Panel’s Recommendations

- Antiretroviral therapy (ART) is recommended for all pregnant people with HIV to reduce the risk of perinatal HIV transmission and to optimize the health of the pregnant person (AII). Initiating ART as soon as possible in pregnant people who have never received antiretroviral (ARV) drugs is recommended, based on data demonstrating that earlier virologic suppression is associated with a lower risk of perinatal HIV transmission (AII).

- The results of ARV drug-resistance studies should guide the selection of ARV regimens in people whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 copies/mL to 1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AII). However, ART initiation should not be delayed while awaiting results of resistance testing. When ART is initiated before the results of the drug-resistance assays are available, the ARV regimen should be modified, if necessary, based on the resistance assay results (AII).

- ARV regimens that are Preferred for the treatment of pregnant people with HIV who are ARV-naive include a dual-nucleoside reverse transcriptase inhibitor combination (abacavir plus lamivudine [3TC], tenofovir disoproxil fumarate plus either emtricitabine [FTC] or 3TC, or tenofovir alafenamide plus either FTC or 3TC) and either a ritonavir-boosted protease inhibitor (atazanavir/ritonavir or darunavir/ritonavir) or an integrase strand transfer inhibitor (dolutegravir irrespective of trimester) or raltegravir (see Table 4 and Recommendations for Use of Antiretroviral Drugs During Pregnancy) (AIII).

- The Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal HIV (the Panel) emphasizes the importance of counseling and informed decision-making with regard to all ARV regimens for pregnant people with HIV (AIII). See Appendix C: Antiretroviral Counseling Guide for Health Care Providers for more information.

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

Pregnant people with HIV should receive standard clinical, immunologic, and virologic evaluations. Consistent with the principles of HIV treatment for nonpregnant adults, clinicians should discuss treatment options with pregnant people and offer antiretroviral (ARV) regimens that contain at least three drugs. These regimens reduce the risk of perinatal HIV transmission and optimize the pregnant person’s health. Use of an ARV regimen that successfully reduces plasma HIV RNA to undetectable levels substantially lowers the risk of perinatal transmission of HIV, minimizes the need to consider elective cesarean delivery as an intervention to reduce the risk of transmission, and reduces the risk of ARV drug resistance.

Decisions about the timing and management of antiretroviral therapy (ART) in people who have not previously received ART should be guided by several key principles:
A suppressed viral load at the time of delivery markedly reduces the risk of perinatal HIV transmission.

In an analysis of 12,486 infants delivered by women with HIV between 2000 and 2011 in the United Kingdom and Ireland, the overall perinatal transmission rate declined from 2.1% in 2000 and 2001 to 0.46% in 2010 and 2011. The transmission risk was significantly lower in women with viral loads <50 copies/mL (0.09%) than in women with viral loads of 50 copies/mL to 399 copies/mL (1.0%), regardless of the type of ARV regimen used or the mode of infant delivery. The decline in perinatal transmission rates over time was attributed to the increasing number of women on ART at the time of conception and reductions in the proportion of women who either initiated ART late in pregnancy or who never received ART before delivery.

Initiating ART early increases the likelihood that a person will achieve viral suppression by the time of delivery, further reducing the risk of perinatal HIV transmission.

Although most perinatal HIV transmission events occur late in pregnancy or during delivery, recent analyses suggest that early control of viral replication may be important in preventing transmission. In the prospective multicenter French Perinatal Cohort, both maternal viral load at delivery and the timing of ART initiation were independently associated with perinatal HIV transmission rate. For women who had achieved viral loads <50 copies/mL at the time of delivery, transmission risk was 0.9% with third-trimester ART initiation, 0.5% with second-trimester initiation, 0.2% with first-trimester initiation, and 0% (of more than 2,500 infants) with preconception ART initiation. Regardless of when ART was initiated, perinatal transmission rate was higher for women with viral loads of 50 copies/mL to 400 copies/mL near delivery than for those with <50 copies/mL, and it was higher for people with viral loads >400 copies/mL at delivery (4.4% for women who initiated ART in the third trimester and who had viral loads >400 copies/mL at delivery). Other studies have similarly found lack of early and sustained viremic control to be strongly associated with increased risk of perinatal HIV transmission.

These data suggest that ART should be initiated as early as possible in ARV-naive pregnant people because early and sustained control of HIV viral replication is associated with a decreased risk of perinatal HIV transmission. Other studies have demonstrated that baseline viral load is significantly associated with the likelihood of viral suppression by the time of delivery; thus, prompt initiation of ART is particularly important in pregnant people who have high baseline viral loads.

The benefits of initiating ART early in pregnancy generally outweigh the risks.

The susceptibility of fetuses to the potential adverse effects of drugs is dependent on multiple factors, including the gestational age of the fetus at the time of medication exposure (see Teratogenicity and Antiretroviral Drug Regimens and Maternal and Neonatal Outcomes). The effects of taking ARV drugs during pregnancy are not fully known; however, in general, the data from observational studies on the incidence of birth defects among fetuses/infants of women who received ARV regimens during pregnancy have been reassuring. No differences have been found between the rates of birth defects among infants with first-trimester exposures to most ARV drugs and the rates among infants with later gestational exposures or the rates reported in the general population. See Teratogenicity for a more detailed discussion of the adverse events that are associated with the use of specific ARV drugs. The decision about when to initiate ART should be discussed by health care providers and
Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States

their patients. The discussion should include an assessment of the pregnant person’s health status, the risks and benefits to the individual’s health, and the potential risks and benefits to the fetus.

**ARV drugs further reduce perinatal HIV transmission risk through infant pre-exposure and post-exposure prophylaxis.**

ARV drugs reduce the risk of perinatal HIV transmission through a number of different mechanisms. Although lowering antenatal viral load is an important component of preventing HIV transmission in people with higher viral loads, ART use during pregnancy reduces transmission even in people with low viral loads.15-19 Additional mechanisms that reduce the risk of perinatal HIV transmission include pre-exposure prophylaxis and post-exposure prophylaxis for the infant.

The passage of an ARV drug across the placenta produces drug levels that inhibit viral replication in the fetus, effectively providing pre-exposure prophylaxis. This is particularly important during the birth process when intensive viral exposure can occur. All **Preferred** nucleoside reverse transcriptase inhibitors (NRTIs), as well as dolutegravir (DTG) and raltegravir (RAL), are known to have high transplacental passage (see **Table 11**). ARV drugs administered to the infant after birth provide a form of post-exposure prophylaxis (see **Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection**).20

**Specific ARV regimens are Preferred for use in pregnancy.**

The decision about which ARV drugs to use during pregnancy should be made by a pregnant person after discussing the known and potential benefits and risks to the individual and the fetus/infant with their health care provider.

All pregnant people with HIV should be counseled that the use of ART is recommended, regardless of viral load, to optimally reduce the risk of perinatal transmission. If, after counseling, a person chooses to forgo the use of ARV drugs during pregnancy, this decision should be re-addressed during subsequent medical appointments. The **Perinatal HIV Hotline** (1-888-448-8765) can provide information to assist with the discussion.

**Table 4** and **Table 5** outline the ARV regimens that are designated by the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission as **Preferred** for treatment of pregnant people with HIV who have never received ARV drugs, people who are continuing or restarting ART in pregnancy, or people who are trying to conceive (see **Pregnant People with HIV Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications** and **Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV**). Drugs or drug combinations are designated as **Preferred** for therapy in pregnant people when clinical trial data in adults have demonstrated efficacy and durability with acceptable toxicity and ease of use, and when pregnancy-specific pharmacokinetic (PK) data are available to guide dosing. In addition, the available data must suggest a favorable risk-benefit balance for the drug or drug combination compared to other ARV drug options; the assessment of risks and benefits should incorporate outcomes for pregnant people, fetuses, and infants. Some **Preferred** drugs or regimens may have minimal toxicity or teratogenicity risks that are offset by other advantages for people with HIV who are pregnant or who are trying to conceive. Therefore, it is important for health care providers to read all the information on each drug in the Perinatal Guidelines before administering any of these medications to patients (see **Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy**) and provide appropriate patient counseling to support informed
decision-making (see Appendix C: Antiretroviral Counseling Guide for Health Care Providers). Preferred regimens include a dual-NRTI combination (abacavir plus lamivudine [3TC] or tenofovir disoproxil fumarate [TDF], or tenofovir alafenamide [TAF] plus emtricitabine [FTC] or 3TC) used with either a ritonavir-boosted protease inhibitor (PI; atazanavir/ritonavir [ATV/r] or darunavir/ritonavir) or an integrase strand transfer inhibitor (INSTI) DTG or RAL.

RAL or DTG has been suggested for use when ART is initiated late in pregnancy, particularly for people who have high viral loads, because of the ability of RAL and DTG to suppress viral load rapidly (a decrease of approximately 2 log10 copies/mL occurs by Week 2 of therapy with these drugs). In the Dolutegravir in Pregnant HIV Women and Their Neonates (DolPHIN 2) study, 268 ART-naive women in Uganda and South Africa were randomized to receive DTG plus two NRTIs or efavirenz (EFV) plus two NRTIs at a median gestational age of 31 weeks. At delivery, women in the DTG arm were significantly more likely to achieve viral loads of <50 copies/mL (74.1% vs. 42.7%; adjusted risk ratio 1.64 [1.31–2.06], P < 0.0001) than women in the EFV arm. Similarly, the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) 1081 trial randomized 408 ART-naive women in South America, Africa, Thailand, and the United States who presented late in pregnancy (20 to <37 weeks gestation) to receive RAL plus two NRTIs or EFV plus two NRTIs. Among 307 women in the primary efficacy analysis, 84% in the EFV group and 94% in the RAL group achieved a viral load of <200 copies/mL at or near delivery (absolute difference 10% [95% CI, 3% to 18%]; P = 0.0015); the difference primarily occurred among women enrolling later in pregnancy (interaction P = 0.040). The median time to achieve a viral load of <200 copies/mL was 8 days for women who received RAL-based ART and 15 days for women who received EFV-based ART. The decline in viral load was greater in the women who received RAL than in those who received EFV at 2, 4, and 6 weeks after initiation.

Resistance tests should be performed, but ART initiation should not be delayed while waiting for results.

Standard ARV drug-resistance testing should be performed before starting an ARV regimen when plasma HIV RNA levels are above the threshold for resistance testing (i.e., >500 copies/mL to 1,000 copies/mL). INSTI-resistance testing is not routinely recommended, but it should be performed for people who are at risk for INSTI resistance (e.g., people with partners who were treated with INSTIs, people who had prior treatment that included INSTIs; see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). For details regarding genotypic and phenotypic resistance testing, see the Adult and Adolescent Antiretroviral Guidelines. Given the association between earlier viral suppression and lower risk of perinatal HIV transmission, ART should be initiated as soon as possible in pregnant people who have never received ARV drugs without waiting for the results of resistance testing. The regimen can be modified, if required, when test results return. Either an INSTI-based or a PI-based ARV regimen can be considered when the results of resistance testing are not available to inform the selection of ARV drugs because clinically significant resistance to PIs and INSTIs is uncommon in ARV-naive individuals.

Regimens other than combination (three-drug) ART are not recommended.

The use of zidovudine (ZDV) monotherapy during pregnancy is not recommended because ART provides clear health benefits to the pregnant individual and helps prevent perinatal HIV transmission. In the past, the use of ZDV monotherapy during pregnancy for prophylaxis of perinatal transmission was an option for people who had low viral loads (i.e., <1,000 copies/mL) on no ARV drugs. Although the Adult and Adolescent Antiretroviral Guidelines recommend some two-drug...
ARV regimens in certain clinical circumstances, two-drug ARV regimens are not recommended for initiation of ART in ARV-naive pregnant people.

**ARV regimens can be modified postpartum.**

ARV regimens that were initiated during pregnancy can be modified after delivery. People may be able to use some simplified regimens that could not be used during pregnancy because the pregnancy, safety, and/or PK data for those regimens were insufficient. Decisions regarding which specific ARV agents to use postpartum should be made by patients after they have discussed their options with their HIV care providers. These decisions should take several factors into consideration, including the current adult ART recommendations, the patient’s plans for contraceptive use and future pregnancies, and individual adherence considerations and medication preferences (see General Principles Regarding Use of Antiretroviral Drugs During Pregnancy).
References


