Prepregnancy Counseling and Care for Persons of Childbearing Age With HIV

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Panel's Recommendations
• Discuss reproductive desires and plans with all persons with HIV of childbearing potential on an ongoing basis throughout the course of their care (AIII). • Provide information about effective and appropriate contraceptive methods to people who do not currently desire pregnancy (AI). Offer all contraceptive methods or refer for contraceptive services. Individuals with HIV can use all available contraceptive methods (e.g., pill, patch ring, injection, implant); however, the presence of other medical co-morbidities and drug -drug interactions between hormonal contraceptives, antiretroviral (ARV) drugs, and other medications should be considered (see Table 3) (AII). • During prepregnancy counseling, provide information on safer sex; ask about the use of alcohol, nicotine products, and other substances. Provide or refer to evidence-based interventions for substance use disorder, including medication-assisted treatment for opiate use disorder (e.g., methadone, buprenorphine), and counsel patients on how to manage health risks (e.g., access to a syringe services program) when indicated. (AII). • Provide education and counseling about interventions to prevent perinatal HIV transmission, including antiretroviral therapy (ART). Explain that persons 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 fully suppressive ART is started before pregnancy and undetectable viral load is maintained throughout pregnancy and at delivery, there is no risk of HIV transmission to the infant. • For people with HIV who are considering or planning a pregnancy, begin to provide patient-centered, evidence-based counseling to support shared decision making about infant feeding (AIII) (see Infant Feeding for Individuals with HIV in the United States).Information and plans for infant feeding should be reviewed throughout pregnancy and again after delivery. • When selecting or evaluating an ARV regimen for persons of childbearing potential with HIV, consider a regimen's effectiveness, a person's hepatitis B status, and the possible adverse outcomes for the pregnant person and their fetus (AII). See Teratogenicity and Recommendations for Use of Antiretroviral Drugs During Pregnancy: Overview for more information. The Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission emphasizes the importance of counseling and shared decision-making regarding all ARV regimens for persons with HIV (AIII).
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 persons of childbearing potential comprehensive family planning and the opportunity to receive prepregnancy counseling and care as a component of routine primary medical care. The purpose of prepregnancy care is to improve the health of each person before conception by identifying risk factors for adverse outcomes for the pregnant person and their fetus, tailoring education and counseling to individual needs, and treating or stabilizing medical conditions to optimize outcomes for the pregnancy and the

fetus/newborn.[1,2] Prepregnancy care is not something that occurs in a single clinical visit; rather, it requires integrating ongoing care and interventions into primary care to address people's needs during the different stages of reproductive life. Integrating comprehensive family planning and prepregnancy care into routine health care visits can help people with HIV reach their desired reproductive outcomes by supporting them to make informed decisions about their fertility and contraceptive use that are aligned with their preferences and reproductive goals.[3–6] Providers should initiate and document a nonjudgmental conversation with all persons of reproductive age about their reproductive desires because they may be reluctant to bring up the subject themselves.[7–11] A meta-analysis of 50 studies found a 42% prevalence of fertility desire among persons with HIV. In a pooled analyses, fertility desire was associated with being on antiretroviral therapy (ART), male sex, age younger than 30, being married/cohabitating, a secondary education or higher, and being childless.[12] Health care providers who routinely care for persons of reproductive age with HIV play an important role in promoting prepregnancy health and informed reproductive decisions. Pregnancy intentions may not be binary and may change over time, thus underscoring the need for health care providers to engage in ongoing discussions to support dynamic pregnancy intentions.[11] However, even among providers who offer primary care to persons with HIV, the delivery of comprehensive reproductive counseling often falls short of the current guidelines.[13–15]

The fundamental principles of prepregnancy 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 prepregnancy counseling and care that are appropriate for all persons of reproductive age, persons with HIV have specific needs that should be addressed.[16–19]

- Discuss reproductive options; actively assess their pregnancy intentions on an ongoing basis throughout the course of care; and, when appropriate, make referrals to HIV and reproductive health specialists, including experts in reproductive endocrinology and infertility when necessary. The HIV status of one or both parents should not be a reason to withhold standard of care infertility treatment and assist individuals and couples in reaching their desired reproductive outcomes.
- Encourage individuals to disclose their HIV status to their partner or co-parent before pregnancy if it is safe to do so. However, this disclosure should not be a requirement of assisting couples in achieving pregnancy.
- Recognize that the primary treatment goal for persons with HIV who are planning a pregnancy should include sustained suppression of plasma viral load below the limit of detection before conception for their own health, to minimize the risk of perinatal HIV transmission, and to prevent sexual HIV transmission to a partner without HIV (see Reproductive Options for Couples When One or Both Partners Have HIV). Inform individuals considering or planning pregnancy that with ART starting before pregnancy and maintained throughout pregnancy and with undetectable viral load at delivery, there is no risk of HIV transmission to the infant.[20,21]
- Explain that persons with HIV who take ART as prescribed and who achieve and maintain an undetectable viral load will not transmit HIV through sex, commonly known as Undetectable = Untransmittable or U=U. For more information, see Let's Stop HIV Together.
- Encourage sexual partners to receive HIV counseling and testing so that they can seek HIV care if they have HIV or seek advice about HIV prevention, including pre-exposure prophylaxis (PrEP), if they do not have HIV (see Pre-exposure Prophylaxis (PrEP) to Reduce the Risk of Acquiring HIV During Periconception, Antepartum, and Postpartum Periods).

- Ask about the use of alcohol, tobacco, and other substance. Provide or refer to evidence-based interventions for substance use disorder, including medication-assisted treatment for opiate use disorder (e.g., methadone, buprenorphine), and counsel patients on how to manage health risks (e.g., access to a syringe services program). Frazier et al.[22] reported that overall, 39% of women with HIV of reproductive age reported current drinking and 10% reported binge drinking. Compared to non-drinkers, binge drinkers were less likely to adhere to ART or be virally suppressed and more likely to smoke and use drugs. Between 2007 and 2019, marijuana use during pregnancy among women with HIV increased from 7.1% to 11.7%, whereas alcohol and opioid use were unchanged. Postpartum alcohol (44.4%), marijuana (13.6%), and concomitant alcohol and marijuana (10%) use were common; marijuana use increased from 10.2% in 2006 to 23.7% in 2019, whereas postpartum alcohol use was unchanged.[2]
- Ask pregnant people whether they feel safe at home and offer assistance or referrals for those experiencing intimate partner violence (IPV) or requesting it.
- Counsel on maintaining a healthy diet and healthy weight before and during pregnancy.
- Counsel people who are contemplating pregnancy to take a daily multivitamin that contains 400 mcg of folic acid to help prevent neural tube defects (NTDs). Individuals with a history of having a child with NTDs, a family history of NTDs, or on certain anti-epileptic medications, especially valproic acid, are candidates for receiving a higher dose (1,000–4,000 mcg) of folic acid. Higher doses of folate may also be considered for persons receiving trimethoprim/sulfamethoxazole (TMP/SMX) who are trying to conceive (see Special Considerations in Pregnancy in *Pneumocystis* Pneumonia).
- Educate and counsel about the risk factors for perinatal HIV transmission, the strategies to reduce those risks, and the potential effects of HIV or taking antiretroviral (ARV) drugs during pregnancy on pregnancy course and outcomes.
- Provide patient-centered, evidence-based counseling to support shared decision-making about infant feeding (see Infant Feeding for Individuals with HIV in the United States). Information about and plans for infant feeding should be reviewed throughout pregnancy and again after delivery
- Support shared decision-making about ART. Educate and counsel on the factors that affect the selection of ARVs for persons who are trying to conceive, are pregnant, or postpartum. 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.
- Consider the following factors when prescribing ART to persons of childbearing potential: the regimen's effectiveness, an individual's hepatitis B virus (HBV) status, the possible adverse outcomes for the pregnant person and their fetus, the likelihood of developing drug resistance, and the possible adverse outcomes for the mother and fetus.[24–26]
- Use the prepregnancy period to modify the ARV regimen for persons who are contemplating pregnancy to optimize virologic suppression and minimize potential adverse effects (see Recommendations for Use of Antiretroviral Drugs During Pregnancy and Table 7). Recognize that individuals with perinatally-acquired HIV may have special needs (e.g., psychosocial support, adherence support)[27] (see Prenatal Care, Antiretroviral Therapy, and HIV Management in People with Perinatal-Acquired HIV Infection).

- Recognize that transgender and gender-diverse people who were assigned female sex at birth may have special needs.[28]. For transgender men attempting pregnancy, the use of testosterone may induce hypothalamic-pituitary-gonadal suppression leading to decreased ovulation.[29]
- 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, tetanus, and SARS-CoV-2. All persons, including those with HIV, should receive Tdap (tetanus, diphtheria, and pertussis) vaccination during pregnancy.
- Offer all persons who currently do not desire pregnancy a full range of contraceptive methods to help them achieve their fertility goals. Persons with HIV can use all available contraceptive methods, including hormonal contraception (e.g., pill, patch, ring, injection, implant) and intrauterine devices (IUDs).[30] Providers should be aware of the presence of other medical co-morbidities and 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 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.[31] ACTG 5375 showed that doubling the dose of LNG from 1.5 mg to 3 mg successfully increased LNG exposure in women receiving efavirenz (EFV)-based ART.[32] 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 health of people with HIV prior to pregnancy (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.[31,33–54] 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 persons with HIV without other contraindications. An alternative or additional contraceptive method may be recommended when drug interactions are known. For persons receiving darunavir/ritonavir (DRV/r)-based ART, an alternative or additional contraception may be considered because the area under the curve (AUC) for oral contraceptive hormones may be decreased.[55] Cobicistat-boosted protease inhibitors (PIs) are

contraindicated with drosperinone-containing hormonal contraceptives due to the potential for hyperkalemia.[51] 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.[34,36,46,56]

Several studies have shown that the use of EFV decreases the effectiveness of hormonal implants and hormonal vaginal rings. Although contraceptive implants (e.g., etonogestrel [ENG], LNG) generally can be used in people who are receiving ARVs, both PK and clinical data suggest that these implants have decreased efficacy when used with EFV-based regimens.[44,57–59] Scarsi et al. reported that 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 Week 36 and Week 48, whereas no pregnancies occurred in the ART-naive or nevirapine (NVP) groups.[48]

In a study of 570 women with HIV in Eswatini, formerly known as Swaziland, who had LNG implants (i.e., Jadelle), none of the women on NVP- or lopinavir/ritonavir-based regimens (n = 208 and n = 13, respectively) became pregnant, whereas 15 women on EFV (n = 121; 12.4%) became pregnant.[44] A prospective study in seven African countries collected data from 5,153 women with HIV who were followed for 1 to 3 years. During the follow-up period, 40% used injectables, 14% used oral contraceptives, and 9% of the women used implants (mostly LNG, which is not available in the United States, where ENG is approved); 31% 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. A potential lesser degree of effectiveness of these methods may be due to their greater dependence on user action, as compared to longer acting methods. ART use did not significantly diminish contraceptive effectiveness, although all methods showed non-significant reduced contraceptive effectiveness when people used EFV concurrently.[60]

In a retrospective study among 1,152 women with HIV using either EFV or NVP and ENG or LNG implants, 115 pregnancies occurred, 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, $P > 0.01$).[61] A study of 42 women in Malawi (30 women with HIV on EFV and LNG, and 12 women without HIV on LNG) showed that EFV users had lower LNG concentrations that non EFV users, and one-third of the EFV/LNG users had LNG concentrations <180 pg/mL, which is the suggested minimum level for efficacy. No pregnancies were reported over 60 women-years of follow-up.[62]

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 all received ENG implants. Women in the EFV group with CYP 2B6 516 G>T had 43% lower ENG minimum plasma concentration (C_{min}) and 34% lower AUC from 0 to 24 h ($AUC_{0–24}$) at

24 weeks. For women on NVP, those with NR1I2 63396 C>T had lower ENG C_{min} and 37% lower $AUC_{0–24}$ at 24 weeks.[52] Haas et al. reported that EFV reduced the median ENG level by at least 93% in CYP2B6 slow metabolizers versus by 75% in normal and intermediate metabolizers. EFV reduced median ethinyl estradiol concentration by 75% in slow metabolizers and 41% in normal and intermediate metabolizers among women using hormonal vaginal ring contraceptive[63].

Other medications, such as those for tuberculosis (TB) treatment and ARVs, also may have drug–drug interactions with contraceptives. A PK 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% of women at Week 12.[64] The authors suggest redosing DMPA more frequently,[65] such as every 8 to 10 weeks. Haas et al. studied the interaction between DMPA, EFV, rifampicin, and isoniazid (INH) during treatment for HIV and tuberculosis. There were no associations between either CYP2B6 or N-acetyltransferase 2 (NAT2) genotype and MPA C_{min} at Week 12. The study was not designed to distinguish inductive effects of rifampicin from possible inhibitory effects of isoniazid on MPA clearance. Nevertheless, the authors recommended that more frequent DMPA dosing may be appropriate for women receiving all these medications.[66]

Because data are limited on pregnancy rates among persons 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% decrease in norethindrone (with DRV/r). The Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission (the Panel) does not recommend any change in ethinyl estradiol dose in people who are receiving etravirine (ethinyl estradiol increased 22%) or rilpivirine (ethinyl estradiol increased 14%). In a secondary analysis of 85 cisgender women enrolled in HPTN 077, compared to women reporting no hormonal contraception (n = 6), oral contraceptive use (n =18) was associated with lower cabotegravir-long acting (CAB-LA) peak concentration but was not associated with other PK parameters, suggesting this association is not likely to be clinically significant. No other hormonal contraceptive type (injectable, implants, and other) was associated with significant differences in CAB-LA PK parameters.[67]

Another contraceptive vaginal ring containing segesterone/ethinyl estradiol (Annovera) has recently been approved by the U.S. Food and Drug Administration. No available drug–drug interaction studies with this contraceptive vaginal ring and ARV and CYP inducers/inhibitors are known. The contraceptive may possibly be metabolized in the same way as ENG and ethinyl estradiol in the NuvaRing. Our recommendation is extrapolated from what is known with the etonogestrel/ethinyl estradiol (NuvaRing) vaginal ring.[54]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives

Note: All recommendations in this table are based on consensus expert opinion. Additional information can be found in CDC's Update to U.S. Medical Eligibility Criteria for Contraceptive Use, 2016: Updated Recommendations for the Use of Contraception Among Women at High Risk for HIV Infection.[68]

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	
Efavirenz (EFV)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, and Etonogestrel Implants	If efficacy is of primary importance, consider an alternative method (or a reliable method of barrier contraception in addition to this method).
Dosing Recommendation/Clinical Comment for DMPA[a]	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No effect on EE concentrations • ↓ active metabolites of norgestimate; LNG AUC ↓ 83% and norelgestromin AUC ↓ 64%[37] • Etonogestrel (in COC) C_{24h} ↓ 61%[43] • Etonogestrel ↓ 79%; EE ↓ 59%[54] DMPA • No effect on DMPA levels[34,36] DMPA AUC ↓ 33-35% when coadministered with EFV, rifampin, and isoniazid. More frequent DMPA dosing may be appropriate.[64] Etonogestrel Implant • ENG ↓ below 90 pg/mL in 60% of people on EFV[69] • ↓ 49% in Etonogestrel concentration[53] • Etonogestrel AUC ↓ 63% to 82%[59,70] LNG Implant • ↓ 61% LNG concentration[53] • LNG AUC ↓ 47%[48] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users[61] • LNG AUC ↓ 40–73% over 30 months of use[62] LNG Emergency Contraception (Oral dosing) • LNG (emergency contraception) AUC ↓ 58%[31]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	• C_{max} was 51% higher with 3 mg LNG (24.9 ng/mL) compared to 1.5 mg (15.1 ng/mL), and the 48-hour concentration was 66% higher (0.6 vs 0.3 ng/mL, respectively). Dose adjustment of LNG EC from 1.5 mg to 3 mg successfully increased LNG exposure on EFV-based ART[32] Vaginally Administered Etonogestrel/EE (Vaginal Ring) • Etonogestrel ↓ 93% in CYP2B6 slow metabolizers and ↓ 75% in normal and intermediate metabolizers[63] • EE ↓ 75% in slow metabolizers and ↓ 41% in normal and intermediate metabolizers[63] Changes in ARV Levels and/or Effects on HIV *COC* • No effect on EFV concentrations[37] • EFV C_{12h} ↓ 22%; was under therapeutic threshold in three of 16 subjects[43] *DMPA* • No effect on HIV disease progression[34,71,72] • No effect on EFV concentrations[34] LNG Implant • No effect on HIV disease progression[48]
Clinical Studies	COC • No difference in pregnancy rates[60] • Pregnancy rate was 13% higher in women using COCs and EFV than in women using COCs alone[58,73] • Progesterone >3 ng/mL (a surrogate for ovulation) in three of 16 women[74] • No ovulations[37] DMPA • No increase in pregnancies[34,58,60,72] • Low endogenous progesterone, consistent with no ovulation[34,36,72] Etonogestrel Implant • Pregnancy rate higher with EFV compared with no ART but still lower with implants than with other hormonal methods of contraception[58] • Presumptive ovulation in 5%[70] Levonogestrel Implant • 12% pregnancy rate[44] • 15% pregnancy rate[48] • Pregnancy rate higher with EFV compared with no ART but still lower with implants than with other hormonal methods of contraception[58] • No increase in pregnancy rate[60]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Justification/Evidence for Recommendation	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 More frequent DMPA dosing may be appropriate for women receiving rifampicin, INH, and EFV. 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.[54]
Etravirine (ETR)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↑ 22%[75] No significant effect on NE[75]
Clinical Studies	COC • No ovulations[75]
Justification/Evidence for Recommendation	For COCs, one study found no ovulations and no significant change in progestin levels. No data on POPs.
Nevirapine (NVP)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 29%;[76] no change in EE AUC[77] NE AUC ↓ 18%[76] Etonogestrel (in COC) C_{24h} ↓ 22%[43] DMPA • No significant change[34] LNG Implant • LNG AUC ↑ 35%[48] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users[61] Changes in ARV Levels and/or Effects on HIV *COC*

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	• No significant effect on NVP levels[74,76,78] *DMPA* • No effect on HIV disease progression[34,71,72,79] *LNG Implant* • No effect on HIV disease progression[48,80]
Clinical Studies	COC • No increase in pregnancy rate[58,60,73,81,82] • No ovulations[74,77,82] DMPA • No increase in pregnancy rates[58,60,72,81] • Low serum progesterone, consistent with no ovulation[34] Etonogestrel Implant • No increase in pregnancy rate[58] LNG Implant • No increase in pregnancy rate[44,48,58,60,80]
Justification/Evidence for Recommendation	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.
Rilpivirine (Oral RPV)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↑ 14%[42] No significant change on NE[42] Changes in ARV Levels and/or Effects on HIV *COC* • No change in RPV levels compared to historical controls[42]
Clinical Studies	COC • No change in progesterone[42]
Justification/Evidence for Recommendation	For COCs, evidence does not show effects on ovulation or progestin levels. No change in RPV levels. No data on POPs

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Doravirine (DOR)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	No clinically significant interaction with EE and LNG[83]
Clinical Studies	N/A
Justification/Evidence for Recommendation	No clinical data
Ritonavir (RTV)-Boosted Protease Inhibitors (PIs)	
Atazanavir/Ritonavir (ATV/r)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 19%[84] Norgestimate AUC ↑ 85%[84] POP • NE AUC ↑ 50%[85] Vaginally Administered Etonogestrel/EE • Etonogestrel ↑ 71% • EE ↓ 38%[54]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, increase in progestin levels seen in only one study. Using a COC with at least 35 mcg/day may decrease breakthrough bleeding. For POPs, increase in progestin levels seen in only one study RTV inhibits CYP3A4, which may increase contraceptive hormone levels.
Darunavir/Ritonavir (DRV/r)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, and Etonogestrel Implants	If efficacy is of primary importance, can consider an alternative method (or a reliable method of barrier contraception in addition to this method)
Dosing Recommendation/Clinical Comment for DMPA[a]	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 44%[55] NE AUC ↓ 14%[55]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, small decrease in progestin levels No data on POPs

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Lopinavir/Ritonavir (LPV/r)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 55%[33] NE AUC ↓ 17% Patch • EE AUC ↓ 45%[33] • Norelgestromin AUC ↑ 83%[33] DMPA • DMPA AUC ↑ 46%[46] Etonogestrel Implant • Etonogestrel AUC ↑ 52%[70] Changes in ARV Levels and/or Effects on HIV *Patch* • LPV/r ↓ 19%[33] *DMPA* • No effect on HIV disease progression[46] • No change in LPV/r levels[46]
Clinical Studies	COC • Trend of increased pregnancy rate, but CIs overlap[58] Patch • Low serum progesterone consistent with no ovulations (n = 8)[33] DMPA • No pregnancies and no ovulations[46] • Trend of increased pregnancy rate, but CIs overlap[58] Etonogestrel Implant • No increase in pregnancy rate[58] LNG Implant • No increase in pregnancy rate[44,58]
Justification/Evidence for Recommendation	For COCs, nonsignificant increase in pregnancy rate. Small decrease in progestin level For patch, no ovulations, and progestin levels increased

