## Table 4. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (Last updated, February 10, 2021; last reviewed, February 10, 2021)

Recommendations for initial therapy are intended for pregnant women **who have never received ART or ARV drugs for prophylaxis** (i.e., women who are ARV-naive) and who show no evidence of significant resistance to regimen components (also see Pregnant Women with HIV Who Have Never Received Antiretroviral Drugs and Table 5).

In general, the Panel recommends that **women who are already on fully suppressive ARV regimens when pregnancy occurs should continue to use those regimens**, unless they are receiving an ARV drug or ARV regimen that is not recommended for use in adults, or there are concerns about safety and inferior efficacy during pregnancy (see Table 5 and Pregnant Women with HIV Who Are Currently Receiving Antiretroviral Therapy). Clinicians may need to consider additional factors when initiating ART in women who previously received ART or ARV drugs for prophylaxis (see Pregnant Women with HIV Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications and Table 5).

Regimens are listed alphabetically within each drug class and recommendation category, so the order does not indicate a ranking of preference. In addition, the Panel makes no recommendation of one agent or regimen over another within each category *(Preferred* or *Alternative)*. The table also indicates antiretroviral drugs or regimens that are available in fixed-dose combination (FDC) tablets.

**Note:** For more information about the use of specific drugs and dosing in pregnancy, see Table 5, the individual drug sections in Appendix B, and Table 10.

| Drug or Drug Combination | Comments |
|---|---|
| **Preferred Initial Regimens in Pregnancy**<br>Drugs or drug combinations are designated as *Preferred* for therapy in pregnant women when clinical trial data in adults have demonstrated efficacy and durability with acceptable toxicity and ease of use, and pregnancy-specific PK data are available to guide dosing. In addition, the available data must suggest a favorable risk-benefit balance for the drug or drug combination compared with other ARV drug options; the assessment of risks and benefits should incorporate outcomes for women, fetuses, and infants. Some *Preferred* drugs or regimens may have minimal toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive. Therefore, it is important to read all the information on each drug in the Perinatal Guidelines before administering any of these medications to patients (also see Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy). | |
| **Preferred Dual-NRTI Backbones** | |
| **ABC/3TC** | Available as an FDC. Can be administered once daily. ABC **should not be used** in patients who test positive for HLA-B*5701 because of the risk of developing a hypersensitivity reaction. ABC/3TC administered with ATV/r or EFV is not recommended if pretreatment HIV RNA is >100,000 copies/mL. |
| **TDF/FTC *or* TDF/3TC** | TDF/FTC is available as an FDC. Either coformulated TDF/FTC or separate doses of TDF and 3TC can be administered once daily. TDF has potential renal toxicity; thus, TDF-based, dual-NRTI combinations should be used with caution in patients with renal insufficiency. |
| **Preferred INSTI Regimens** | |
| **DTG/ABC/3TC (FDC) *or* DTG plus a Preferred Dual-NRTI Backbone[a]** | Administered once daily. The use of DTG/ABC/3TC requires HLA-B*5701 testing, because this FDC contains ABC. INSTI-based regimens may be particularly useful when drug interactions or the potential for preterm delivery with a PI-based regimen are a concern.In nonpregnant adults, DTG is associated with lower rates of INSTI resistance than RAL; like RAL, DTG has been shown to rapidly decrease viral load in ARV-naive pregnant women who present to care |

| Preferred INSTI Regimens | |
|---|---|
| | later in pregnancy. DTG is *Preferred* for the treatment of pregnant women with acute HIV infection and for women who present to care late in pregnancy. There are specific timing and/or fasting recommendations if DTG is taken with calcium or iron (e.g., in prenatal vitamins; see Table 10). The use of DTG at conception and in very early pregnancy has been associated with a small, but statistically significant, increase in the risk of NTDs; this information should be discussed with patients to ensure informed decision-making. For more information, see Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 5, Teratogenicity, and Appendix C: Antiretroviral Counseling Guide for Health Care Providers. |
| **RAL plus a Preferred Dual-NRTI Backbone** | PK data are available for RAL in pregnancy when using the twice-daily formulation (400 mg twice daily), but data are not available for the once-daily 1,200 mg (2 x 600 mg) extended-release formulation "raltegravir HD". Twice-daily dosing is required in pregnancy. RAL has been shown to produce rapid viral load decline to undetectable levels in women who present for initial therapy late in pregnancy. INSTI-based regimens may be particularly useful when drug interactions or the potential for preterm delivery with PI-based regimens are a concern. There are specific timing and/or fasting recommendations if RAL is taken with calcium or iron (e.g., in prenatal vitamins; see Table 10). |
| **Preferred PI Regimens** | |
| **ATV/r plus a Preferred Dual-NRTI Backbone** | Once-daily administration. Extensive experience with use in pregnancy. Maternal hyperbilirubinemia; no clinically significant neonatal hyperbilirubinemia or kernicterus reported, but neonatal bilirubin monitoring is recommended. Cannot be administered with PPIs. Specific timing recommended for dosing with H2 blockers (see Table 10). |
| **DRV/r plus a Preferred Dual-NRTI Backbone** | Better tolerated than LPV/r. Experience with use in pregnancy is increasing. Must be used twice daily in pregnancy. |
| **Drug** | **Comments** |
| **Alternative Initial Regimens in Pregnancy**<br>Drugs or drug combinations are designated as *Alternative* options for therapy in pregnant women when clinical trial data in adults show efficacy, and the data in pregnant individuals are generally favorable but limited. Most *Alternative* drugs or regimens are associated with more PK, dosing, tolerability, formulation, administration, or interaction concerns than those in the *Preferred* category, but they are acceptable for use in pregnancy. Some *Alternative* drugs or regimens may have known toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive. Therefore, it is important to read all the information on each drug in the Perinatal Guidelines before administering any of these medications to patients (also see Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy). | |
| **Alternative Dual-NRTI Backbones** | |
| **TAF/FTC** | Available as an FDC. Data about the use of TAF at conception and during pregnancy are limited. For both boosted and non-boosted regimens, plasma TAF exposures in pregnant adults are similar to those seen in nonpregnant adults; a change in dosing is not required. |
| **ZDV/3TC** | Available as an FDC. Although not recommended for initial therapy in nonpregnant adults, ZDV/3TC is the NRTI combination with most experience for use in pregnancy. It has the disadvantages of requiring twice-daily administration, which increases the potential for hematologic toxicities and other toxicities. |

| Alternative NNRTI Regimens | |
|---|---|
| **EFV/TDF/FTC (FDC)** ***or*** **EFV/TDF/3TC (FDC)** ***or*** **EFV plus a Preferred Dual-NRTI Backbone** | Birth defects have been reported in primate studies of EFV, no evidence has been found of an increased risk of birth defects in human studies and extensive experience in pregnancy; cautionary text remains in the package insert (see Teratogenicity, Efavirenz, and Table 10). These regimens are useful for women who require treatment with drugs that have significant interactions with *Preferred* agents or who need the convenience of a coformulated, single-tablet, once-daily regimen and are not eligible for DTG or RPV. Screening for antenatal and postpartum depression is recommended. Higher rate of adverse events than some *Preferred* drugs. |
| **RPV/TDF/FTC (FDC)** ***or*** **RPV/TAF/FTC (FDC)** **RPV plus a Preferred Dual-NRTI Backbone** | RPV **is not recommended** in patients with pretreatment HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm$^3$. Do not use with PPIs. PK data are available for pregnant individuals, but there is relatively little experience with use in pregnancy. PK data suggest lower drug levels and risk of viral rebound in second and third trimesters; if used, consider monitoring viral load more frequently. Should be taken with food. Available in a coformulated, single-tablet, once-daily regimen. |
| **Drug** | **Comments** |
| **Insufficient Data in Pregnancy to Recommend for Initial Regimens in ART-Naive Women**<br>These drugs are approved for use in adults,but lack adequate pregnancy-specific PK or safety data. | |
| **BIC/TAF/FTC (FDC)** | Limited data on the use of BIC in pregnancy. |
| **DOR** | No data on the use of DOR in pregnancy. |
| **IBA** | No data on the use of IBA in pregnancy. |
| **Drug** | **Comments** |
| **Not Recommended for Initial ART or Use in Pregnancy**<br>These drugs and drug combinations are recommended for use in adults but **are not recommended** for use during pregnancy because of limited data about use in pregnancy and/or concerns about maternal or fetal safety **or** PK changes **or** inferior efficacy, including viral breakthroughs in the second and third trimester (see Table 5 and Table 10).<br><br>**Note:** When a pregnant woman presents to care while virally suppressed on one of these drugs or drug combinations, providers should consider whether to continue her current regimen or switch to a recommended ARV regimen (see Pregnant Women with HIV Who Are Currently Receiving Antiretroviral Therapy and Table 5). | |
| **ATV/c** | Limited data on the use of ATV with COBI in pregnancy. Substantial reductions in trough levels of ATV in the second and third trimesters have been reported when taken with COBI. |
| **DRV/c (FDC)** ***or*** **DRV/c/FTC/TAF (FDC)** | Limited data on the use of DRV with COBI in pregnancy. Inadequate levels of both DRV and COBI in second and third trimester, as well as viral breakthroughs, have been reported. |
| **EVG/c/FTC/TAF (FDC)** | Limited data on the use of EVG with COBI (see above). Inadequate levels of both EVG and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Specific timing and/or fasting recommendations, especially if taken with calcium or iron (e.g., in prenatal vitamins; see Table 10). |
| **EVG/c/FTC/TDF (FDC)** | Limited data on the use of EVG with COBI in pregnancy. Inadequate levels of both EVG and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Specific timing and/or fasting recommendations, especially if taken with calcium or iron (e.g., in prenatal vitamins; see Table 10). |

| Drug | Comments |
|---|---|
| **Not Recommended for Initial ART in Pregnancy and Not Recommended, Except in Special Circumstances, for Treatment-Experienced Women in Pregnancy**<br>These drugs **are not recommended** for use in pregnant women who have never received ART. With the exception of NVP and LPV/r, data about the PKs, safety, and efficacy of these drugs during pregnancy are limited.<br><br>Some of these drugs are also categorized as not recommended except in special circumstances during pregnancy, because the Panel recognizes that circumstances may exist in which pregnant women who are ART-experienced may need to initiate or continue these drugs to reach or maintain viral suppression (see Table 5). | |
| **ETR** | Not recommended for use in ART-naive populations. Data about the use of ETR in pregnancy are limited. |
| **LPV/r plus a Preferred Dual-NRTI Backbone** | Abundant experience and established PKs in pregnancy. Has been associated with an increased risk of preterm delivery; see Antiretroviral Drug Regimens and Maternal and Neonatal Outcomes. More nausea than with *Preferred* or *Alternative* agents. Twice-daily administration. A dose increase is recommended during the third trimester (see Table 10). Once-daily LPV/r **is not recommended** for use in pregnant women. |
| **MVC** | Not recommended for use in ART-naive populations. MVC requires tropism testing before use. Available PK data suggest that using the standard adult dose is appropriate for pregnant patients, although data about use in pregnancy are limited. |
| **NVP** | Not recommended because of the potential for adverse events, complex lead-in dosing, and low barrier to resistance. NVP should be used with caution when initiating ART in women with CD4 counts >250 cells/mm$^3$. Use NVP and ABC together with caution; both can cause hypersensitivity reactions in the first few weeks after initiation. |
| **T-20** | Not recommended for use in ART-naive populations. |

**Note: The following drugs and drug combinations (not listed above) should not be used during pregnancy;** women who become pregnant while taking these medications should switch to a recommended regimen: d4T, ddI, FPV, FPV/r, IDV, IDV/r, NFV, RTV (as the sole PI), SQV, SQV/r, TPV, TPV/r, two-drug ARV regimens, or a three-NRTI ARV regimen (e.g., ABC/ZDV/3TC). See Archived Drugs in the Perinatal Guidelines and What Not to Use in the Adult and Adolescent Antiretroviral Guidelines for individual ARV drugs, ARV combinations, and ARV regimens that are not recommended or that should not be used in adults.

**Key:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CD4 = CD4 T lymphocyte cell; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IBA = ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; NVP = nevirapine; the Panel = the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine