



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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Panel's Recommendations

- Plasma HIV RNA levels should be monitored at the initial visit (**AI**); 2 to 4 weeks after initiating (or changing) antiretroviral (ARV) drug regimens (**BI**); monthly until RNA levels are undetectable (**BIII**); and then at least every 3 months during pregnancy (**BIII**). HIV RNA levels also should be assessed at approximately 34 to 36 weeks' gestation to inform decisions about mode of delivery (see [Transmission and Mode of Delivery](#)) and to inform decisions about optimal treatment of the newborn (see [Infant ARV Prophylaxis](#)) (**AIII**).
- CD4 T lymphocyte (CD4) cell count should be monitored at the initial antenatal visit (**AI**) and every 3 to 6 months during pregnancy (**BIII**). Monitoring of CD4 cell count can be performed every 6 months in patients on combination antiretroviral therapy (ART) with consistently suppressed viral load who have CD4 counts well above the threshold for opportunistic infection risk (**CIII**).
- HIV drug-resistance studies should be performed before starting ARV regimens in all ARV-naïve pregnant women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) unless they have already been tested for ARV resistance (**AIII**). HIV drug-resistance studies should be performed before modifying ARV regimens for those entering pregnancy with detectable HIV RNA levels that are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) while receiving ARV drugs or who have suboptimal virologic response to ARV drugs started during 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**).
- Monitoring for complications of ARV drugs during pregnancy should be based on what is known about the adverse effects of the drugs a woman is receiving (**AIII**).
- HIV-infected women taking ART during pregnancy should undergo standard glucose screening at 24 to 28 weeks' gestation (**AIII**). Some experts would perform earlier glucose screening in women receiving ongoing protease inhibitor (PI)-based regimens initiated before pregnancy, similar to recommendations for women with risk factors for glucose intolerance (**BIII**). For further information on PIs see [Combination Antiretroviral Drug Regimens and Pregnancy Outcome](#).
- **Ultrasound in the first trimester, or as soon as possible thereafter**, is recommended to confirm gestational age and, if scheduled cesarean delivery is necessary, to guide timing of the procedure (see [Transmission and Mode of Delivery](#)) (**AI**).
- In women on effective antiretroviral therapy (ART), no perinatal transmissions have been reported after amniocentesis, but a small risk of transmission cannot be ruled out. Amniocentesis should be performed on HIV-infected women only after initiation of an effective ART regimen and, ideally, when HIV RNA levels are undetectable (**BIII**). In women with detectable HIV RNA levels in whom amniocentesis is deemed necessary, consultation with an expert should be considered (**BIII**).

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

More frequent viral load monitoring is recommended in pregnant than non-pregnant individuals because of the importance of rapid and sustained viral suppression in preventing perinatal HIV transmission. In individuals who are adherent to their antiretroviral (ARV) regimen and do not harbor resistance mutations to the prescribed drugs, viral suppression is generally achieved in 12 to 24 weeks—although it may take longer in some patients and may be dependent on starting viral load. Most patients with adequate viral response at 24 weeks of treatment have had at least a 1 log viral load decrease within 1 to 4 weeks after starting therapy.^{1,2} Viral load should be monitored in HIV-infected pregnant women at the initial visit, 2 to 4 weeks after initiating or changing ARV regimens, monthly until undetectable, and at least every 3 months thereafter. If adherence is a concern, more frequent monitoring is recommended because of the potential increased risk of perinatal HIV infection associated with detectable HIV viremia during pregnancy.³

Viral load also should be assessed at approximately 34 to 36 weeks' gestation to inform decisions about mode of delivery and about optimal treatment of newborns (see [Transmission and Mode of Delivery](#)).

In HIV-infected pregnant women, CD4 T lymphocyte (CD4) cell count should be monitored at the initial visit and at least every 3 months during pregnancy. CD4 cell counts can be performed every 6 months in patients who are clinically stable with consistently suppressed viral load who have CD4 counts well above the threshold for opportunistic infection risk.^{1,4,5}

Whenever feasible, ARV drug-resistance testing should be performed before initiation of ARV drugs if HIV RNA levels are above the threshold for resistance testing, but therapy should not be delayed once the blood is drawn and results are pending. If the results demonstrate resistance, then the regimen can subsequently be adjusted. Testing also should be performed on women taking an ARV regimen who have suboptimal viral suppression or who have persistent viral rebound to detectable levels after prior viral suppression on an ARV regimen (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)). Drug-resistance testing in the setting of virologic failure is most useful if performed while patients are receiving ARV drugs or within 4 weeks after discontinuation of drugs. Even if more than 4 weeks have elapsed since the ARVs were discontinued, resistance testing can still provide useful information to guide therapy, though it may not detect previously selected resistance mutations. Genotypic testing is preferable to phenotypic testing because it costs less, has a faster turnaround time, and is more sensitive for detection of mixtures of wild-type and resistant virus.

Monitoring for potential complications of ARV drugs during pregnancy should be based on what is known about the adverse effects of the drugs a woman is receiving. For example, routine hematologic monitoring is recommended for women receiving zidovudine-containing regimens and routine renal monitoring should be recommended for women on tenofovir. Liver function should be monitored in all women receiving ARV drugs. Hepatic dysfunction has been observed in pregnant women on protease inhibitors (PI), and hepatic steatosis and lactic acidosis in pregnancy have been related to nucleoside reverse transcriptase inhibitor use. **Pregnant women in general are more likely to have elevated liver enzymes than their non-pregnant counterparts.**^{6,7}

Pregnancy increases the risk of hyperglycemia. PI drugs have been associated with increased risk of hyperglycemia, new-onset diabetes mellitus, exacerbation of existing diabetes mellitus, and diabetic ketoacidosis.⁸⁻¹¹ However, the majority of studies in HIV-infected pregnant women have not shown an increased risk of glucose intolerance with PI-based regimens during pregnancy. A prospective study including detailed evaluations for glucose intolerance and insulin resistance among HIV-infected pregnant women did not find differences between women on PI-containing and non-PI-containing regimens.¹² In both groups, the rate of impaired glucose tolerance was high (38%), but that may be related to high body mass index and race/ethnicity among trial subjects. HIV-infected women receiving antiretroviral therapy (ART) during pregnancy should receive the standard glucose screening at 24 to 28 weeks' gestation that is recommended for all pregnant women. Some experts would perform earlier glucose screening in women receiving ongoing PI-based ART initiated before pregnancy, similar to recommendations for women with risk factors for glucose intolerance.

Accurate estimation of date of delivery is critical to planning elective cesarean deliveries at 38 weeks' gestation to prevent perinatal transmission in HIV-infected women with elevated HIV RNA viral loads. Therefore, first-trimester ultrasound is recommended to confirm gestational age and to provide the most accurate estimation of gestational age at delivery (see [Transmission and Mode of Delivery](#)).¹³⁻¹⁵ In patients who are not seen until later in gestation, second-trimester ultrasound can be used for both anatomical survey and determination of gestational age.

Although data are still somewhat limited, the risk of HIV transmission does not appear to be increased with amniocentesis or other invasive diagnostic procedures in women receiving effective ART resulting in viral suppression. This is in contrast to the era before effective ART, during which invasive procedures such as amniocentesis and chorionic villus sampling (CVS) were associated with a two- to four-fold increased risk of perinatal transmission of HIV.¹⁶⁻¹⁹ Although no transmissions have occurred among 159 cases reported to date of amniocentesis or other invasive diagnostic procedures among women on effective ART, a small increase in risk of transmission cannot be ruled out.²⁰⁻²³ HIV-infected women who have indications for invasive testing in pregnancy (e.g., abnormal ultrasound or aneuploidy screening) should be counseled about the potential risk of transmission of HIV along with other risks of the procedure and allowed to make an informed decision about testing. Some experts consider CVS and cordocentesis too risky to offer to HIV-infected women, and they recommend limiting invasive procedures to amniocentesis. At a minimum, HIV-infected pregnant

women should receive effective ART before undergoing any invasive prenatal testing and, ideally, have an undetectable HIV RNA level at the time of the procedure, and every effort should be made to avoid inserting the needle through, or very close to, the placenta. Consideration can also be given to the use of noninvasive methods of prenatal risk assessment, using tests with high sensitivity and low false-positive rates, such as serum screening alone or combined with nuchal translucency, anatomic ultrasound, and noninvasive molecular prenatal testing.^{24,25} In women with detectable HIV RNA levels for whom amniocentesis is deemed necessary, consultation with an expert should be considered.

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