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	For DMPA, evidence shows no effect on pregnancy rate or ovulations. Progestin levels increased. For implants, evidence shows no effect on pregnancy rate. Progestin levels increased.
Cobicistat (COBI)-Boosted Protease Inhibitors (PIs)	
Atazanavir/Cobicistat (ATV/c)	
Dosing Recommendation/Clinical Comment for COC/P/R	**Contraindicated** with drospirenone-containing hormonal contraceptives due to potential for hyperkalemia
Dosing Recommendation/Clinical Comment for POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Drospirenone AUC ↑ 2.3-fold[51] No change in LNG concentration 25% decrease in EE C24[50]
Clinical Studies	N/A
Justification/Evidence for Recommendation	No data on POPs
Darunavir/Cobicistat (DRV/c)	
Dosing Recommendation/Clinical Comment for COC/P/R	Clinical monitoring is recommended when DRV/c is used in combination with drospirenone-containing COCs as a result of the potential for hyperkalemia.
Dosing Recommendation/Clinical Comment for POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Drospirenone AUC ↑ 1.6-fold EE AUC ↓ 30%[51]
Clinical Studies	N/A
Justification/Evidence for Recommendation	No data on POPs.
Protease Inhibitors (PIs) Without Ritonavir (RTV)	
Atazanavir (ATV)	
Dosing Recommendation/Clinical Comment for COC/P/R	Prescribe oral contraceptive that contains no more than 30 mcg of EE or recommend alternative contraceptive method.
Dosing Recommendation/Clinical Comment for POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • EE AUC ↑ 48%[86] • NE AUC ↑ 110%[86]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, increased concentrations of estrogen and progestin, but the only data available are from the product label. No data on POPs
CCR5 Antagonist	
Maraviroc (MVC)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No significant effect on EE or LN[87]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE or progestin. No clinical data No data on POPs
Integrase Strand Transfer Inhibitors (INSTIs)	
Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/FTC/TAF)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	No significant drug interactions with EE or norgestimate
Clinical Studies	N/A
Justification/Evidence for Recommendation	No clinical data
Dolutegravir (DTG)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No significant effect on etonogestrel implants[69] • No significant effect on norgestimate or EE • No change in DTG AUC[47]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE or progestin. No clinical data No data on POPs

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Elvitegravir/Cobicistat (EVG/c)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • Norgestimate AUC ↑ 126% • EE AUC ↓ 25%[88,89]
Clinical Studies	N/A
Justification/Evidence for Recommendation	When administered as the 4-drug regimen EVG/c/FTC/TDF, increases in progestin and a small decrease in EE were observed. No clinical data No data on POPs
Raltegravir (RAL)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No change in EE • Norgestimate AUC ↑ 14%[90]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE and a small increase in progestin. No clinical data No data on POPs.
Cabotegravir-Long Acting (CAB-LA)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], Etonogestrel Implants	No additional contraceptive protection needed
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Oral contraceptive use was associated with ↓ CAB-LA Cmax compared to women not on any hormonal contraception (GMR 0.75; 90%CI:0.59-0.93; P=0.033). However, oral contraceptive use did not result in significant differences in other CAB-LA PK parameters.
Clinical Studies	N/A
Justification/Evidence for Recommendation	Although oral contraceptive use was associated with lower CAB-LA peak concentration, no other PK parameters PK parameters seen suggesting the association is not likely to be clinically significant.

[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: 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; CDC = Centers for Disease Control and Prevention; CI = confidence interval;

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

$C_{max;}$ = minimum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; COC = combined oral contraceptives; COC/P/R = COC/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; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; LNG = levonorgestrel; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NE = norethindrone; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; POP = progesterone-only oral contraceptive pills; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Sources: Panel on Antiretroviral Guidelines for Adults and Adolescents; Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV; Table 24a, Table 24b, and Table 24d

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