People With HIV Who Are Taking Antiretroviral Therapy When They Become Pregnant

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Panel's Recommendations
• In most cases, people with HIV who are receiving antiretroviral therapy (ART) and who present for pregnancy care should continue their ART during pregnancy, provided that the regimen is tolerated, safe, and effective in suppressing viral replication (defined as a regimen that maintains an HIV viral load less than lower limits of detection of the assay) (AII). • When considering changes in ART during pregnancy, the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission recommends patient counseling to support informed decision-making (AIII). See Appendix C: Antiretroviral Counseling Guide for Health Care Providers. • For pregnant people on ART, antiretroviral (ARV) drug-resistance testing should be performed prior to changing an ARV regimen if HIV RNA is above the threshold for standard genotypic drug resistance testing (AI) (usually >500 copies/mL to 1,000 copies/mL) (AIII), but may be possible for HIV RNA >200 to <500 copies/mL in some laboratories (CIII). See Antiretroviral Drug Resistance and Resistance Testing in Pregnancy. • Clinicians need to consider whether pharmacokinetic changes in pregnancy, especially in the second and third trimester, may lead to a lower plasma level of some ARV drugs and necessitate increased doses, more frequent dosing, boosting, more frequent viral load monitoring, or a change in the ARV regimen (AII). See Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy. • Although there are no data on the use of two-drug oral regimens during pregnancy (e.g., dolutegravir [DTG] plus lamivudine [3TC], DTG plus rilpivirine [RPV]), the component drugs are recommended as *Preferred* or *Alternative* for use in pregnancy. Pregnant persons who present to care on DTG/3TC or DTG/RPV and have successfully maintained viral suppression can continue the two-drug regimen (BIII) with more frequent viral load monitoring every 1 to 2 months throughout pregnancy (CIII). • Data about the use of long-acting injectable cabotegravir (CAB-LA) and RPV during pregnancy are extremely limited and insufficient to make a recommendation for or against use in pregnancy. Pregnant people who present to care on this regimen should be counseled about limited data. Clinicians and pregnant people should reach a shared decision about continuing this regimen with frequent viral load monitoring or switching to one of the *Preferred* or *Alternative* three-drug ARV regimens (CIII). • The use of cobicistat-containing regimens during pregnancy is associated with lower plasma drug exposures due to physiologic changes associated with pregnancy. These lower drug exposures pose an increased risk of virologic failure during the second and third trimesters of pregnancy. When pregnant people present to care on one of these regimens, clinicians and pregnant people should reach a shared decision about whether to continue the regimen with frequent viral load monitoring or to switch to a different regimen that is recommended for use during pregnancy (BIII) (see Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive and Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs). If one of these regimens is continued, absorption should be optimized by taking the drugs with food and following instructions for administration (e.g., spacing administration of vitamins containing iron and calcium) (AII). Viral load should be monitored more frequently (i.e., every 1–2 months) (CIII). • People who present during pregnancy on drugs that are not recommended for use because of toxicity (e.g., stavudine, didanosine) should stop taking these drugs and be switched to other ARV drugs that are recommended for use during pregnancy (AIII). See Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs for more information. • If an ARV regimen is altered during pregnancy, drugs in the new regimen should include ARV drugs that are recommended for use in pregnancy (BIII) (see Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive and Table 7. Situation-Specific Recommendations for Use of ARVs), and more frequent virologic monitoring is warranted until viral suppression is stably observed (CIII).

Please see Intrapartum Care for People with HIV for guidance about use of intrapartum intravenous zidovudine prophylaxis and scheduled cesarean delivery for pregnant people who have not achieved viral suppression on antiretroviral therapy at delivery.
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*

People on Fully Suppressive Antiretroviral Therapy

In general, **people who are already on a fully suppressive antiretroviral regimen when pregnancy occurs should continue their antiretroviral therapy (ART) regimens.** Discontinuing or altering therapy could cause an increase in viral load, leading to disease progression, a decline in immune status, and an increased risk of perinatal HIV transmission.[1] In a study from the French Perinatal cohort among 1,797 women with HIV RNA level <50 copies/mL before 14 weeks gestation, change in antiretroviral (ARV) regimen in 411 women due to safety concerns based on existing guidelines at the time of pregnancy did not result in loss of virologic control.[2] However, among 662 pregnancies that were followed in Italy between 2001 and 2008, treatment modification during pregnancy was independently associated with HIV RNA level >400 copies/mL in late pregnancy (adjusted odds ratio [aOR] 1.66; 95% CI, 1.07–2.57; $P = 0.024$).[3] This highlights the importance of using potent and well-tolerated regimens during pregnancy to maximize effectiveness and minimize the need for modification of treatment in pregnancy. The findings also highlight the importance of not changing effective ARV regimens in people who become pregnant while taking ART that is safe in pregnancy.

One key exception is regimens that involve medications that are not recommended for use in adults because of high risk for toxicity (e.g., stavudine, indinavir, didanosine, and treatment-dose ritonavir) or inferior virologic efficacy (nelfinavir [NFV]); these drugs are now rarely used. In this case, these drugs should be stopped and people switched to other ARV drugs that are recommended for use in pregnancy (see Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive and Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive).

Physiologic changes that occur during pregnancy may result in lower levels of certain ARVs, resulting in loss of virologic control with the potential for perinatal transmission. **For patients who have achieved viral suppression and become pregnant while receiving regimens with a potential increased risk of virologic failure during pregnancy due to pharmacokinetic (PK) concerns (e.g., cobicistat [COBI]-boosted regimens) or regimens with insufficient data about dosing and/or safety in pregnancy (e.g., bictegravir [BIC], doravirine [DOR], oral two-drug regimens, and long-acting injectable cabotegravir/rilpivirine [CAB/RPV]),** clinicians need to consider whether to continue the regimen or switch to a different regimen that is recommended for use during pregnancy.[4-6] (See Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive and Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive) For regimens with PK concerns or those with insufficient data about dosing in pregnancy, pregnant people and clinicians may elect to continue the suppressive regimen with frequent viral load monitoring (e.g., every 1–2 months, understanding that switching may be needed later in pregnancy, when viral rebound may increase vertical transmission risk and lead to cesarean

delivery), or they may elect to switch to recommended oral regimens as soon as pregnancy is recognized. In these cases, the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission (the Panel) emphasizes the importance of patient counseling and informed decision-making, including consideration of individual factors (such as ARV resistance or intolerance, or difficulty with adherence to other regimens) that may increase the risk of virologic failure with a switch to a new regimen. When choosing to switch any ART regimen in pregnancy in people who are already virologically suppressed, clinicians should closely monitor tolerability of the new regimen, evaluate for adverse effects, and consider more frequent viral load monitoring (i.e., every 1–2 months). For additional information, see Appendix C: Antiretroviral Counseling Guide for Health Care Providers.

COBI-Boosted Regimens

Clinicians and pregnant people should be aware that the use of atazanavir/cobicistat, darunavir/cobicistat, or elvitegravir/cobicistat (EVG/c) is associated with lower plasma drug exposures during the second and third trimesters of pregnancy due to the physiologic changes associated with pregnancy. These low drug exposures pose an increased risk of virologic failure in the second and third trimesters and potential perinatal HIV transmission. When a pregnant person presents to care on one of these regimens, providers should consider continuing the regimen with more frequent viral load monitoring or switching to a different regimen that is recommended for use during pregnancy (see Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant People and Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive).[4-6] A recent multicenter, retrospective study of 134 pregnant women with HIV who received elvitegravir (EVG)-containing ART at any time during pregnancy reported that 81.3% of study participants had viral suppression at delivery (HIV RNA <40 copies/mL); among 68 women who initiated EVG before pregnancy and continued receiving EVG through delivery, the rate of viral suppression at delivery was 88.2%. The perinatal HIV transmission rate was 0.8% in this study.[7] If one of these regimens is continued, absorption should be optimized by taking the drugs with food. Pregnant people who are taking regimens that include EVG/c should take ARV drugs and prenatal vitamins ≥2 hours apart.

BIC and DOR-Based Regimens

There are currently very limited PK data on BIC in human pregnancy[8,9] and only pharmacokinetic modeling data based on *ex vivo* studies of placental transfer for DOR in pregnancy.[8,10] Patients who become pregnant while receiving regimens with BIC or DOR with viral suppression should be counseled about limited available data. Clinicians and patients should reach a shared decision about continuing such regimens with frequent viral load monitoring (every 1–2 months) or switching to one of the *Preferred* or *Alternative* regimens.

Oral Two-Drug Regimens

Currently, no data exist on the use of oral two-drug regimens in pregnancy (e.g., dolutegravir [DTG] plus lamivudine and DTG plus rilpivirine [RPV])**.** However, for both DTG plus lamivudine (3TC) and DTG/RPV, there are data in nonpregnant persons showing noninferiority when compared to a standard three-drug regimen.[11,12] The component drugs in each of the oral two-drug regimens (DRG, 3TC, RPV) have well described PKs that are adequate in pregnancy, and the individual drug components are recommended as *Preferred* or *Alternative* ARV drugs by the Panel. Note that although PK data indicate that RPV plasma concentration is reduced during the second and third

trimesters of pregnancy, the reduction is less than the reductions seen with the COBI-containing regimens described above, and most pregnant people will have adequate exposure. A recent observational study of 188 pregnant people on oral RPV as part of a three-drug regimen at delivery found that 182 (96.8%) had viral load <200 copies/mL.[13] Standard RPV dosing is recommended when used as part of a three-drug regimen, and viral load should be monitored frequently (e.g., every 1–2 months; see Rilpivirine, Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive, and Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive.

Long-Acting Injectable CAB and RPV

Data on long-acting injectable **CAB and RPV** are currently limited to a small number of patients without HIV who became pregnant while enrolled in trials of long-acting injectable CAB for pre-exposure prophylaxis and stopped the medication once pregnancy was recognized, usually in the first trimester.[14,15] In these patients, the pharmacologic washout was similar in pregnant and non-pregnant adults.[14,16] No data are available about the pharmacokinetics of CAB in the second and third trimesters, with either oral or injectable formulations. While data in non-pregnant adults suggest slower washout (and thus potentially higher CAB levels) with intramuscular CAB among people with obesity,[17] this may not be applicable to the weight gain that is due to pregnancy, as the volume of distribution in pregnancy differs from that in obesity. No data exist on the PKs of injectable RPV in pregnancy. Prior data have shown concern for lower concentrations of oral RPV in the third trimester,[18] as above. Some patients who have achieved virologic suppression on injectable CAB and RPV experienced previous challenges with oral ART, such that switching back to oral ART could increase the risk of virologic rebound. When switching from long-acting injectable CAB and RPV to an oral regimen in pregnancy, the timing of the switch must take into account the long half-life of the long-acting injectable formulation (median 5.6–11.5 weeks) with persistence of the drug for up to 12 months.[19] When the dosing schedule is monthly, the change to an oral regimen should occur within 4 weeks of the last CAB and RPV injections.[20] When the dosing schedule is every 2 months, the change to an oral regimen should occur within 8 weeks of the last CAB and RPV injections.[21,22] Dosing recommendations, including guidance for switching to an oral regimen, can be found in the prescribing information.[19,22] For additional information, see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression and Discontinuation or Interruption of Antiretroviral Therapy in the Adult and Adolescent Antiretroviral Guidelines.

People Not on Fully Suppressive ART When Becoming Pregnant

People who are not fully suppressed and who are currently taking ART should be evaluated carefully for adherence and HIV drug resistance, with every effort made to achieve rapid and full viral suppression through adherence interventions or medication changes (see Pregnant People Who Have Not Achieved Viral Suppression on Antiretroviral Therapy).

Resistance testing should be performed when considering altering an ARV regimen in a pregnant person who is experiencing virologic failure and who has HIV RNA levels above the threshold for resistance testing (usually >500 to 1,000 copies/mL). In individuals who have HIV RNA levels >200 copies/mL but <500 copies/mL, testing may be unsuccessful, but it still should be considered. The results can be used to select a new regimen with a greater likelihood of suppressing viral replication to undetectable levels. See Antiretroviral Drug Resistance and Resistance Testing in Pregnancy.

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