Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 1 of 3)

These recommendations are for pregnant women **who have never received antiretroviral therapy (ART) previously (i.e., antiretroviral-naive)** and who have no evidence of significant resistance to regimen components. See Table 9 for more information on specific drugs and dosing in pregnancy.

Within each drug class and recommendation category, regimens are listed alphabetically, and the order does not indicate a ranking of preference. In addition, The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (the Panel) makes no recommendation of one agent or regimen over another within each category (Preferred or Alternative).

It is recommended that **women who become pregnant while on a stable ART regimen with viral suppression** remain on that same regimen, with the exception of regimens containing didanosine, stavudine, or treatment-dose ritonavir, and (until more data are available) elvitegravir/cobicistat.

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; pregnancy-specific PK data are available to guide dosing; in addition, there have been 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 FDC. Can be administered once daily. ABC **should not be used** in patients who test positive for HLA-B*5701 because of risk of hypersensitivity reaction. ABC/3TC 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 available as FDC. Either TDF/FTC (coformulated) 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 PI Regimens	
ATV/r plus a Preferred Two-NRTI Backbone	Once-daily administration. Extensive experience in pregnancy. Maternal hyperbilirubinemia; no clinically significant neonatal hyperbilirubinemia or kernicterus reported, but neonatal bilirubin monitoring recommended. Cannot be administered with proton-pump inhibitors; specific timing recommended for dosing with H2 blockers (see Table 9).
DRV/r plus a Preferred Two-NRTI Backbone	Better tolerated than LPV/r. PK data available. Increasing experience with use in pregnancy. Must be used twice daily in pregnancy.
Preferred Integrase Inhibitor Regimen(s)	
RAL plus a Preferred Two-NRTI Backbone	PK data available and increasing experience in pregnancy. Rapid viral load reduction (potential role for women who present for initial therapy late in pregnancy). Useful when drug interactions with PI regimens are a concern. Twice-daily dosing required.
Alternative Initial Regimens in Pregnancy: • Regimens with clinical trial data demonstrating efficacy in adults and adequate serum drug levels in pregnancy, but one or more of the following 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 Two-NRTI Backbones	
ZDV/3TC	Available as FDC. NRTI combination with most experience for use in pregnancy but has disadvantages of requirement for twice-daily administration and increased potential for hematologic toxicities.
Alternative PI Regimens	
LPV/r plus a Preferred Two-NRTI Backbone	Abundant experience and established PK in pregnancy. More nausea than with preferred agents. Twice-daily administration. Dose increase recommended in third trimester (see Table 9). Once-daily LPV/r is not recommended for use in pregnant women.

Table 6. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (page 2 of 3)

Drug	Comments
Alternative Integrase Inhibitor Regimens	
DTG plus a Preferred Two-NRTI Backbone	PK data available only in abstract form. No safety problems identified in limited but increasing experience in pregnancy. Available as FDC (with ABC, requiring HLA B5701 testing). Administered once daily. Useful when drug interactions with a PI are a concern. In non-pregnant adults, associated with lower rates of INSTI resistance than RAL, and therefore suggested for women with acute infection in pregnancy. Specific timing and/or fasting recommendations if taken with calcium or iron (e.g., in prenatal vitamins; Table 9).
Alternative NNRTI Regimens	
EFV plus a Preferred Two-NRTI Backbone	Concern because of birth defects seen in primate studies, but data not borne out in human studies and extensive experience in pregnancy; cautionary text remains in package insert (see Teratogenicity and Table 9). Preferred regimen in women who require co-administration 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 RPV. Screening for antenatal and postpartum depression is recommended. Higher rate of adverse events than drugs in Preferred category
RPV/TDF/FTC (or RPV plus a Preferred Two-NRTI Backbone)	RPV not recommended with pretreatment HIV RNA >100,000 copies/mL or CD4 cell count <200 cells/mm^3. Do not use with PPIs. PK data available in pregnancy but relatively little experience with use in pregnancy. Available in coformulated single-pill, once-daily regimen.
Insufficient Data in Pregnancy to Recommend Routine Use in Initial Regimens for ART-Naive Women: • Drugs that are approved for use in adults but lack adequate pregnancy-specific PK or safety data	
TAF/FTC Fixed Drug Combination	No data on use of TAF in pregnancy.
RPV/TAF/FTC Fixed Drug Combination	No data on use of TAF in pregnancy.
Not Recommended for Initial ART in Pregnancy: • Drugs whose use is not recommended as part of initial regimens in pregnancy because of toxicity, lower rate of viral suppression, or pharmacologic data suggesting insufficient serum drug levels in pregnancy, or because these drugs are not recommended in ART-naive populations. **Note:** Drugs not recommended for initial use because of toxicity (stavudine [d4T], didanosine [ddI], treatment-dose ritonavir [RTV], marked below with *) should also be stopped in women who present during pregnancy while taking these medications. For women who present on drugs not recommended for initial use because of concerns about viral breakthrough (EVG/COBI/TDF/FTC or EVG/COBI/TAF/FTC, marked below with **), providers should consider switching to more effective, recommended regimens. If an EVG/COBI regimen is continued, viral load should be monitored frequently, and therapeutic drug monitoring (if available) may be useful. Other medications listed below may be continued in women who present during pregnancy, as long as they are well tolerated and result in sustained virologic suppression.	
EVG/COBI/TDF/FTC** Fixed Drug Combination	Limited data on use of EVG/COBI component in pregnancy. Inadequate levels of both EVG and COBI in 2nd and 3rd 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 9).
EVG/COBI/TAF/FTC** Fixed Drug Combination	Limited data on use of EVG/COBI as above; additionally, no data on use of TAF in pregnancy. Inadequate levels of both EVG and COBI in 2nd and 3rd 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 9).
ABC/3TC/ZDV As a complete regimen, in absence of other antiretroviral medications	Generally not recommended due to inferior virologic efficacy.
COBI	Limited data on use of COBI (including coformulations with ATV or DRV) in pregnancy.
d4T*	Not recommended due to toxicity.
ddI*	Not recommended due to toxicity.

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

Drug	Comments
FPV	Limited data on use in pregnancy. Not recommended in ART-naive populations.
IDV/r	Nephrolithiasis, maternal hyperbilirubinemia.
MVC	MVC requires tropism testing before use. Few case reports of use in pregnancy. Not recommended in ART-naive populations.
NFV	Lower rate of viral suppression with NFV compared to LPV/r or EFV in adult trials.
RTV*	RTV as a single PI is not recommended because of inferior efficacy and increased toxicity.
SQV/r	Not recommended based on potential toxicity and dosing disadvantages. Baseline ECG is recommended before initiation of SQV/r because of potential PR and QT prolongation; contraindicated with preexisting cardiac conduction system disease. Limited data in pregnancy. Large pill burden. Twice-daily dosing required.
ETR	Not recommended in ART-naive populations.
NVP	Not recommended because of greater 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 count >250 cells/mm^3. Use NVP and ABC together with caution; both can cause hypersensitivity reactions within the first few weeks after initiation.
T20	Not recommended in ART-naive populations.
TPV/r	Not recommended in ART-naive populations.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; CD4 = CD4 T lymphocyte cell; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FDC = fixed-drug combination; FPV = fosamprenavir; FTC = emtricitabine; IDV/r = indinavir/ritonavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV/r = saquinavir/ritonavir; T20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine