Women with HIV  

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Key Considerations and Recommendations

- **Antiretroviral therapy (ART)** is recommended for all persons living with HIV to improve their health and to reduce the risk of HIV transmission to sexual partners without HIV **(A1)**.

- When prescribing antiretroviral (ARV) drugs, clinicians should take into account that some ARV drugs have significant pharmacokinetic (PK) interactions with hormonal contraceptives; an alternative or additional effective contraceptive method is recommended to prevent unplanned pregnancy **(AIIII)**. Switching to an ARV drug that does not have interactions with hormonal contraceptives may also be considered **(BIII)**.

- A pregnancy test should be performed for those of childbearing potential prior to initiation of ART **(AIII)**.

- Preliminary data suggest there may be an increased risk of neural tube defects (NTDs) (0.9%) in infants born to women who were receiving dolutegravir (DTG) at the time of conception. Updated results have shown that the prevalence of NTDs in infants who were exposed to DTG at the time of conception is lower (0.3%) than reported in the preliminary data, but still higher than in infants born to women who received ART that did not include DTG (0.1%).

- Providers should discuss the potential risks and benefits of using DTG with individuals of childbearing potential and provide appropriate counseling so that individuals can make informed decisions.

- **Before initiating an integrase strand transfer inhibitor-based regimen in a person of childbearing potential, clinicians should review Table 6b for information to consider when choosing an ART regimen**.

- In a patient with multidrug-resistant HIV who has no alternatives to DTG, the decision of whether to use DTG should be made after carefully considering the risk of NTDs in the infant if pregnancy occurs while a patient is taking DTG, and the risks of persistent viremia in the patient and potential HIV transmission to the fetus if pregnancy occurs while the patient is not on effective ART.

- During pregnancy, an additional goal of ART is to maintain a viral load below the limit of detection throughout pregnancy to reduce the risk of transmission to the fetus and newborn **(A1)**.

- When selecting an ARV combination regimen for a pregnant woman, clinicians should consider the available safety, efficacy, and PK data on use during pregnancy for each agent. The risks and benefits of ARV use during pregnancy should be discussed with all individuals of childbearing potential **(AIII)** and clinicians should consult the most current Perinatal Guidelines when designing a regimen **(AIII)**.

**Rating of Recommendations:**  
**A** = Strong; **B** = Moderate; **C** = Optional

**Rating of Evidence:** **I** = Data from randomized controlled trials; **II** = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; **III** = Expert opinion

This section focuses on some unique clinical and therapeutic issues to consider and basic principles to follow when caring for cisgender women living with HIV. Cisgender women are defined as women who were assigned female at birth and who identify themselves as women. Some topics discussed in this section, such as contraception, drug-drug interactions between antiretroviral (ARV) drugs and hormonal therapy, and pregnancy, also apply to transgender men (men assigned female at birth), and individuals assigned female at birth who identify as nonbinary (gender identities that are not exclusively feminine or masculine) or gender fluid (gender identity is not fixed). See Transgender People with HIV for more information on the specific HIV care needs of these individuals. Clinicians who care for pregnant patients should consult the current Perinatal Guidelines for a more in-depth discussion on treating pregnant patients and guidance on managing these patients.

**Sex Difference Considerations in Antiretroviral Therapy**

In general, studies to date have not shown sex differences in virologic responses to antiretroviral therapy (ART).1-4 However, there are limited data showing that pharmacokinetics (PKs) for some ARV drugs may differ between men and women, possibly because of variations in factors such as body weight, plasma volume, gastric emptying time, plasma protein levels, cytochrome P 450 activity, drug transporter function, and excretion activity.5-7
Adverse Effects

Several studies with older ARV drugs have suggested that sex may influence the frequency, presentation, and severity of some ARV-related adverse events. Most notably, women are more likely to develop severe symptomatic hepatotoxicity with nevirapine (NVP) use⁸,⁹ and are more likely to develop symptomatic lactic acidosis with prolonged use of older nucleoside reverse transcriptase inhibitors (NRTIs) such as zidovudine (ZDV), stavudine, and didanosine.¹⁰ These agents are no longer recommended for use in people with HIV in the United States; although ZDV is still administered intravenously (IV) to some patients during delivery, it is not generally recommended for long-term use.

