Preconception Counseling and Care for Women of Childbearing Age with HIV

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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. With the increasing prevalence of the opioid epidemic, 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., access to a syringe services program) **(AII)**. • Women with HIV should attain maximum viral suppression before attempting conception for their own health to prevent sexual HIV transmission to partners without HIV **(AI)** and to minimize the risk of *in utero* HIV transmission to the infant **(AI)**. • When selecting or evaluating an antiretroviral (ARV) regimen for women of childbearing age with HIV, consider a regimen's effectiveness, a woman's hepatitis B status, the teratogenic potential of the drugs in the ARV regimen, and the possible adverse outcomes for the mother and fetus **(AII)**. See Teratogenicity and Recommendations for Use of Antiretroviral Drugs During Pregnancy for more information. The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission emphasizes the importance of counseling and shared decision making regarding all ARV regimens for people with HIV **(AIII)**. • HIV infection does not preclude the use of any contraceptive method; however, drug-drug interactions between hormonal contraceptives, antiretrovirals, and other medications should be considered (see Table 3). **(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, tailoring education and counseling 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 requires integrating ongoing care and interventions into primary care to address the needs of women during the different stages of reproductive life. Integrating comprehensive family planning and preconception care into routine health care visits is important because almost half of all pregnancies in the United States are unplanned.[2–5] Providers should initiate and document a nonjudgmental conversation with all women of reproductive age about their reproductive desires because women may be reluctant to bring up the subject themselves.[6–10] Health care providers who routinely care for women of reproductive age with HIV play an important role in promoting preconception health and informed reproductive decisions. However, even among providers who offer primary care to women with HIV, the delivery of comprehensive reproductive counseling often falls short of the current guidelines.[11–13]

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 with HIV have specific needs that should be addressed.[14–17] 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 the experts of HIV and women's health, including experts in reproductive endocrinology and infertility when necessary.[6,18]
- Recognize that the primary treatment goal for women who are on antiretroviral therapy (ART) and are planning a pregnancy should include sustained suppression of plasma viral load below the limit of detection before conception, which is important for the health of the woman because the risk of perinatal HIV transmission is minimized and sexual HIV transmission to a partner without HIV is prevented (see Reproductive Options for Couples When One or Both Partners Have HIV).
- Explain to women that people with HIV who take ART as prescribed and who achieve and maintain an undetectable viral load have effectively no risk of transmitting HIV through sex, commonly known as Undetectable = Untransmittable or U=U. For more information, see Let's Stop HIV Together from CDC.
- 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. The use of opioids should be treated (e.g., with methadone or buprenorphine) and managed appropriately (e.g., provide access to syringe services program) when elimination is not feasible.
- Counsel women on maintaining a healthy diet and healthy weight before and during pregnancy.
- Counsel women who are contemplating pregnancy to take a daily multivitamin that contains 400 mcg of folic acid to help prevent neural tube defects (NTDs). Women with a history of having a child with NTDs, a family history of NTDs, or on certain anti-epileptic medications are candidates for receiving a higher dose (1–4 mg) of folic acid.
- Educate and counsel women about the risk factors for perinatal HIV transmission, the strategies to reduce those risks, and the potential effects of HIV or taking antiretroviral drugs (ARVs) during pregnancy on pregnancy course and outcomes. Education and counseling also should be directed at helping women to understand the recommendation that women 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 alternatives to infant feeding.
- Support women's shared decision making about ART and educating and counseling them about the factors that affect the selection of ARVs for women who are trying to conceive, pregnant women, or postpartum women. This support includes discussing the small but statistically significant increase in the risk of infant NTDs when dolutegravir (DTG) is taken around the time of conception with women who currently are receiving DTG as part of their ART regimen or with women who wish to be started on DTG. For more information, see Teratogenicity, updated guidance about the use of dolutegravir in pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy, Dolutegravir, and Appendix C: Antiretroviral Counseling Guide for Health Care Providers: Pregnant Women and Women who are Trying to Conceive.
- Consider the following factors when prescribing ART to women of childbearing age: the regimen's effectiveness, an individual's hepatitis B virus (HBV) status, the potential for teratogenicity, the likelihood of developing drug resistance, and the possible adverse outcomes for mother and fetus.[19–21]
- Use the preconception period to modify the ARV regimen for women who are contemplating pregnancy to optimize virologic suppression and minimize potential adverse effects (see Recommendations for Use of Antiretroviral Drugs During Pregnancy and Table 5).
- Recognize that women with perinatally acquired HIV may have special needs[22] (see Prenatal Care, Antiretroviral Therapy, and HIV Management in Women with Perinatal HIV Infection).
- Evaluate and manage therapy-associated adverse effects (e.g., hyperglycemia, anemia, hepatotoxicity) that may affect 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), which includes vaccination for influenza, pneumococcus, HBV, and tetanus. All women, including those with HIV, should receive Tdap (tetanus, diphtheria, and pertussis) vaccination during pregnancy.
- Offer all women who currently do not desire pregnancy the effective and appropriate contraceptive methods to reduce the likelihood of an unintended pregnancy. Women with HIV 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, hormonal contraceptives, and other medications that could lower contraceptive efficacy or increase the risk of such adverse effects as blood clots (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). Emergency contraceptive pills that contain estrogen and progestin and those that only contain levonorgestrel (LNG) may have interactions with ARV drugs that are similar to the ones observed with combined oral contraceptives.[24] No data are available on potential interactions between ARV drugs and ulipristal acetate, a progesterone receptor modulator; however, ulipristal acetate is metabolized predominantly by cytochrome P450 (CYP) 3A4, so interactions may occur (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 ARVs and hormonal contraceptives primarily come from drug labels and several studies on the pharmacokinetics (PKs) and pharmacodynamics among the different forms of contraception and ARVs.[24–45] The contraceptive effectiveness of the levonorgestrel IUD is largely through local (i.e., intrauterine) release of levonorgestrel, not through systemic absorption. CDC's U.S. Medical Eligibility Criteria for Contraceptive Use lists the levonorgestrel IUD 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 the use of an IUD.

Hormonal contraceptives can be used with ARVs in women without other contraindications. Additional or alternative methods of contraception may be recommended when drug interactions are known. For women who are using ritonavir (RTV)-boosted protease inhibitors (PIs) and who are also on combination hormonal contraceptives (e.g., pills, patches, rings) or progestin-only pills, the use of an alternative or additional method of contraception may be considered because the area under the curve (AUC) of hormones may be decreased with the use of some RTV-boosted PIs (i.e., darunavir/ritonavir [DRV/r], fosamprenavir/ritonavir, and lopinavir/ritonavir [LPV/r]) but not 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 ARVs.[26,28,38,46] Doses of hormonal contraceptives do not need to be adjusted in patients who are receiving nucleoside reverse transcriptase inhibitors.

Although contraceptive implants (e.g., etonogestrel [ENG]/LNG) generally can be used in women who are receiving ARVs, both PK and clinical data suggest that these implants have decreased efficacy when used with efavirenz (EFV)-based regimens.[36,47–49] Scarsi et al. reported on three groups of Ugandan women with HIV: those who were not on ART (17 women), those taking nevirapine (NVP)-based ART (20 women), and those taking EFV-based ART (20 women) who had LNG implants placed and had LNG PK levels assessed at 1, 4, 12, 24, 36, and 48 weeks post-insertion. The geometric mean ratios of LNG concentrations (patients taking EFV-

based ART vs. ART-naive patients) were 0.53 at 24 weeks and 0.43 at 48 weeks. Three pregnancies occurred in the EFV group (15%) between weeks 36 and 48, whereas no pregnancies occurred in the ART-naive or NVP groups.[40]

In a study of 570 women with HIV in Swaziland who had LNG implants (i.e., Jadelle), none of the women on NVP- or LPV/r-based regimens (n = 208 and n = 13, respectively) became pregnant, whereas 15 women on EFV (n = 121; 12.4%) became pregnant.[36] Because of their overall efficacy, implants remain as effective as or more effective than oral and injectable contraceptives among women with HIV who are using EFV, and all hormonal contraceptives remain more effective than no contraception among these women.[48,50] 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 percent of the women used implants (mostly LNG), 40 percent used injectables, and 14 percent used oral contraceptives; 31 percent of these women took ART during the follow-up period, mostly NVP-containing (75%) or EFV-containing (15%) regimens. Among women who were 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% confidence interval [CI], 0.01–0.45) and women who were not on ART (aHR 0.05; 95% CI, 0.02–0.11). Injectables and oral contraceptives also reduced pregnancy risk but to lesser degrees. ART use did not significantly diminish contraceptive effectiveness, although all methods showed nonstatistically significant reduced contraceptive effectiveness when a woman used EFV concurrently.[50]

In a retrospective study among 1,152 women with HIV and using either EFV or NVP and ENG or LNG implants, there were 115 pregnancies, yielding a pregnancy incidence rate of 6.32 (5.27–7.59), with a rate of 9.26 among ENG and 4.74 among LNG implant users, respectively. Pregnancy incidence rates did not differ between EFV- and NVP-based regimens (incidence rate ratio [IRR] = 1.00; 95%CI, 0.71–1.43). No pregnancies were recorded among women on PI-based regimens. Pregnancy rates of EFV- and NVP-containing regimens were similar at 6.41 (4.70–8.73) and 6.44 (5.13–8.07), respectively. Pregnancy rates differed by implant type with LNG implant users half as likely to become pregnant as ENG implant users (IRR = 0.51; 95% CI, 0.33–0.73, $P > 0.01$).[51]

Genetic contributions also may influence observed drug-drug interactions between contraceptives and ARVs. In a study of 19 women not on ART (control group), 19 women on EFV, and 19 women on NVP with ENG implants, the women in the EFV group with cytochrome P450 2B6 (CYP2B6) 516 G>T were associated with 43% lower ENG C_{min} and 34 percent lower $AUC_{0–24}$ at 24weeks. For patients on NVP, NR1I2 63396 C>T had lower ENG C_{min} and 37 percent lower $AUC_{0–24}$ at 24weeks.[44]

Other medications, such as those for tuberculosis (TB) treatment and ARVs, also may have drug-drug interactions with contraceptives. A pharmacokinetic study of DMPA among women with HIV/TB coinfection who received EFV-based treatment and rifampicin-based TB treatment showed that among 42 evaluable women, five women (11.9%; 95% CI, 4.0–25.6%) had medroxyprogesterone acetate (MPA) <0.1 ng/ml at week 12, the level above which ovulation is prevented; of these women, one had MPA <0.1 ng/ml at week 10. The median clearance of MPA was higher in women on EFV compared with women with HIV who were not on ART, thus leading to subtherapeutic concentrations of MPA in 12 percent of women at week 12.[52] The authors suggest redosing DMPA more frequently, such as every 8–10 weeks.

Because data are limited on pregnancy rates among women on different hormonal contraceptives and ARVs, some of 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 ARVs and combined hormonal methods, DMPA, and LNG and ENG implants. The smallest decrease in PK for which an alternative method was recommended was a 14 percent decrease in norethindrone (with DRV/r). For women who are using

atazanavir without RTV 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 the use of oral contraceptives that contain ≤30 µg ethinyl estradiol. The Panel does not recommend any change in ethinyl estradiol dose in women who are receiving etravirine (ethinyl estradiol increased 22%), rilpivirine (ethinyl estradiol increased 14%), or indinavir (ethinyl estradiol increased 25%, norethindrone increased 26%).

