



Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Pregnant Women Living with HIV Who Have Never Received Antiretroviral Drugs (Antiretroviral Naive) (Last updated November 14, 2017; last reviewed November 14, 2017)

Panel's Recommendations

- Antiretroviral therapy (ART) should be recommended to all pregnant women living with HIV to reduce the risk of perinatal transmission of HIV and to optimize the health of the mother (AI). Initiation of ART as soon as HIV is diagnosed during pregnancy is recommended based on data demonstrating that earlier virologic suppression is associated with lower risk of transmission (AII).
- Antiretroviral (ARV) drug-resistance studies should be performed to guide selection of regimens in women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 copies/mL) unless drug-resistance studies have already been performed (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)) (AI). If 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 (BIII).
- The choice of regimen should be informed by current adult treatment guidelines, what is known about the use of specific drugs in pregnancy, and the risk of teratogenicity (see [Table 6](#) and [Table 9](#)) and maternal factors such as nausea, vomiting, and comorbid conditions. ART regimens that are preferred for the treatment of pregnant women living with HIV who are ARV-naive include: a dual nucleoside reverse transcriptase inhibitor combination (abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine or lamivudine) and either a ritonavir-boosted protease inhibitor (atazanavir/ritonavir or darunavir/ritonavir) or an integrase strand transfer inhibitor (raltegravir) (see [Table 6](#)) (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

Pregnant women living with HIV infection should receive standard clinical, immunologic, and virologic evaluation. They should be counseled about and offered antiretroviral therapy (ART) containing at least three drugs for their own health and for the prevention of perinatal transmission of HIV, consistent with the principles of treatment for non-pregnant adults.¹ Use of an ART regimen that successfully reduces plasma HIV RNA to undetectable levels substantially lowers the risk of perinatal transmission of HIV, minimizes the need for consideration of elective cesarean delivery as an intervention to reduce risk of transmission, and reduces risk of antiretroviral (ARV) drug resistance in the mother. In an analysis of perinatal transmission in a total of 12,486 infants delivered by women living 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 (0.09%) in women with viral loads <50 copies/mL compared with a risk of 1.0% in women with viral loads of 50 to 399 copies/mL, regardless of the type of ARV regimen or mode of delivery.² The continued decline in perinatal transmission rates was attributed to the increasing number of women on ART at the time of conception and reductions in the proportion of women either initiating ART late in pregnancy or never receiving ART prior to delivery. Similar data from Canada in 1,707 pregnant women living with HIV followed between 1997 and 2010 showed perinatal transmission was 1% in all mothers receiving ART and 0.4% if more than 4 weeks of ART was received.³

ARV drug-resistance testing should be performed before starting an ARV regimen if plasma HIV RNA levels are above the threshold for resistance testing (i.e., >500 copies/mL). For details regarding genotypic and phenotypic resistance testing, see the [Adult and Adolescent Guidelines](#)). Given the association of earlier viral suppression with lower risk of transmission as discussed above, during pregnancy, ART should be initiated as soon as HIV is diagnosed without waiting for the results of resistance testing, with modification of the regimen, if required, when test results return. **Either a protease inhibitor (PI)-based or integrase strand transfer inhibitor (INSTI)-based** ART regimen can be considered when the results of resistance testing are not available to inform selection of ARV drugs because clinically significant resistance to PIs **and INSTIs** is uncommon in ARV-naive individuals.

[Table 6](#) outlines the ARV regimens that are preferred for treatment of pregnant women living with HIV who have never received ARV drugs. These recommendations are based on available data indicating acceptable

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toxicity profiles, ease of use, pharmacokinetic data in pregnancy, and lack of evidence of teratogenic effects or established adverse outcomes for mother, fetus, or newborn in addition to optimal ARV efficacy and durability. Preferred regimens include a dual nucleoside reverse transcriptase inhibitor (NRTI) combination (abacavir/lamivudine or tenofovir disoproxil fumarate with emtricitabine or lamivudine) in combination with either a ritonavir-boosted PI (atazanavir/ritonavir or darunavir/ritonavir) or an INSTI (raltegravir). **Raltegravir is the preferred INSTI for women who are ARV-naïve and experience with its efficacy and safety in pregnant women is increasing.** Selection of these regimens should be based on individual patient characteristics and needs (see [Table 9](#)).

Susceptibility of fetuses to the potential teratogenic effects of drugs is dependent on multiple factors, including the gestational age of the fetus at exposure (see the [Teratogenicity](#) section). Although fetal effects of ARV drugs are not fully known, in general, reports of birth defects in fetuses/infants of women enrolled in observational studies who receive ARV regimens during pregnancy have been reassuring. There have been no differences in the rates of birth defects for first-trimester compared with either later gestational exposures or with rates reported in the general population.⁴⁻⁷ The decision about when to initiate ART should be carefully considered by health care providers and their patients. The discussion should include an assessment of a woman's health status and the benefits and risks to her health and the potential risks and benefits to the fetus.

