Appendix C: Antiretroviral Counseling Guide for Health Care Providers

(Last updated, February 10 2021; last reviewed, February 10, 2021)

Decision-making about Antiretroviral Drugs for Pregnant Women and Women Who Are Trying to Conceive

This counseling guide summarizes information, based on currently available data, to support the process of informed decision-making by health care providers and their patients about the use of antiretroviral (ARV) drugs and antiretroviral therapy (ART) options by women who are pregnant or are trying to conceive.

For pregnant women and women who are trying to conceive, effective ART with sustained viral suppression maximizes both women’s health and the prevention of perinatal HIV transmission. The risk of perinatal HIV transmission is reduced to the lowest levels (<1%) in women with HIV who initiate ART prior to conception and who have sustained viral suppression to undetectable levels throughout pregnancy.

When making decisions about ART, it is important to weigh the available data on the risks and benefits of all Preferred and Alternative ARVs, gestational age, tolerance of and satisfaction with the current ARV regimen, and the potential loss of virologic control with regimen changes. Patients should receive the information needed to help them make informed decisions about ARV drugs and regimens.

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

When discussing ARV drug options, it is important to point out that some ARV drugs that are recommended for use in adults and nonpregnant women are not Preferred or Alternative options for women who are pregnant or who are trying to conceive for the following reasons:

- Not enough is known about the safety of using certain ARV drugs before or during pregnancy because studies about their use 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 all the possible effects when using these drugs during pregnancy (e.g., bictegravir).
- For some ARV drugs (e.g., cobicistat-boosted regimens), pharmacokinetic (PK) changes occur in pregnancy that decrease blood levels of those agents, potentially leading to a loss of virologic control and an increased risk of perinatal transmission or adverse effects on maternal HIV infection.
- For newer ARV drugs, PK data may not be available to guide dosing in pregnancy.

General Antiretroviral Counseling for Pregnant Women and Women Who Are Trying to Conceive

- It is important to help women consider the available information about the advantages, disadvantages, and potential risks associated with the use of ARV drugs, such as other birth defects or other adverse pregnancy outcomes (e.g., preterm delivery); see the section on Counseling Regarding the Risk of Neural Tube Defects (NTDs) below, and refer to Table 4, Teratogenicity, and Antiretroviral Drug Regimens and Maternal and Neonatal Outcomes for additional information.
- Changes in ART during pregnancy can lead to an increase in viral load, which increases the risk of perinatal HIV transmission; this viral rebound may affect choices for future ARV regimens due to the possible development of resistance.
- Women who are receiving ARVs that are not Preferred or Alternative options for pregnant women and women who are trying to conceive should receive counseling about the risks and benefits of continuing their current ART or switching to another ARV regimen. Panel recommendations about the continuation of specific ARV drugs are summarized in Table 5.
- When assessing the benefits and risks of switching a patient’s ARV regimen, clinicians and patients should consider such factors as the feasibility of switching to another ARV drug, the tolerability of each drug, the...
ability to maintain viral suppression, the risk of perinatal HIV transmission, and the risk of NTDs or other adverse outcomes, such as preterm birth.

- Women who are trying to conceive should receive information about the use of specific ARV regimens during pregnancy, which will enable them to make informed decisions before they become pregnant.
- All cases of ARV drug exposure during pregnancy should be reported to the Antiretroviral Pregnancy Registry.

**Antiretroviral Drugs That Are Recommended for Use in Pregnancy**

**Preferred** ARV drug options for women who are initiating ART while pregnant or while trying to conceive include dolutegravir (DTG), raltegravir, atazanavir/ritonavir, and darunavir/ritonavir. A moderate amount of data exists about pregnancy outcomes and birth defects with each of these drugs and drug combinations. Although these data are reassuring, it is important to note that a rigorous, systematic birth surveillance program that includes large numbers of women with periconceptional exposure, like the Botswana study, is available only for DTG and efavirenz (EFV).

- EFV and rilpivirine are recommended as Alternative ARV drug options in pregnancy. Alternative drugs may have more limited data on use in pregnancy than Preferred drugs (e.g., rilpivirine) or may be associated with more PK, dosing, tolerability, drug interaction, or resistance concerns than those in the Preferred category, but they are acceptable for use in pregnancy.
- Recommendations regarding the use of specific ARV agents or ARV regimens often change as more information on the safety, tolerability, and PK changes of these drugs in pregnancy becomes available. Current updates include the following:
  - DTG is now a Preferred ARV for women who are trying to conceive, in addition to being a Preferred ARV for women who are pregnant, irrespective of trimester.
  - Lopinavir/ritonavir, formerly categorized as an Alternative ARV, now is Not Recommended Except in Special Circumstances. This change is based on data on increased risks of preterm delivery and small-for-gestational-age infants—as well as on requirements for twice-daily dosing and potential nausea and vomiting; see Antiretroviral Drug Regimens and Maternal and Neonatal Outcomes.
  - With the availability of additional data, the Panel now recommends tenofovir alafenamide as an Alternative nucleoside reverse transcriptase inhibitor for ARV regimens.
  - Regimens that contain atazanavir/cobicistat, darunavir/cobicistat, or elvitegravir/cobicistat are not recommended for use in pregnant women because of PK changes that may lead to increased viral loads later in pregnancy. Health care providers should discuss with their patients whether to continue the regimen or switch to one that is recommended for use during pregnancy (see Table 5 and Pregnant Women with HIV Who Are Currently Receiving Antiretroviral Therapy). If a regimen with PK concerns is continued, it is important that the patient follow the instructions for taking the regimen to optimize absorption (e.g., taking certain drugs with or without food, avoiding antacids or divalent cation-containing vitamins). Viral load should be monitored more frequently in these patients (i.e., every 1–2 months).
  - If an ARV regimen is changed during pregnancy, drugs in the new regimen should be recommended for use in pregnancy (see Table 4 and Table 5), and viral load should be checked 2 to 4 weeks after the switch.

**Counseling Regarding the Risk of NTDs in Pregnant Women and Women Who Are Trying to Conceive**

In 2018, the preliminary data from a study in Botswana identified an increased risk of infant NTDs in women who were taking DTG around the time of conception. Subsequent data and findings from later, planned analyses found that the risk of infant NTDs was lower than previously reported in the preliminary data, but there was still a very small, potentially increased risk of infant NTDs among women who were taking DTG around the time of conception or in early pregnancy.

Because the updated data indicate that the increased risk of NTDs associated with DTG use is very small and because DTG has the advantages of once-daily dosing, being generally well tolerated, and producing rapid,
The Panel recommends DTG as a Preferred ARV drug for use throughout pregnancy and also recommends it as a Preferred ARV drug for women who are trying to conceive. The Panel strongly recommends that the use of DTG and all ARV drugs be accompanied by appropriate counseling to allow patients and their health care providers to make informed decisions about treatment. Considerations that should be addressed in counseling are summarized below. For additional information, see Teratogenicity, Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 4, Table 5, and Pregnant Women with HIV Who Are Currently Receiving Antiretroviral Therapy.

- Because of mandatory food folate fortification, the overall risk of NTDs in the United States is low in the general population. A background risk of NTDs exists, regardless of the ARV regimen used or a woman’s HIV status. In the United States, the background risk of NTDs in the general population is 0.07%, or 7 infants with NTDs per 10,000 pregnancies. The Centers for Disease Control and Prevention (CDC) notes that 3,000 pregnancies are affected by infant NTDs every year in the United States. Most NTDs occur before the neural tube closes at 4 weeks postconception (approximately 6 weeks after the last menstrual period), often before a woman realizes she is pregnant. After 6 weeks’ gestation, the additional risk of NTDs developing is thought to be much less likely.

- The most recent data from Botswana indicate that there is still a very small statistically significant increase in the risk of infant NTDs with DTG compared to EFV exposure at the time of conception. The prevalence of infant NTDs was slightly higher in women who were taking DTG around the time of conception (0.19%, or 19 infants with NTDs per 10,000 deliveries) than in women who were taking EFV or in women without HIV infection (0.07%, 7 infants with NTDs per 10,000 deliveries in both groups). However, the risk of NTDs in infants exposed to DTG around the time of conception was no longer significantly elevated when compared with infants exposed to any non-DTG ARV regimen around the time of conception in this setting.

- Data available studies have not shown an increase in the risk of NTDs in infants born to women who initiated DTG during pregnancy.

- Currently, insufficient DTG periconceptional exposures have been reported to the Antiretroviral Pregnancy Registry to determine whether an increased risk of NTDs exists in the United States.

- Folic acid is known to lower the risk of NTDs in the general population. The U.S. Public Health Service recommends that all pregnant women and women who might conceive take at least 400 mcg of folic acid daily and continue to do so throughout pregnancy. Unlike in Botswana, food in the United States is fortified routinely with folate. However, no established link exists between the use of DTG and impaired folate metabolism, nor does any evidence show that folate supplementation prevents NTDs associated with the periconceptional use of DTG.

- It is important to help women weigh the available information about the risks of NTDs when using DTG against what is known (or not known) about the risks of NTDs associated with other ARV drugs recommended for use in pregnancy. With the exception of EFV, not enough data are available to determine the risk of NTDs that may be associated with periconceptional use of any of the other currently recommended Preferred and Alternative ARV drugs in the United States. With data from Botswana, we now can rule out a threefold (or greater) increase in the risk of NTDs in infants who were exposed to EFV, which the Panel recommends as an Alternative ARV drug for pregnant women and women who are trying to conceive (see Table 4, Table 5, and Efavirenz).

Footnotes

- Guidance on the care of pregnant women and women who are trying to conceive also applies to transgender and nonbinary people of childbearing potential.
- Raltegravir requires twice-daily dosing during pregnancy and has a lower barrier to resistance than DTG.
- The first trimester is less than 14 weeks (up to 13 6/7 weeks) gestational age by last menstrual period.