A contraceptive vaginal ring containing segesterone/ethinyl estradiol (Annovera) has been approved by the U.S. Food and Drug Administration. No available drug-drug interaction studies with this new contraceptive vaginal ring and ARV and CYP inducers/inhibitors are known. The contraceptive possibly could be metabolized in the same way as ENG and ethinyl estradiol in the NuvaRing. Our recommendation is extrapolated from what is known with the NuvaRing.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives

Note: All recommendations in this table are based on consensus expert opinion. More details can be found in 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 for POPs	Dosing Recommendation/ Clinical Comment for DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs							
EFV	**COC:** • No effect on EE concentrations • ↓ active metabolites of norgestimate; LNG AUC ↓ 83% and norelgestromin AUC ↓ 64%[29] • Etonogestrel (in COC) C_{24h} ↓ 61%[35] **DMPA:** • No effect on DMPA levels[26,28] **Etonogestrel Implant:** • ↓ 49% in Etonorgestrel concentration [45] • Etonogestrel AUC ↓ 63% to 82%[49,53] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users.[51]	**COC:** • No difference in pregnancy rates[50] • Pregnancy rate was 13% higher in women using COCs and EFV than in women using COCs alone[48,57] • Progesterone >3 ng/mL (a surrogate for ovulation) in three of 16 women[58] • No ovulations[29] **DMPA:** • No increase in pregnancy rates [26,48,50,55]	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.

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
	LNG Implant: • ↓61% LNG concentration [45] • LNG AUC ↓ 47%[40] • LNG (emergency contraception) AUC ↓ 58%[24] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users.[51] **Changes in ARV Levels and/or Effects on HIV** *COC*: • No effect on EFV concentrations[29] • EFV C_{12h} ↓ 22%; was under therapeutic threshold in three of 16 subjects[35] *DMPA:* • No effect on HIV disease progression[26,54,55] • No effect on EFV concentrations[26]	• Low progesterone[26,28,55] **Etonogestrel Implant:** • Pregnancy rate higher with EFV compared with no ART, but still lower with implants than with other hormonal methods of contraception[48] • Presumptive ovulation in 5%[53] **LN Implant:** • 12% pregnancy rate[36] • 15% pregnancy rate[40] • Pregnancy rate higher with EFV compared with no ART, but still lower with implants than with other hormonal-					For implants, some studies suggest higher pregnancy rate and decreased hormone levels. For vaginally administered etonogestrel/EE, PK evaluation showed that etonogestrel levels were 79% lower and EE levels were 59% lower in participants on EFV than in controls after 21 days.[56]

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
	LNG Implant: • No effect on HIV disease progression[40] **Vaginally Administered Etonogestrel/EE:** • Etonogestrel ↓ 79% EE ↓ 59%[56]	methods of contraception[48] • No increase in pregnancy rate[50]					For implants, some studies suggest higher pregnancy rate and decreased hormone levels. For vaginally administered etonogestrel/EE, PK evaluation showed that etonogestrel levels were 79% lower and EE levels were 59% lower in participants on EFV than in controls after 21 days.[56]
ETR	EE AUC ↑ 22%[59] No significant effect on NE[59]	**COC:** No ovulations[59]	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 data on POPs.

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
NVP	EE AUC ↓ 29%;[60] no change in EE AUC[61] NE AUC ↓ 18%[60] Etonogestrel (in COC) C_{24h} ↓ 22%[35] **DMPA:** • No significant change[26] **LNG Implant:** • LNG AUC ↑ 35%[40] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users.[51] **Changes in ARV Levels and/or Effects on HIV** *COC:* • No significant effect on NVP levels[58,60,62] *DMPA:* • No effect on HIV disease progression[26,54,55,63] *LNG Implant:* • No effect on HIV disease progression[40,64]	**COC:** • No increase in pregnancy[48,50,57,65,66] • No ovulations[58,61,66] **DMPA:** • No increase in pregnancy rate[48,50,55,65] • No ovulations[26] **Etonogestrel Implant:** • No increase in pregnancy rate[48] **LNG Implant:** No increase in pregnancy[36,40,48,50,64]	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. No effect on NVP levels. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. No effect on HIV disease progression. For implants, evidence does not show effects on pregnancy rate or HIV disease progression.