Although most perinatal 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, maternal viral load at delivery and timing of ART initiation were both independently associated with perinatal transmission rate. The perinatal transmission rate increased from 0.2% for women starting ART before conception to 0.4%, 0.9%, and 2.2% for those starting in the first, second, or third trimester (respectively). Regardless of when ART was initiated, the perinatal transmission rate was higher for women with viral loads of 50 to 400 copies/mL near delivery than for those with <50 copies/mL.⁸ In an earlier publication involving the same cohort, lack of early and sustained control of maternal viral load appeared strongly associated with residual perinatal transmission of HIV.⁹ That study evaluated risk factors for perinatal transmission in women with HIV RNA <500 copies/mL at the time of delivery; overall HIV transmission was 0.5%. Women who transmitted were less likely to have received ARV drugs at the time of conception than non-transmitters and were less likely to have HIV RNA <500 copies/mL at 14, 28, and 32 weeks' gestation. By multivariate analysis, plasma viral load at 30 weeks' gestation was significantly associated with transmission. Among women starting ARV drugs during pregnancy, the gestational age at initiation of therapy did not differ between groups (30 weeks), but viral load tended to decrease earlier in the non-transmitters, although this was not statistically significant. The number of patients initiating therapy during pregnancy was too small to assess whether initiation of ARV drugs in the first trimester was associated with lower rates of transmission. These data suggest that early and sustained control of HIV viral replication is associated with decreasing residual risk of transmission and favor initiating ART sufficiently early in ARV-naïve women to suppress viral replication by the third trimester. Other studies have demonstrated that baseline viral load is significantly associated with the likelihood of viral suppression by delivery, and thus, prompt initiation of ART would be particularly important in pregnant women who have high baseline viral loads.¹⁰⁻¹² However, the potential benefits of earlier initiation of ART must be balanced against the unknown long-term outcome of first-trimester ARV exposure to the fetus.

ART is recommended for all pregnant women living with HIV, regardless of viral load. Although rates of perinatal transmission are low in women with undetectable or low HIV RNA levels, there is no threshold below which lack of transmission can be ensured.¹³⁻¹⁵ The mechanism by which ARV drugs reduce perinatal transmission of HIV is multifactorial. Although lowering maternal antenatal viral load is an important component of prevention in women with higher viral load, ARV prophylaxis is effective even in women with low viral load.¹⁶⁻²⁰ Additional mechanisms of protection include pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis of the infant. With PrEP, passage of the ARV drug across the placenta results in presence of drug levels sufficient for inhibition of viral replication in the fetus, particularly during the birth process when there is intensive viral exposure. Therefore, whenever possible, ART regimens initiated during

pregnancy should include an NRTI with high transplacental passage, such as lamivudine, emtricitabine, tenofovir, or abacavir (see [Table 9](#)).²¹⁻²⁴ With post-exposure prophylaxis, ARV drugs are administered to the infant after birth.

The use of zidovudine monotherapy during pregnancy is no longer recommended because of the clear health benefit of ART to the mother and for the prevention of perinatal transmission of HIV. In the past, use of zidovudine alone during pregnancy for prophylaxis of perinatal transmission was considered to be an option for women with low viral loads (i.e., <1,000 copies/mL) on no ARV drugs.

All pregnant women living with HIV infection should be counseled that ART is recommended, regardless of viral load, to optimally reduce the risk of perinatal transmission. If, after counseling, a woman chooses to forgo the use of ARV drugs during pregnancy, this decision should be re-addressed during subsequent medical appointments. The Perinatal Hotline is a resource that can be accessed to assist with the discussion (www.hivpregnancyhotline.org).

Raltegravir has been suggested for use in late pregnancy in women who have high viral loads because of its ability to rapidly suppress viral load (approximately 2 log copies/mL decrease by Week 2 of therapy).²⁵⁻²⁸ Two case series have reported the effect of adding raltegravir to ART regimens. In one, 4 women diagnosed with HIV infection in the third trimester experienced a mean viral load decline per week of 1.12 log after raltegravir was added to a standard ARV regimen.²⁹ In the second publication, raltegravir was either initiated as part of an ART regimen in 9 ARV-naïve women or added to an existing ARV regimen in 5 women who conceived on ART but had persistent viremia. Raltegravir was initiated at a gestational age of 34 weeks or later.³⁰ The median exposure time to raltegravir was 17 days and the mean viral load decline was 2.6 log. Although no raltegravir-related adverse effects were noted in these reports, marked elevations in hepatic transaminases were reported in a single pregnant woman living with HIV when raltegravir was added to an ART regimen.³¹ Although raltegravir is the preferred INSTI for women who are ARV-naïve, the efficacy and safety of this approach has only been described in anecdotal reports and, therefore, cannot be routinely recommended at this time.

The ART regimen initiated during pregnancy can be modified after delivery to include simplified regimens that were not used in pregnancy because safety data were insufficient. Decisions regarding continuation of an ART regimen or which specific ARV agents to use should be made by women in consultation with their HIV care providers, taking into account current recommendations and life circumstances (see [General Principles Regarding Use of Antiretroviral Drugs during Pregnancy](#)).

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