other progesterone-based contraception, and limited studies have shown no significant interaction between DMPA and ARV drugs.[28,30,40,43] Nucleoside reverse transcriptase inhibitors have no effect on hormonal contraceptive doses.

While contraceptive implants (e.g., etonogestrel/levonorgestrel) generally can be used in women on ART, both pharmacokinetic (PK) and clinical data suggest that these implants have decreased efficacy when used with efavirenz-based regimens.[38,44-46] Scarsi et al. reported on three groups of Ugandan women living with HIV (those who were not on ART [17 women], those taking nevirapine-based ART [20 women], and those taking efavirenz-based ART [20 women]) who had levonorgestrel implants placed and had levonorgestrel PK levels assessed at 1, 4, 12, 24, 36, and 48 weeks post-insertion. The geometric mean ratio of levonorgestrel (patients taking efavirenz-based ART vs. ART-naive patients) was 0.53 at 24 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.[42]

In a study of 570 women with HIV in Swaziland who had levonorgestrel implants (i.e., Jadelle), none of the women on nevirapine- or LPV/r-based regimens (n = 208 and n = 13, respectively) became pregnant, whereas 15 women on efavirenz (n = 121; 12.4%) became pregnant.[38] Because of their overall efficacy, implants remain equally effective as or more effective than oral and injectable contraceptives among women with HIV who are using efavirenz, and all hormonal contraceptives remain more effective than no contraception among these women.[45,47] A study collected data from 5,153 women with HIV who were followed prospectively for 1 to 3 years. During the follow-up period, 9% of the women used implants (mostly levonorgestrel), 40% used injectables, and 14% used oral contraceptives; 31% of these women took ART during the follow-up period, mostly nevirapine (75%) or efavirenz (15%). Among women not using

contraception, pregnancy rates were 13.2 per 100 person-years for those who were on ART and 22.5 per 100 person-years for those who were not on ART. Implants greatly reduced the incidence of pregnancy among women on ART (adjusted hazard ratio[aHR] 0.06; 95% CI, 0.01–0.45) and not on ART (aHR 0.05; 95% CI, 0.02–0.11). Injectables and oral contraceptives also reduced pregnancy risk, though to lesser degrees. ART use did not significantly diminish contraceptive effectiveness, although all methods showed nonstatistically significant reduced contraceptive effectiveness when a woman was using efavirenz concurrently.[47]

Because data are limited 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 levonorgestrel and etonogestrel implants. The smallest decrease in PK for which an alternative method was recommended was a 14% decrease in norethindrone (with DRV/r). For women using atazanavir without ritonavir boosting (ethinyl estradiol increase 48%, norethindrone increase 110%), the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (the Panel) recommends use of oral contraceptives containing ≤30 µg ethinyl estradiol. The Panel does 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%).

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

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	COC: • No effect on EE concentrations • ↓ active metabolites of norgestimate LN AUC ↓ 83%; norelgestromin AUC ↓ 64%[31] • Etonogestrel (in COC) C_{24h} ↓ 61%[37] DMPA: • No effect on DMPA levels[28,30] Etonogestrel Implant: • Etonogestrel AUC ↓ 63% to 82%[46,48] LN Implant: • LN AUC ↓ 47%[42] • LN (emergency contraception) AUC ↓ 58%[26] Changes in ARV Levels and/or Effects on HIV *COC:* • No effect on EFV concentrations[31] • EFV C_{12h} ↓ 22%; was under therapeutic threshold in 3/16 subjects[37] *DMPA:* • No effect on HIV disease progression[28,49,50] • No effect on EFV concentrations[28]	COC: • No difference in pregnancy rates[47] • Pregnancy rate higher (13%) in women using COCs and EFV than COCs alone[45,51] • Progesterone >3 ng/mL (a surrogate for ovulation) in 3/16 women[52] • No ovulations[31] DMPA: • No increase in pregnancy rates[28,45,47,50] • Low progesterone[28,30,50] Etonogestrel Implant: • Pregnancy rate higher with EFV compared with no ART, but still lower than other hormonal methods of contraception[45] • Presumptive ovulation in 5%[48] LN Implant: • 12% pregnancy rate[38] • 15% pregnancy rate[42] • Pregnancy rate higher with EFV compared with no ART, but still lower than other hormonal methods of contraception[45]	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.	For COCs, some studies suggest higher pregnancy rate and ovulation rate and decreased progestin levels. EFV may decrease, but clinical significance unclear. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. Also, no effect on HIV disease progression or EFV levels. For implants, some studies suggest higher pregnancy rate and decreased hormone levels.