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
RPV	EE AUC ↑ 14%[34] No significant change on NE[34] **Changes in ARV Levels and/or Effects on HIV** *COC:* No change in RPV levels compared to historical controls[34]	**COC:** No change in progesterone[34]	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. No change in RPV levels. No data on POPs.
DOR	No clinically significant interaction with EE and LNG[67]	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.
RTV-Boosted PIs							
ATV/r	EE AUC ↓ 19%[68] Norgestimate AUC ↑ 85%[68] **POP:** • NE AUC ↑ 50%[69] **Vaginally Administered Etonogestrel/EE:** • Etonogestrel ↑ 71% • EE ↓ 38%[56]	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 one study. For POPs, increase in progestin levels seen in only one study. RTV inhibits CYP3A4, which may increase contraceptive hormone levels.

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
DRV/r	EE AUC ↓ 44%[70] NE AUC ↓ 14%[70]	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 data on POPS.
LPV/r	EE AUC ↓ 55%[25] NE AUC ↓ 17% **Patch:** • EE AUC ↓ 45%[25] • Norelgestromin AUC ↑ 83%[25] **DMPA:** • DMPA AUC ↑ 46%[38] **Etonogestrel Implant:** • Etonogestrel AUC ↑ 52%[53]	**COC:** • Increased pregnancy rate, but CIs overlap[48] **Patch:** • No ovulations[25] **DMPA:** • No pregnancies and no ovulations[38] • Increased pregnancy rate, but CIs overlap[48]	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. Progestin levels increased.

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
	Changes in ARV Levels and/or Effects on HIV *Patch:* • LPV/r ↓ 19%[25] *DMPA:* • No effect on HIV disease progression[38] • No change in LPV/r levels[38]	**Etonogestrel Implant:** • No increase in pregnancy rate[48] **LN Implant:** No increase in pregnancy rate[36,48]					For implants, evidence shows no effect on pregnancy rate. Progestin levels increased.
COBI-Boosted PIs							
ATV/c	Drospirenone AUC ↑ 2.3-fold No change in LNG concentration 25% decrease in EE C_{24}[42]	N/A	**Contraindicated** with drospirenone-containing hormonal contraceptives due to potential for hyperkalemia. Consider alternative or additional contraceptive method.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No data on POPs.
DRV/c	Drospirenone AUC ↑ 1.6-fold EE AUC ↓ 30%[43]	N/A	Clinical monitoring is recommended when DRV/c is used in combination with	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No data on POPs

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
COBI-Boosted PIs, continued							
			drospirenone-containing COCs as a result of the potential for hyperkalemia. Consider alternative or additional contraceptive method.				
PIs without RTV							
ATV	**COC:** • EE AUC ↑ 48%[71] • NE AUC ↑ 110%[71]	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 the only data available are from the product label. No data on POPs
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 data on POPs

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
INSTIs							
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 • No change in DTG AUC[39]	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 data on POPs.
EVG/c	**COC:** • Norgestimate AUC ↑ 126% • EE AUC ↓ 25%[73,74]	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 four-drug regimen EVG/c/FTC/ TDF, increases in progestin and a small decrease in EE were observed. No clinical data. No data on POPs.
RAL	**COC:** • No change in EE • Norgestimate AUC ↑ 14%[75]	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 a small increase in progestin. No clinical data.

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 DMPAa	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
INSTIs, continued							
							No data on POPs.

[a] Because the hormonal levels achieved with DMPA are substantially higher than the levels that are required for contraception, any small reduction in hormonal level attributed to ARV drugs is unlikely to reduce contraceptive effectiveness.

Key to Symbols:
↑ = increase
↓ = decrease

Key: APV = amprenavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{12h} = concentration at 12 hours post-dose; C_{24h} = concentration at 24 hours post-dose; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; CHC = combination hormonal contraceptives; CI = confidence interval; Cmin = minimum plasma concentration; COBI = cobicistat; COC/P/R = combined oral contraceptives/patch/ring; CYP = cytochrome P450; DMPA = depot medroxyprogesterone acetate; DOR= doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EE = ethinyl estradiol; EFV = efavirenz; ENG = etonogestrel; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LNG = 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 = protease inhibitor/ritonavir; 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 = tipranavir; 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 21a, 21b, and 21d.

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