Pregnant People with HIV Who Are Currently Receiving Antiretroviral Therapy

(Last updated December 30, 2021; last reviewed December 30, 2021)

Panel's Recommendations
• 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. • Persons 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 antiretroviral (ARV) drugs that are recommended for use during pregnancy **(AIII).** See Table 5: Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive for more information. • 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 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 with more frequent viral load monitoring, every 1 to 2 months throughout pregnancy **(CIII)**. • Because data about the use of long-acting injectable cabotegravir (CAB) and RPV during pregnancy are extremely limited, pregnant persons who present to care on this regimen should be switched to one of the *Preferred* or *Alternative* three-drug ARV regimens **(CIII)**. • The use of atazanavir/cobicistat, darunavir/cobicistat, or elvitegravir/cobicistat 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 (see Table 4 What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive and Table 5: Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive). When a pregnant person presents to care on one of these regimens, providers should decide whether to continue the regimen or to switch to a different regimen that is recommended for use during pregnancy **(BIII).** If one of these regimens is continued, absorption should be optimized by taking the drugs with food, and viral load should be monitored frequently (i.e., every 1–2 months). • If an ARV regimen is altered during pregnancy, drugs in the new regimen should include ARV drugs that are recommended for use in pregnancy (see Table 4 What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive and Table 5: Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive) **(BIII),** and more frequent virologic monitoring is warranted **(CIII).** • ARV drug-resistance testing should be performed to assist the selection of active drugs when changing ARV regimens in pregnant people who are experiencing virologic failure on ART and who have HIV RNA levels >500 copies/mL to 1,000 copies/mL **(AII).** In individuals who have HIV RNA levels >500 copies/mL but <1,000 copies/mL, testing may be unsuccessful but still should be considered **(BII).** See Pregnant People Who Have Not Achieved Viral Suppression on Antiretroviral Therapy for more information.

- Clinicians should discuss future reproductive plans and timing, the risks and benefits of conceiving on specific ARV medications, and use of appropriate contraceptive options to prevent unintended pregnancy **(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

People who are taking antiretroviral therapy (ART) for HIV infection should continue their ART regimen during pregnancy, provided it is well tolerated, safe, and effective in suppressing viral replication. 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] Maintenance of viral suppression is paramount for both maternal health and the prevention of perinatal transmission. However, a change in ART may be indicated or considered in specific circumstances. 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 when changing ARV regimens during pregnancy. For additional information, see Appendix C: Antiretroviral Counseling Guide for Health Care Providers.

Persons with HIV 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 switch to other antiretroviral (ARV) drugs that are recommended for use in pregnancy (see Table 4: What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant People and Table 5: Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive).

No data exist on the use of oral two-drug regimens in pregnancy (e.g., dolutegravir [DTG] plus lamivudine and DTG plus rilpivirine [RPV]; if a pregnant person presents to care on these regimens and has successfully maintained viral suppression, the regimen can be continued without adding a third agent, but more frequent viral load (i.e., every 1–2 months) monitoring is recommended. For both regimens, there are data in nonpregnant persons showing noninferiority when compared to a standard three-drug regimen.[2,3] Pharmacokinetics (PK) have been well described and are adequate in pregnancy, and the components of each of the two-drug oral regimens are recommended as *Preferred* or *Alternative* ARV drugs by the Panel.

Because there are insufficient data on pregnancy PK and safety data for cabotegravir (CAB), persons who become pregnant on long-acting injectable CAB and rilpivirine (RPV) should be switched to an oral regimen recommended for use in pregnancy for the remainder of the pregnancy.[4] 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.[5] With the current dosing schedule of monthly injections, change to an oral regimen should occur within 4 weeks of the last CAB and RPV injections.[6] Dosing recommendations, including guidance for switching to an oral regimen, can be found in the prescribing information[5,7] and the Adult and Adolescent Antiretroviral Guidelines.

For persons with HIV who have achieved virologic suppression and become pregnant while receiving ARV drugs with insufficient data about their use in pregnancy—such as bictegravir or doravirine—clinicians should consider whether to continue or change the regimen because a regimen change carries a risk for viral rebound at the time of the switch.[8] If a decision is made with the patient

to continue the same regimen, viral load should be monitored more frequently (i.e., every 1–2 months).

The use of regimens containing 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 4: What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant People and Table 5: Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive).[9-11] 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.[12] 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. In addition, viral load should be monitored more frequently (e.g., every 1–2 months) in patients taking cobicistat-boosted regimens (see Monitoring During Pregnancy).[10] Lack of viral suppression on subsequent testing indicates a need for a regimen change, and a pregnant person may need a scheduled cesarean delivery if the lack of suppression is detected late in pregnancy.

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 cobicistat-containing regimens described above, and most pregnant people will have adequate exposure. Standard RPV dosing is recommended, and viral load should be monitored frequently (e.g., every 1–2 months; see Recommendations for Use of Antiretroviral Drugs During Pregnancy).

As newer, highly effective ARV drugs are approved by the Food and Drug Administration, people with HIV may present for prenatal care on ART regimens that include ARV drugs for which significant experience in pregnancy is lacking and PK and safety data are limited. If questions arise about specific drugs in an ART regimen, providers are encouraged to consult with an HIV perinatal specialist before discontinuing or altering a fully suppressive regimen that is well tolerated. In addition, more frequent virologic monitoring is warranted when an ARV regimen is altered during pregnancy. Because little is known about the use of newly approved drugs during pregnancy, providers should make every effort to report all ART exposures in pregnant people to the Antiretroviral Pregnancy Registry.

Pregnant people with HIV who are on ART and who present for care during the first trimester should be counseled regarding the benefits and potential risks of receiving ARV drugs during this period. Providers should emphasize that continuing an effective ARV regimen is recommended, see Appendix C: Antiretroviral Counseling Guide for Health Care Providers and Teratogenicity.

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 >1,000 copies/mL. In individuals who have HIV RNA levels >500 copies/mL but <1,000 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.

During and after pregnancy, clinicians should discuss future reproductive plans and timing, risks and benefits of conceiving on specific ARV medications, and contraceptive options to prevent unintended pregnancy (see Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV).

References

1. Floridia M, Ravizza M, Pinnetti C, et al. Treatment change in pregnancy is a significant risk factor for detectable HIV-1 RNA in plasma at end of pregnancy. *HIV Clin Trials*. 2010;11(6):303-311. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21239358.

2. Cahn P, Madero JS, Arribas JR, et al. Durable efficacy of dolutegravir plus lamivudine in antiretroviral treatment-naive adults with HIV-1 infection: 96-week results from the GEMINI-1 and GEMINI-2 randomized clinical trials. *J Acquir Immune Defic Syndr*. 2020;83(3):310-318. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31834000.

3. van Wyk J, Ajana F, Bisshop F, et al. Efficacy and safety of switching to dolutegravir/lamivudine fixed-dose 2-drug regimen vs. continuing a tenofovir alafenamide–based 3- or 4-drug regimen for maintenance of virologic suppression in adults living with human immunodeficiency virus type 1: phase 3, randomized, noninferiority TANGO study. *Clin Infect Dis*. 2020;71(8):1920-1929. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31905383.

4. Patel P, Thiagarajah S, Ford S, et al. Cabotegravir pharmacokinetic tail in pregnancy and neonatal outcomes. Abstract 775. Presented at: Conference on Retroviruses and Opportunistic Infections. 2020. Boston, MA. Available at: https://www.croiconference.org/abstract/cabotegravir-pharmacokinetic-tail-in-pregnancy-and-neonatal-outcomes/.

5. Cabenuva (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension), co-packaged for intramuscular use [package insert]. Food and Drug Administration. 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212888s000lbl.pdf.

6. Panel on Antiretroviral Guidelines for Adults and Adolescents. Optimizing antiretroviral therapy in the setting of viral suppression. 2021. Available at: https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/optimizing-antiretroviral-therapy-setting-virologic-suppression

7. Vocabria (cabotegravir) [package insert]. Food and Drug Administration. 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212887s000lbl.pdf.

8. Frange P, Tubiana R, Sibiude J, et al. Rilpivirine in HIV-1-positive women initiating pregnancy: to switch or not to switch? *J Antimicrob Chemother*. 2020;75(5):1324-1331. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32157283.

9. Crauwels HM, Osiyemi O, Zorrilla C, Bicer C, Brown K. Reduced exposure to darunavir and cobicistat in HIV-1-infected pregnant women receiving a darunavir/cobicistat-based regimen. *HIV Med*. 2019;20(5):337-343. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30873741.

10. Momper J, Best BM, Wang J, et al. Elvitegravir/cobicistat pharmacokinetics in pregnant and postpartum women with HIV. *AIDS*. 2018;32(17):2507-2516. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30134297.

11. van der Galien R, Ter Heine R, Greupink R, et al. Pharmacokinetics of HIV-integrase inhibitors during pregnancy: mechanisms, clinical implications and knowledge gaps. *Clin Pharmacokinet*. 2018;58(3):309-323. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29915921.

12. Badell ML, Sheth AN, Momplaisir F, et al. A multicenter analysis of elvitegravir use during pregnancy on HIV viral suppression and perinatal outcomes. *Open Forum Infect Dis*. 2019;6(4):ofz129. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31037241