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 POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
EFV, continued	LN Implant: • No effect on HIV disease progression[42]	No increase in pregnancy rate[47]					
ETR	EE AUC ↑ 22%[53] NE: • No significant effect[53]	COC: • No ovulations[53]	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, 1 study found no ovulations and no significant change in progestin levels. No evidence on POPs.
NVP	EE AUC ↓ 29%;[54] no change in EE AUC[55] NE AUC ↓ 18%[54] Etonogestrel (in COC) C_{24h} ↓ 22%[37] DMPA: • No significant change[28] LN Implant: • LN AUC ↑ 35%[42] Changes in ARV Levels and/or Effects on HIV *COC:* • No significant effect on NVP levels[52,54,56] *DMPA:* • No effect on HIV disease progression[28,49,50,57] *LN Implant:* • No effect on HIV disease progression[42,58]	COC: • No increase in pregnancy rate[45,47,51,59,60] • No ovulations[52,55,60] DMPA: • No increase in pregnancy rate[45,47,50,59] • No ovulations[28] Etonogestrel Implant: • No increase in pregnancy rate[45] LN Implant: • No increase in pregnancy rate[38,42,45,47,58]	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. Evidence 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 POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
RPV	EE AUC ↑ 14%[36] NE: • No significant change[36] Changes in ARV Levels and/or Effects on HIV *COC:* • No change in RPV levels compared to historical controls[36]	COC: • No change in progesterone[36]	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 POPs.
RTV-Boosted PIs							
ATV/r	EE AUC ↓ 19%[61] Norgestimate AUC ↑ 85%[61] POP: • NE AUC ↑ 50%[62]	N/A	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, increase in progestin levels seen in only 1 study. For POPs, increase in progestin levels seen in only 1 study. RTV inhibits CYP3A4, which may increase contraceptive hormone levels.
DRV/r	EE AUC ↓ 44%[63] NE AUC ↓ 14%[63]	N/A	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 POPs.
FPV/r	EE AUC ↓ 37%[64] NE AUC ↓ 34%[64] No change in FPV/r levels[64]	N/A	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 POPs.

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 POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
LPV/r	EE AUC ↓ 55%[27] NE AUC ↓ 17% Patch: • EE AUC ↓ 45%[27] • Norelgestromin AUC ↑ 83%[27] DMPA: • DMPA AUC ↑ 46%[40] Etonogestrel Implant: • Etonogestrel AUC ↑ 52%[48] Changes in ARV Levels and/or Effects on HIV *Patch:* • LPV/r level ↓ 19%[27] *DMPA:* • No effect on HIV disease progression[40] • No change in LPV/r levels[40]	COC: • Increased pregnancy rate, but CIs overlap[45] Patch: • No ovulations[27] DMPA: • No pregnancies, no ovulations[40] • Increased pregnancy rate, but CIs overlap[45] Etonogestrel Implant: • No increase in pregnancy rate[45] LN Implant: • No increase in pregnancy rate.[38,45]	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 increased. 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.
SQV/r	↓ EE[65] Changes in ARV Levels and/or Effects on HIV *COC:* • No change in SQV/r levels[66]	N/A	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.	No information on progestin levels for CHCs or POPs. 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.

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 POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
TPV/r	EE AUC ↓ 48%[67] NE: • No significant change[67] Changes in ARV Levels and/or Effects on HIV: • No change in TPV levels[67]	N/A	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, no significant change in progestin levels but only from product label. No evidence on POPs. 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.
COBI-Boosted PIs							
ATV/c	Drospirenone AUC ↑ 2.3-fold; EE AUC ↓ 22%[68]	N/A	**Contraindicated** with drospirenone-containing hormonal contraceptives due to potential for hyperkalemia. Consider alternative or additional contraceptive method.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	No evidence on POPs.

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 POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
COBI-Boosted PIs, continued							
DRV/c	Drospirenone AUC ↑ 1.6-fold; EE AUC ↓ 30%[68]	N/A	In combination with drospirenone-containing COCs, clinical monitoring is recommended due to the potential for hyperkalemia. Consider alternative or additional contraceptive method.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	No evidence on POPs.
PIs without RTV							
ATV	COC: • EE AUC ↑ 48%[69] • NE AUC ↑ 110%[69]	N/A	Prescribe oral contraceptive that contains no more than 30 mcg of EE, or recommend alternative contraceptive method.	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 POPs.
FPV	COC *APV:* • No change in EE AUC; C_{min} ↑ 32% • NE AUC ↑ 18%; C_{min} ↑ 45%[64] FPV with EE/Norethindrone: • APV AUC ↓ 22% and C_{min} 20%)[64]	N/A	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 FPV alone with ethinyl estradiol/ norethindrone may lead to loss of virologic response. No evidence on POPs.

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 POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
PIs without RTV, continued							
IDV	COC: • EE AUC ↑ 22% • NE AUC ↑ 26%[70]	COC: • No pregnancies among women taking IDV and COCs[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, small increases in EE and progestin have been observed, and 1 clinical study did not suggest any efficacy concerns. No evidence on POPs.
NFV	COC: • EE AUC ↓ 47% • NE AUC ↓ 18%[71] DMPA: • No change[28] NFV: • AUC ↓ 18%	COC: • 1 small study suggested that women using COCs and NFV may have had higher pregnancy rates than those using COCs alone[51] DMPA: • No pregnancies, no ovulations[28,50] • CD4 count/HIV RNA: no change[28,50]	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, a small decrease in progestin and a decrease in estrogen have been observed; 1 small clinical study suggests possible higher pregnancy rate with COC and NFV use. DMPA, PK, and clinical data demonstrate no change. However, NFV AUC slightly decreased. No evidence on POPs or implants.
CCR5 Antagonist							
MVC	COC: • No significant effect on EE or LN[72]	N/A	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 or progestin. No clinical data. No evidence on POPs.

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 POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
Integrase Inhibitors							
BIC/FTC/ TAF	No significant drug interactions with EE or norgestimate.	N/A	No additional contraceptive protection is needed	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No clinical data.
DTG	COC: • No significant effect on norgestimate or EE • DTG AUC no change[41]	N/A	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 POPs.
EVG/c	EVG/COBI *COC:* • Norgestimate AUC ↑ 126% EE AUC ↓ 25%[74]	N/A	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 EE were observed. No clinical data. No evidence on POPs.
RAL	COC: • EE no change • Norgestimate AUC ↑ 14%[73]	N/A	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 POPs.

[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 Symbols:

↑ = increase ↓ = decrease

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CD4 = CD4 T lymphocyte; CHC = combination hormonal contraceptives; CI = confidence interval; C_{min} = minimum plasma concentration; COBI = cobicistat; COC/P/R =combined oral contraceptives/patch/ring; CYP = cytochrome P450 3A4; DMPA = depot medroxyprogesterone acetate; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EE = ethinyl estradiol; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IDV =

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives

indinavir; LN =levonorgestrel; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NE = norethindrone; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; P = progestin; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PK = pharmacokinetic; POP = progesterone-only oral contraceptive pills; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Tables 15a, 15b, and 15d.

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