APPENDIX C: ANTIRETROVIRAL COUNSELING GUIDE FOR HEALTH CARE PROVIDERS

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Decision-Making About Antiretroviral Drugs During Pregnancy or When Trying to Conceive

This guide summarizes current information about recommendations of the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission (the Panel) to support counseling about the use of antiretroviral (ARV) drugs and antiretroviral therapy (ART) options during pregnancy or when trying to conceive.

During pregnancy or when trying to conceive, effective ART with sustained viral suppression maximizes their health and the prevention of perinatal HIV transmission. The risk of perinatal HIV transmission is reduced to the lowest levels (1% or less) when ART for HIV is initiated prior to conception and sustained viral suppression to undetectable levels throughout pregnancy has been achieved. See Use of Antiretroviral Drugs to Prevent Perinatal HIV Transmission and Improve Health During Pregnancy.

Before, during, and after pregnancy, it is important to discuss future childbearing desires and plans, the potential benefits and risks of conceiving while taking specific ARV medications, and contraceptive options to prevent unintended pregnancy.

General Antiretroviral Counseling During Pregnancy or When Trying to Conceive

- As part of shared decision-making, information should be provided during pregnancy or when trying to conceive to help the understanding and consideration of the benefits, advantages, disadvantages, and potential risks associated with the use of each individual ARV drug they are currently receiving or will be initiating. These factors include dosing frequency, side effects or tolerability issues, and adverse pregnancy outcomes (e.g., preterm birth, birth defects). For additional information, refer to Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy When Antiretroviral Therapy Has Never Been Received, Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs During Pregnancy and When Trying to Conceive, Teratogenicity, and Antiretroviral Drug Regimens and Pregnancy Outcomes.
- When trying to conceive, information should be provided about the use of specific ARV regimens during pregnancy to enable informed decisions before pregnancy occurs.
- It should be explained that not enough is known about the safety of using certain ARV drugs around the time of conception or during pregnancy or about the need for dosing changes during pregnancy, when relevant, because studies in pregnancy are limited. **It is important to emphasize that a lack of data does not indicate the absence or presence of risk; rather, it means that we do not have all the information about the possible effects when using these drugs during pregnancy.**

- The Antiretroviral Pregnancy Registry (APR) prospectively collects and reviews data about birth defects in order to detect any major teratogenic effect(s) involving ARV drug exposure during pregnancy. Clinicians are encouraged to report all cases of ARV drug exposure during pregnancy or when conception occurred while receiving ARV drugs to the Antiretroviral Pregnancy Registry. The APR provides updated birth defect data for ARV drugs twice a year through an interim report released in June and December.
    - When discussing the risks of birth defects with ARV medication exposure, it is important to point out the overall risk of defects in the general population and explain during which weeks of gestation the fetus is at risk for developing that defect. For example, a background risk of neural tube defects (NTDs) exists, regardless of the ARV regimen used or the HIV status during pregnancy. Most NTDs occur before the neural tube closes at 4 weeks post-conception (approximately 6 weeks after the last menstrual period), often before pregnancy is known. After 6 weeks' gestation, the additional risk of NTDs developing is thought to be much less likely. Folic acid supplementation should always be encouraged when trying to conceive and in early pregnancy (see Prepregnancy Counseling and Care).
    - Early data from the Tsepamo study in Botswana raised concerns about a possible higher rate of NTDs among infants born to mothers who received dolutegravir (DTG) at the time of conception. Sufficient data now exist to indicate that DTG is not associated with an increased risk of NTDs. See Dolutegravir for additional information.
    - The Antiretroviral Pregnancy Registry report has monitored sufficient numbers of first-trimester exposures to bictegravir (BIC) to detect at least a twofold increase in the risk of overall birth defects. No such increase in birth defects has been detected with BIC. Previously, not enough reported data had existed to assess the risk of birth defects with BIC.
    - Clinicians are encouraged to report all cases of ARV drug exposure during pregnancy or when conception occurred while receiving ARV drugs to the APR.
- The risk of other adverse pregnancy outcomes, many of which are more common than birth defects, also should be discussed. Some ARV regimens may increase the risk of preterm birth (see Antiretroviral Drug Regimens and Pregnancy Outcomes).
- In most cases, the Panel recommends continuing the current regimen during pregnancies impacted by HIV, provided that the regimen is tolerated and effective in suppressing viral replication (defined as a regimen that maintains an HIV viral load less than the lower limits of detection of the assay).
    - Explain that changes in ART during pregnancy can lead to an increase in viral load, which increases the risk of perinatal HIV transmission and may affect choices for future ARV regimens because of the possible development of drug resistance.
    - When ARVs that are not *Preferred* or *Alternative* options for use during pregnancy are being taken, counsel about the benefits and risks of continuing the current ART or switching to another ARV regimen.
    - When ARVs for which data about use in pregnancy are insufficient (e.g., long-acting cabotegravir [CAB-LA], doravirine) or ARVs with pharmacokinetic (PK) changes that could lead to lower drug levels and loss of viral suppression (e.g., cobicistat-boosted regimens) are being taken, discuss whether to continue the current regimen with frequent viral load monitoring (i.e., every 1 to 2 months) or consider switching to another ARV drug or drug regimen. In making this decision, consider the tolerability of each drug, the ability to maintain viral suppression, the risk of perinatal HIV transmission, and the risk of potential adverse outcomes.

- The Panel recognizes that to reach or maintain viral suppression in the context of ART experience, ARV drugs that have insufficient data regarding use in pregnancy or are not recommended for use in pregnancy except in special circumstances may need to be taken.
- For additional information, see Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs During Pregnancy and When Trying to Conceive and When Antiretroviral Therapy is Being Taken When Pregnancy Occurs.

Antiretroviral Drugs That Are Recommended for Use in Pregnancy

- When making recommendations about the use of ARV drugs in pregnancy, the Panel considers available data from multiple sources about efficacy, PK, dosing, safety, and toxicity during pregnancy and in nonpregnant adults. The Panel requires adequate PK, dosing, and teratogenicity data during pregnancy to categorize a drug as *Preferred* or *Alternative* for use in pregnancy or when trying to conceive. ARV drugs are assigned to one of the five categories (see Recommendations for the Use of Antiretroviral Drugs During Pregnancy: Overview).
- ARV regimens for treating HIV-2 mono-infection or HIV-1/HIV-2 coinfection should include drugs that are active against HIV-2 (see HIV-2 Infection and Pregnancy).
- Moderate amounts of data about pregnancy outcomes and birth defects exist for each of the drugs and drug combinations that are *Preferred*. Although these data are reassuring, it is important to note that among the *Preferred* drugs, a rigorous, systematic birth surveillance program that includes large numbers of women with periconception exposure is available only for DTG.
- *Preferred* ARV drug regimens include DTG or BIC used in combination with two nucleoside reverse transcriptase inhibitors (NRTIs).
  - DTG plus tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC) or lamivudine (3TC)
  - Fixed-dose combination of BIC/FTC/TAF
- DTG- and BIC-based regimens are *Preferred* for treating early (acute or recent) HIV infection during pregnancy unless there is a history of prior exposure to CAB-LA for pre-exposure prophylaxis. After CAB-LA exposure, a regimen of darunavir/ritonavir (DRV/r) with TDF or TAF plus FTC or 3TC is the *Preferred* ART regimen pending results of genotype testing that includes integrase resistance testing. For additional information, see Early (Acute and Recent) HIV Infection.
- Raltegravir, atazanavir/ritonavir (ATV/r), DRV/r, efavirenz, rilpivirine (RPV), and the NRTI abacavir are recommended as *Alternative* ARV drug options in pregnancy. *Alternative* drugs may have more limited data on use in pregnancy than *Preferred* drugs or may be associated with more concerns about PK, dosing, tolerability, drug interaction, efficacy, or resistance than those in the *Preferred* category, but they are acceptable for use in pregnancy.
- To maximize ARV absorption and effectiveness, it is important to reinforce the need to check and follow the instructions for taking the regimen (e.g., taking DRV and RPV with food, spacing administration of integrase strand transfer inhibitors and RPV with antacids or divalent cation–containing vitamins, avoiding proton pump inhibitors and spacing administration of H2 blockers with ATV/r and RPV). See Appendix B: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy for instructions about dosing and administration.

- Cobicistat-boosted regimens (atazanavir/cobicistat, darunavir/cobicistat, or elvitegravir/cobicistat) are not recommended for use during pregnancy. PK studies suggest increased drug metabolism and lower therapeutic drug levels of cobicistat-boosted ARV drugs during pregnancy. When the decision is made to continue one of these regimens, more frequent viral load monitoring (i.e., every 1 to 2 months) should be performed.
- If an ARV regimen is changed during pregnancy, drugs in the new regimen should include those that are recommended for use in pregnancy whenever possible (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) and viral load should be monitored more frequently (i.e., every 1 to 2 months).
- Recommendations regarding the use of specific ARV agents or ARV regimens change as more information on the safety, tolerability, and PK changes of these drugs in pregnancy becomes available. For additional information, see Recommendations for the Use of Antiretroviral Drugs During Pregnancy: Overview, Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy When Antiretroviral Therapy Has Never Been Received, Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs During Pregnancy and When Trying to Conceive, and Appendix B: Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy.