Previous Experience With Antiretroviral Medications but Not Currently on Antiretroviral Therapy During Current Pregnancy

Updated: March 31, 2026
Reviewed: March 31, 2026

Panel's Recommendations
• In choosing an antiretroviral therapy (ART) regimen in pregnancy when antiretroviral (ARV) medications have been used previously but are not currently being used, clinicians should obtain an accurate history of all prior ARV medications used for HIV treatment or prevention of HIV transmission, including virologic efficacy, tolerance of the medications, results of prior resistance testing, and barriers to adherence **(AIII).** • ART should be restarted before receiving the results of ARV drug-resistance testing because longer durations of ART during pregnancy have been associated with reduced perinatal transmission rates. ART should be modified, if necessary, based on the results of resistance assays **(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*

Initiating Antiretroviral Therapy After Previous Exposure to Antiretroviral Medications

The choice to discontinue antiretroviral therapy (ART) may be made for a variety of reasons, and the length of time off treatment before pregnancy may vary. HIV treatment history and all prior drug resistance test results should be considered when choosing ART for pregnancy when antiretroviral (ARV) medications have been used previously, even when the results of drug-resistance testing performed during the current pregnancy are not yet available.

When ARV medications have been discontinued, interpreting resistance testing results can be complex because resistance testing is most accurate when performed while ART is still being used or within 4 weeks of discontinuing treatment. In the absence of selective drug pressure, resistant virus may revert to wild type; thus, a negative finding does not rule out the presence of archived resistant virus that could re-emerge once ART is restarted. Therefore, when selecting a new ART regimen, all information—including prior regimens received, virologic response, laboratory testing (including HLA-B*5701 results), tolerance or adherence problems, food requirements, concomitant medications, prior medical conditions, and results of all prior resistance testing—should be considered.

Resistance testing should be performed before initiating a new ART regimen when ARVs have been used previously (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). In general, **ART should be initiated before receiving the results of ARV drug-resistance testing,** especially because longer durations of ART during pregnancy have been associated with reduced perinatal transmission rates compared with shorter treatment periods.[1,2] ART should be modified, when necessary, based on subsequent resistance assay results. Careful monitoring of virologic response is essential. For specific guidance on timing and frequency, see Initial Evaluation and Continued Monitoring of HIV During Pregnancy.

A previous ART regimen that successfully suppressed viral load may be restarted if the regimen was tolerated well and no evidence of resistance to that regimen is identified. Ideally, the regimen should also be recommended currently as a *Preferred* or *Alternative* regimen for initial ART in pregnancy (see Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy When Antiretroviral Therapy Has Never Been Received and Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs During Pregnancy and When Trying to Conceive). Drugs that are not recommended for initial use because of concerns about viral breakthrough during pregnancy should be avoided if *Preferred* or *Alternative* regimens are feasible options; if *Preferred* or *Alternative* regimens are not feasible options, consideration of ARV drugs that are not recommended should be discussed with the patient using a shared decision-making approach. Regimens that require specific test results (e.g., HIV resistance assay results, hepatitis B status, HIV viral load) to be available before initiation should not be used empirically for people who have previously taken ARV drugs (see Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy When Antiretroviral Therapy Has Never Been Received); rather, a *Preferred* regimen should be started and modified later, if necessary, based on resistance assays and other test results. Even experienced health care providers may have difficulty selecting appropriate ART in advanced HIV disease, when there is a history of extensive prior ART, or in cases exhibiting previous significant toxicity or nonadherence. In addition to obtaining genotypic resistance testing, it is strongly recommended that specialists in the treatment of HIV be consulted early in the pregnancy about the choice of a suitable ART regimen for such instances. Consultation is also available through the National HIV Perinatal Hotline (1-888-448-8765).

If ART produces an insufficient viral response (e.g., a 1 $\log_{10}$ drop or less within 4 weeks), clinicians should repeat resistance testing, including testing for resistance to integrase strand transfer inhibitors (INSTIs), if indicated (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). Clinicians should also assess medication adherence, food requirements, and potential drug interactions—including relevant pharmacokinetic studies when available—to inform potential regimen changes. Consultation with an HIV treatment specialist is recommended (see Lack of Viral Suppression While on Antiretroviral Therapy in Pregnancy).

History of Intermittent or Time-Limited Use of Antiretroviral Therapy

History of limited ARV drug use could have occurred in some pregnancies when ARV medication was used for personal health (i.e., ART) or to prevent HIV transmission to the infant (i.e., perinatal prevention) or the sexual partner. ARV drugs may also have been taken previously for post-exposure prophylaxis or pre-exposure prophylaxis (PrEP) for preventing HIV acquisition.[3,4]

Data show that prior time-limited use of ART during pregnancy to prevent perinatal transmission may lead to resistance and, thus, reduced efficacy if these ARV medications are used as a part of subsequent ART.[5-9] Standard genotyping has shown that rates of resistance after time-limited use of ART appear to be low. Resistance seems to be a concern primarily in patients who received time-limited non-nucleoside reverse transcriptase inhibitor–based therapy[10-12] but not in those who previously received protease inhibitor (PI)–based therapies.[10] To date, there are no data on the risk of developing resistance when long-acting ART (e.g., long-acting cabotegravir [CAB-LA] and long-acting rilpivirine) is discontinued without starting alternative ART.

Antiretroviral Therapy After Long-Acting Pre-exposure Prophylaxis

In contrast to time-limited exposure to ART for HIV, recent studies suggest that there may be risk for selection of integrase inhibitor mutations if HIV is acquired while receiving CAB-LA for PrEP.[13-16]

Therefore, when there is a history of using CAB-LA as PrEP, genotypic resistance testing performed before starting ART should also include screening for INSTI-resistance mutations.[17] For this reason, the Panel on Treatment of HIV in Pregnancy and Prevention of Perinatal Transmission recommends the use of the PI darunavir boosted with ritonavir with (tenofovir alafenamide or tenofovir disoproxil fumarate) plus (emtricitabine or lamivudine), rather than the INSTI dolutegravir, as the *Preferred* ART regimen in the context of prior CAB-LA exposure and pending genotype test results. The ART regimen should be modified, when necessary, based on subsequent resistance assay results. See Early (Acute and Recent) HIV Infection in the Adult and Adolescent Antiretroviral Guidelines, Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy When Antiretroviral Therapy Has Never Been Received, and Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs During Pregnancy and When Trying to Conceive for more information.

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