Some studies have investigated how metabolic complications that are associated with the use of ARV drugs differ between women and men. At 96 weeks after initiation of ART, women with HIV were less likely to have decreases in limb fat but more likely to have decreases in bone mineral density (BMD) than men with HIV.¹¹,¹² Women have an increased risk of osteopenia, osteoporosis, and fractures, particularly after menopause, and this risk is exacerbated by HIV and ART.¹³-¹⁶ ART regimens that contain tenofovir disoproxil fumarate (TDF), ritonavir-boosted protease inhibitors (PI/r), or both are associated with a significantly greater loss of BMD than regimens that contain other NRTIs and raltegravir (RAL).¹⁷-²⁰ Abacavir (ABC), NRTI-sparing regimens, and tenofovir alafenamide may be considered as alternatives to TDF for patients who are at risk of osteopenia or osteoporosis. Recommendations for the management of bone disease in people with HIV have been published.²¹

Adults and Adolescents with HIV Who Are of Childbearing Potential

All adults and adolescents with HIV who are of childbearing potential should be offered comprehensive reproductive and sexual health counseling and care as part of routine primary medical care. Topics for discussion should include safe sex practices, reproductive desires and options for conception, the HIV status of sexual partner(s), and the use of effective contraception to prevent unplanned pregnancy. Counseling should also include discussion of special considerations pertaining to ARV use when using hormonal contraceptives, when trying to conceive, and during pregnancy (see the Perinatal Guidelines).

Antiretroviral Regimen Considerations for Individuals Who Are Trying to Conceive or Who Cannot Use Effective Contraception

Efavirenz (EFV) is teratogenic in nonhuman primates. However, a meta-analysis that included data from 23 studies found no evidence for an increased risk of birth defects in infants born to women who received EFV during the first trimester compared with infants born to women who received other ARV drugs during the first trimester.²² EFV can be used in individuals of childbearing potential who are not using effective contraception or who are contemplating pregnancy. Individuals who become pregnant on EFV-containing regimens should continue their current regimens.

Preliminary data from a study in Botswana suggested that there is an increased risk of neural tube defects (NTDs) (0.9%) in infants born to women who were receiving dolutegravir (DTG) at the time of conception.²³,²⁴ Updated results have shown that the prevalence of NTDs in infants who were exposed to DTG at the time of conception is lower (0.3%) than reported in the preliminary data, but still higher than in infants who were exposed to ART that did not contain DTG (0.1%).²⁵,²⁶ Providers should discuss with individuals of childbearing potential the potential risks and benefits of taking DTG and provide appropriate counseling so that individuals can make informed decisions.

Before initiating an integrase strand transfer inhibitor (INSTI)-based regimen in a person of childbearing potential, clinicians should review Table 6b for information to consider when choosing an ART regimen. The key recommendations are listed below:

• **For individuals who are trying to conceive**, the Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating one of the following regimens, which are designated as *Preferred*
regimens during pregnancy in the Perinatal Guidelines: RAL, atazanavir/ritonavir, or darunavir/ritonavir plus TDF/emtricitabine, TDF/lamivudine (3TC), or ABC/3TC. DTG would be an Alternative, rather than a Preferred, option (BII).

- **For individuals who are not planning to conceive but who are sexually active and not using contraception,** consider a regimen’s effectiveness and tolerability, the available data on potential teratogenicity, and the person’s preferences (e.g., pill burden) when choosing between regimens that are recommended for initial therapy (see Table 6a). In this situation, DTG would be an Alternative, rather than Preferred, option (BII). If the person becomes pregnant, changes to the ARV regimen may be warranted. Clinicians should refer to the Perinatal Guidelines for recommendations.

- **For individuals who are using effective contraception,** a DTG-based regimen is one of the recommended options; however, clinicians should discuss the risks and benefits of using DTG with patients to allow them to make informed decisions (AIII).

- **An approach similar to that outlined for DTG should be considered for bictegravir-containing ART (AIII).**

**Reproductive Options for Serodiscordant Couples**

An individual who wishes to conceive with a serodiscordant partner should be informed of options to prevent sexual transmission of HIV while attempting conception. Interventions include screening and treating both partners for sexually transmitted infections (STIs), the use of ART to maximally suppress and maintain the viral load of the partner with HIV, the use of pre-exposure prophylaxis by the partner without HIV, male circumcision, and/or self-insemination with the sperm of the partner without HIV during the periovulatory period of the individual with HIV.

**Hormonal Contraception**

Safe and effective reproductive health and family planning services to prevent unplanned pregnancies and perinatal transmission of HIV are an essential component of care for individuals with HIV of childbearing age. These individuals should receive ongoing counseling on reproductive issues. Regardless of hormonal contraceptive use, individuals with HIV should be advised to consistently use condoms (male or female) during sex and to adhere to an HIV regimen that effectively maintains viral suppression. Both strategies are crucial to prevent transmission of HIV to partners without HIV and to protect against infection with other STIs. The following sections describe some factors to consider when hormonal contraceptives are used.

**Drug-Drug Interactions**

PK interactions between ARV drugs and hormonal contraceptives may reduce contraceptive efficacy. However, there are limited clinical data regarding interactions between ARV drugs and hormonal contraceptives, and the clinical implications of these interactions are unclear. The magnitudes of changes in drug concentrations that may reduce contraceptive efficacy or increase the risk of adverse effects are not known for all forms of contraceptives.

- **Combined Oral Contraceptives (COCs):** Several PIs, EFV, and elvitegravir/cobicistat (EVG/c)-based regimens have drug interactions with COCs. Interactions include either a decrease or an increase in blood levels of ethinyl estradiol, norethindrone, or norgestimate (see Tables 21a, 21b, and 21d), which potentially decreases contraceptive efficacy or increases the risk of estrogen- or progestin-related adverse effects (e.g., thromboembolism). EFV can decrease etonogestrel bioavailability and plasma progestin concentrations of COCs that contain ethinyl estradiol and norgestimate. Several regimens that include
a cobicistat-boosted PI, PI/r, or EVG/c decrease oral contraceptive estradiol levels.\textsuperscript{32-35} One PK study showed that DTG did not affect ethinyl estradiol or norgestimate levels.\textsuperscript{36} Several studies have shown that the use of etravirine, rilpivirine, and NVP did not significantly affect estradiol or progestin levels in individuals with HIV who were using COCs.\textsuperscript{37-39}

- **Injectable Contraceptives:** Small studies of women with HIV who were receiving injectable depot-medroxyprogesterone acetate (DMPA) while on ART showed no significant interactions between DMPA and EFV, lopinavir/ritonavir (LPV/r), NVP, nelfinavir, or NRTI drugs.\textsuperscript{40-43}

- **Contraceptive Implants:** Contraceptive failure of the etonogestrel implant in women on EFV-based therapy has been reported.\textsuperscript{44,45} Studies of women with levonorgestrel- and etonogestrel-releasing implants reported that participants who received EFV-based ART had decreased bioavailability of levonorgestrel and etonogestrel.\textsuperscript{46-48} These studies did not identify any change in hormone concentrations when the implants were used in those taking NVP\textsuperscript{46,48} or LPV/r.\textsuperscript{47} Similarly, two retrospective cohort evaluations that were conducted in Swaziland and Kenya showed an increased risk of contraceptive failure in women using contraceptive implants and receiving EFV.\textsuperscript{49,50}

Concerns about PK interactions between oral or implantable hormonal contraceptives and ARV drugs should not prevent clinicians from prescribing hormonal contraceptives for individuals on ART who prefer this contraceptive method. However, an alternative or additional effective contraceptive method is recommended when there are significant drug interactions between hormonal contraceptives and ARV drugs (see Tables 21a, 21b, and 21d and the Perinatal Guidelines).

**Risk of HIV Acquisition and Transmission**

Studies have produced conflicting data on the association between hormonal contraception and the risk of acquisition of HIV.\textsuperscript{51} Most of the retrospective studies involved couples in which the partners with HIV were not taking ART. A retrospective secondary analysis of two studies of serodiscordant couples in Africa in which the partner with HIV was not receiving ART found that, compared to women who did not use hormonal contraception, those using hormonal contraception (the majority of study participants were using injectable DMPA) had a two-fold increased risk of acquiring or transmitting HIV. Higher genital HIV RNA concentrations have been found in women with HIV who were using hormonal contraception than in those who were not using hormonal contraceptives.\textsuperscript{52} Oral contraceptive use was not significantly associated with transmission of HIV; however, the number of women who were using oral contraceptives in this study was insufficient to adequately assess risk.

A World Health Organization expert group reviewed all available evidence regarding hormonal contraception use and HIV transmission to a partner without HIV and recommended that individuals with HIV can continue to use all existing hormonal contraceptive methods without restriction.\textsuperscript{53} Further research is needed to definitively determine whether hormonal contraceptive use is an independent risk factor for acquisition and transmission of HIV, particularly in the setting of ART. Regardless, the potential association between hormonal contraception use and HIV transmission in the absence of ART underscores the importance of ART-induced viral suppression to reduce transmission risk.

Intrauterine devices (IUDs) appear to be a safe and effective contraceptive option for individuals with HIV.\textsuperscript{54-56} Although studies have focused primarily on IUDs that do not contain hormones (e.g., copper IUDs), several small studies have found that levonorgestrel-releasing IUDs are also safe and are not associated with increased genital tract shedding of HIV.\textsuperscript{57-59}

**Pregnancy**

Clinicians who are caring for pregnant adults and adolescents with HIV should review the Perinatal Guidelines. The use of combination ARV regimens is recommended for all pregnant persons with HIV,
regardless of virologic, immunologic, or clinical parameters, for their own health and to prevent HIV transmission to the fetus (AI). Pregnant individuals with HIV should be counseled regarding the known benefits and risks of using ARV drugs during pregnancy to the woman, fetus, and newborn. They should be strongly encouraged to receive ART for their own health and their infants’ health. Open, nonjudgmental, and supportive discussion should be used to encourage them to adhere to care.

**Prevention of Perinatal HIV Transmission**

The use of ART and the resultant reduction of HIV RNA levels decrease the risk of perinatal HIV transmission. The goal of ART is to achieve maximal and sustained viral suppression throughout pregnancy. Long-term follow-up is recommended for all infants who were exposed to ART in utero, regardless of the infant’s HIV status (see the Perinatal Guidelines).

**Antiretroviral Regimen Considerations**

Pregnancy should not preclude the use of optimal ARV regimens. As in nonpregnant individuals, genotypic resistance testing is recommended for all pregnant persons before initiating ARV drugs (AIII) and for those with detectable HIV RNA while on ART (AI). However, ART initiation should not be delayed pending genotypic resistance test results. The ARV regimen can be modified, if necessary, once the resistance test results are available (BIII). Unique considerations that influence recommendations on the ARV drugs to use during pregnancy include the following:

- Physiologic changes that are associated with pregnancy and that potentially change the PKs of ARV drugs, which may affect ARV dosing at different stages of pregnancy;
- Potential ARV-associated adverse effects in pregnancy;
- Potential for nonadherence to a particular regimen during pregnancy; and
- Potential short-term and long-term effects of an ARV drug on the fetus and newborn, which are unknown for many drugs.

ART is considered the standard of care for pregnant individuals with HIV, both to treat HIV infection and prevent perinatal transmission of HIV. Clinicians should review the Perinatal Guidelines for ARV drug recommendations, including recommendations on the use of DTG and other INSTIs, for individuals who have recently received an HIV diagnosis or those who become pregnant while on ART.

If maternal HIV RNA is ≥1,000 copies/mL (or unknown) near delivery, IV infusion of ZDV during labor is recommended regardless of the mother’s antepartum regimen and resistance profile and the mode of infant delivery (AI). Administration of combination ART should continue during labor and before a cesarean delivery (oral medications can be administered with sips of water during this time).

Clinicians who are treating pregnant individuals with HIV are strongly encouraged to report cases of prenatal exposure to ARV drugs (either administered alone or in combination) to the Antiretroviral Pregnancy Registry. The registry collects observational data regarding exposure to Food and Drug Administration-approved ARV drugs during pregnancy to assess potential teratogenicity.

**Postpartum Management**

Following delivery, clinical, immunologic, and virologic follow-up should continue as recommended for nonpregnant adults and adolescents. Individuals with HIV should be counseled to avoid breastfeeding; maternal ART reduces, but does not eliminate, the risk of HIV transmission of HIV in breast milk, and postnatal transmission can occur despite maternal ART. Persons with HIV should not premasticate food and feed it to their infants, because the practice has been associated with transmission of HIV. ART is currently recommended for all individuals with HIV (AI); therefore, maternal ART should be continued after delivery. For more information regarding postpartum management of HIV, refer to the Perinatal Guidelines.
Several studies have demonstrated that adherence to ART may decline during the postpartum period. Clinicians should address ART adherence at each postpartum clinic visit, including an evaluation of specific factors that facilitate adherence or that present a barrier to adherence. Clinicians may recommend an intervention to improve adherence (see Adherence to the Continuum of Care).

**References**


Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV