Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 1 of 4)

Recommendations for initial therapy are intended for pregnant women **who have never received ART or ARV prophylaxis** (i.e., women who are ARV-naive) and who have no evidence of significant resistance to regimen components (see Pregnant Women Living with HIV Who Have Never Received Antiretroviral Drugs and Table 7).

The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (the Panel) recommends that **women who become pregnant while on a stable ART regimen that results in viral suppression remain on that same regimen**, unless they are receiving an ARV drug or ART regimen that is not recommended for use in adults or there are concerns about safety and inferior efficacy during pregnancy (see Table 7 and Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy). Women who have previously received ART or ARV drugs for prophylaxis may warrant specific considerations (see Pregnant Women Living with HIV Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications and Table 7). Additionally, new data have identified a possible increased risk of NTDs in the infants of women who become pregnant while taking DTG (see table below and Recommendations for Use of Antiretroviral Drugs During Pregnancy).

Regimens are listed alphabetically within each drug class and recommendation category, and 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).

Note: For more information about the use of specific drugs and dosing in pregnancy, see Table 7, the individual drug sections in Appendix B, and Table 10.

Drug	Comments
Preferred Initial Regimens in Pregnancy: • Drugs or drug combinations are designated as preferred for initiating ART in ARV-naive pregnant women when clinical trial data in adults have demonstrated optimal efficacy and durability with acceptable toxicity and ease of use and when pregnancy-specific PK data are available to guide dosing. In addition, drugs or drug combinations must have no established associations with teratogenic effects (from animal and/or human studies), and no clinically significant adverse outcomes for mothers, fetuses, or newborns have been reported.	
Preferred Two-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 a hypersensitivity reaction. ABC/3TC administered with ATV/r or with 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 TDF with separate 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 (After the First Trimester)[a]** Dolutegravir **is not recommended** for use in pregnant women during the first trimester (see Interim Panel Recommendations Regarding the Use of Dolutegravir in Pregnancy and Interim Guidance about the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy).	Should not be initiated during the first trimester (less than 14 weeks [up to 13 6/7 weeks] gestational age by last menstrual period) due to concerns about a possible increased risk of NTDs. No safety problems have been identified when DTG is initiated during pregnancy; however, a possible increased risk of NTDs was observed among infants born to women who conceived while taking DTG. Available as an FDC (coformulated with 3TC and ABC, requiring HLA-B*5701 testing). Administered once daily. Useful when drug interactions with a PI are a concern. In nonpregnant adults, DTG is associated with lower rates of INSTI resistance than RAL; therefore, the use of DTG is suggested for women with acute HIV infection in pregnancy (after the first trimester) and for women who present to care late in pregnancy. There are specific timing and/or fasting recommendations if taken with calcium or iron (e.g., in prenatal vitamins; see Table 10).

Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 2 of 4)

Drug	Comments
Preferred INSTI Regimens, continued	
RAL plus a Preferred 2-NRTI Backbone	PK data are available for RAL use in pregnancy, and there is increasing experience with use in pregnancy. Associated with rapid viral load reduction (which may be useful for women who present for initial therapy late in pregnancy). Useful when drug interactions with PI regimens are a concern. Twice-daily dosing required. There are specific timing and/or fasting recommendations if taken with calcium or iron (e.g., in prenatal vitamins; see Table 10).
Preferred PI Regimens	
ATV/r plus a Preferred 2-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 recommended. Cannot be administered with PPIs. Specific timing recommended for dosing with H2 blockers (see Table 10).
DRV/r plus a Preferred 2-NRTI Backbone	Better tolerated than LPV/r. Increasing experience with use in pregnancy. Must be used twice daily in pregnancy.
Drug	**Comments**
Alternative Initial Regimens in Pregnancy: • These regimens have clinical trial data that demonstrates efficacy in adults and adequate serum drug levels during pregnancy, but 1 or more of the following conditions apply: experience in pregnancy is limited; data are lacking or incomplete on teratogenicity; or regimen is associated with dosing, formulation, toxicity, or interaction issues.	
Alternative 2-NRTI Backbones	
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 and having an increased potential for hematologic toxicities and other toxicities.
Alternative PI Regimens	
LPV/r plus a Preferred 2-NRTI Backbone	Abundant experience and established PKs in pregnancy. More nausea than with preferred agents. Twice-daily administration. Dose increase recommended in third trimester (see Table 10). Once-daily LPV/r **is not recommended** for use in pregnant women.
Alternative NNRTI Regimens	
EFV/TDF/FTC (FDC) ***or*** **EFV/TDF/3TC (FDC)** ***or*** **EFV plus a Preferred 2-NRTI Backbone**	Birth defects have been seen in primate studies of EFV, but there has been no evidence of an increased risk of birth defects in human studies and extensive experience in pregnancy; cautionary text remains in package insert (see Teratogenicity and Table 10). Preferred regimen in women who require coadministration of drugs with 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 other preferred drugs.
RPV/TDF/FTC (FDC) ***or*** **RPV plus a Preferred 2-NRTI Backbone**	RPV **is not recommended** in patients with pretreatment HIV RNA >100,000 copies/mL or CD4 cell counts <200 cells/mm^3. Do not use with PPIs. PK data available for pregnant individuals but relatively little experience with use in pregnancy. Available in coformulated, single-tablet, once-daily regimen. PK data suggest lower drug levels and risk of viral rebound in second and third trimesters; if used, consider monitoring viral load more frequently.
Drug	**Comments**
Insufficient Data in Pregnancy to Recommend for Initial Regimens in ART-Naive Women: • These drugs are approved for use in adults but lack adequate pregnancy-specific PK or safety data.	
BIC/TAF/FTC (FDC)	No data on use of BIC in pregnancy. Limited data on use of TAF in pregnancy.
DOR	No data on the use of DOR in pregnancy.
IBA	No data on the use of IBA in pregnancy.
TAF/FTC (FDC) ***and*** **RPV/TAF/FTC (FDC)**	Plasma TAF exposures in pregnant adults are similar to those seen in nonpregnant adults, whether TAF is administered with a boosting agent or not. TAF has been studied in pregnant women, but data are not yet sufficient to recommend initiating TAF in pregnancy.

Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 3 of 4)

Drug	Comments
Not Recommended for Initial ART or Use in Pregnancy:[b] • These drugs and drug combinations are recommended for use in adults but are not recommended for use during pregnancy or during a defined time in pregnancy (e.g., specific trimester[s]) because of concerns about maternal or fetal safety or inferior efficacy, including viral breakthroughs in the second and third trimester (see Table 7 and Table 10). **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 ART regimen (see Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy and Table 7).	
DTG (during the first trimester)[a]	Should not be initiated during the first trimester (less than14 weeks [up to 13 6/7 weeks] gestational age by last menstrual period) due to concerns about a possible increased risk of NTDs. No safety problems identified when DTG is initiated during pregnancy; however, the possible increased risk of NTDs was observed among infants born to women who conceived while taking DTG (see Preferred INSTI Regimens above for information on the use of DTG after the first trimester).
ATV/COBI	Limited data on the use of ATV with COBI in pregnancy. Concerns regarding low levels of COBI in second and third trimesters when used with DRV or EVG, leading to low levels of DRV or EVG and poor virologic suppression. PK data on ATV/COBI are not yet available, but low levels of these drugs are also expected to occur during the second and third trimesters.
DRV/COBI (FDC) ***or*** **DRV/COBI/FTC/TAF (FDC)**	Limited data on 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. Insufficient data about the use of TAF in pregnancy (see above).
EVG/COBI/FTC/TAF (FDC)	Limited data on use of EVG with COBI and insufficient data on the use of TAF in pregnancy (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/COBI/FTC/TDF (FDC)	Limited data on 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: • These drugs **are not recommended** for use in pregnant women who have never received ART. With the exception of NVP, data about the PKs, safety, and efficacy of these drugs during pregnancy are limited. • Some of these drugs are also categorized as not recommended except in special circumstances during pregnancy, because the Panel recognizes that may be circumstances where pregnant women who are ART-experienced may need to initiate or continue these drugs to reach or maintain viral suppression (see Table 7).	
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.
ETR	Not recommended for use in ART-naive populations.
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 cell 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.

[a] DTG is a preferred INSTI for pregnant women after the first trimester. This classification is based on available PK, safety, and efficacy data. However, because of concerns about congenital anomalies that may have occurred both during and after neural tube closure (which occurs around 4 weeks post-conception and 6 weeks after the last menstrual period), the Panel **does not recommend** use of DTG **during the first trimester.** The first trimester is less than 14 weeks (up to 13 6/7 weeks) gestational age by last menstrual period. This is intended to be a conservative, interim recommendation and will be revised, if indicated, as additional data become available in 2019. Although DTG is not FDA-approved for use in the first trimester, some Panel members would consider using DTG at 12 weeks gestational age by last menstrual period on an individual patient basis (for more information, see Interim Panel Recommendations Regarding the Use of Dolutegravir in Pregnancy in Recommendations for the Use of Antiretroviral Drugs During Pregnancy).

Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 4 of 4)

Note: The following drugs and drug combinations (that are not listed above) should not be used during pregnancy; if women become pregnant while taking these medications, they should switch to a recommended regimen: d4T, ddI, FPV, FPV/r, IDV, IDV/r, NFV, RTV (as a sole PI), SQV, SQV/r, TPV, TPV/r, DTG/RPV (FDC) as a 2-drug ART regimen, or a three-NRTI ART regimen (e.g., ABC/ZDV/3TC). See Table 10 and What Not to Use in the Adult and Adolescent Antiretroviral Guidelines for individual ARV drugs, ARV combinations, and ART regimens that are not recommended or should not be used in adults.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CD4 = CD4 T lymphocyte cell; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FDA = Food and Drug Administration; 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; 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