Appendix C: Antiretroviral Counseling Guide for Health Care Providers

(Last updated March 17, 2022; last reviewed March 17, 2022)

Decision-making About Antiretroviral Drugs for People Who Are Pregnant or Are Trying to Conceive

This guide summarizes information, based on currently available data, to support counseling about the use of antiretroviral (ARV) drugs and antiretroviral therapy (ART) options during pregnancy for people who are pregnant or are trying to conceive. Patients should be counseled about the benefits and potential risks of ARV drugs in order to promote informed, individual decision-making.

For people who are pregnant or are 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%) in people with HIV who initiate ART prior to conception and have sustained viral suppression to undetectable levels throughout pregnancy.

Before, during, and after pregnancy, clinicians and patients should 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.

When discussing risks of birth defects, it is important to point out that the overall risk of neural tube defects (NTDs) in the United States is low in the general population because of mandatory food folate fortification. A background risk of NTDs exists, regardless of the ARV regimen used or a person's HIV status in pregnancy. 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 person is known to be pregnant. After 6 weeks' gestation, the additional risk of NTDs developing is thought to be much less likely. Folic acid supplementation should be encouraged for all people trying to conceive and in early pregnancy (see Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV).

General Antiretroviral Counseling for People Who Are Pregnant or Are Trying to Conceive

- Provide information to help patients understand and consider the benefits, advantages, disadvantages, and potential risks associated with the use of the individual ARV drug they are currently receiving or will be initiating when making decisions about their ARV regimen. These factors include dosing frequency, side effects or tolerability issues, and adverse pregnancy outcomes (e.g., preterm delivery, birth defects). Refer to Table 4, Table 5, Teratogenicity, and Antiretroviral Drug Regimens and Maternal and Neonatal Outcomes for additional information.

- Explain to patients 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 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 all the possible effects when using these drugs during pregnancy.

- Explain to patients that 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 because of the possible development of drug resistance.

- Counsel patients who are receiving ARVs that are not *Preferred* or *Alternative* options for use during pregnancy about the risks and benefits of continuing their current ART or switching to another ARV regimen. Discuss and consider 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 potential adverse outcomes. Panel recommendations about the continuation of specific ARV drugs are summarized in Table 5 and in Pregnant People with HIV Who Are Currently Receiving Antiretroviral Therapy.

- Patients who are trying to conceive should receive information about the use of specific ARV regimens during pregnancy to enable them to make informed decisions before they become pregnant.

Clinicians are encouraged to report all cases of ARV drug exposure during pregnancy or in patients who conceived while receiving ARV drugs to the Antiretroviral Pregnancy Registry.

Antiretroviral Drugs That Are Recommended for Use in Pregnancy

- When making recommendations, the Panel considers available data about a drug's effectiveness in nonpregnant adults and adolescents, tolerability, and ease of use, as well as pregnancy-specific data about potential risks—such as birth defects, pre-term birth, and pharmacokinetic (PK) changes—that could affect effectiveness and dosing. Some ARV drugs recommended for use in nonpregnant adults—such as bictegravir—are not recommended for use in pregnancy because there are insufficient data about their use in pregnancy.

- *Preferred* ARV drug options for use in ARV regimens for people who are pregnant or are trying to conceive include dolutegravir (DTG), raltegravir,[a] atazanavir/ritonavir (ATV/r), or darunavir/ritonavir (DRV/r) used in combination with two *Preferred* nucleoside reverse transcriptase inhibitors (NRTIs): abacavir plus lamivudine (3TC) or emtricitabine (FTC), tenofovir disoproxil fumarate plus 3TC or FTC, or tenofovir alafenamide (TAF) plus 3TC or FTC. DTG-based regimens are *Preferred* for people with Acute HIV during pregnancy. A moderate amount of data about pregnancy outcomes and birth defects exist for 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 is available only for DTG and efavirenz (EFV).

- EFV and rilpivirine (RPV) are recommended as *Alternative* ARV drug options in pregnancy. *Alternative* drugs may have more limited data on use in pregnancy than *Preferred* drugs

[a] Raltegravir requires twice-daily dosing during pregnancy and has a lower barrier to resistance than DTG; DRV/r also requires twice-daily dosing in pregnancy.

(e.g., RPV) or may be associated with more PKs, dosing, tolerability, drug interaction, or resistance concerns than those in the *Preferred* category, but they are acceptable for use in pregnancy. Zidovudine is an *Alternative* NRTI for use in pregnancy.

- Early data from a study in Botswana showed that the use of DTG around the time of conception was associated with a very small increase in the prevalence of infant NTDs. Later, additional data have shown a modest decline in the prevalence of NTDs with the use of DTG at conception. In the most recent analysis of data through March 2021, the prevalence of NTDs among infants born to women on DTG at conception did not differ significantly from those born to women receiving non-DTG regimens. Data from available studies have not shown an increase in the prevalence of NTDs in infants born to women who initiated DTG during pregnancy.

- The risk of other adverse pregnancy outcomes, many of which are more common than birth defects, also should be discussed. ARV regimens that contain ritonavir-boosted protease inhibitors may increase the risk of preterm delivery.

- 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. With the availability of additional data, the Panel now recommends TAF as a *Preferred* NRTI for ARV regimens in pregnancy.

- 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 ARVs during pregnancy. Patients who choose to continue one of these regimens should have more frequent viral load monitoring (i.e., every 1–2 months). It is also important to reinforce the need to 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).

- If an ARV regimen is changed during pregnancy, drugs in the new regimen should include those that are recommended for use in pregnancy (see Table 4 and Table 5), and viral load should be monitored more frequently (i.e., every 1–2 months).

- For additional information, see Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 4, and Table 5.