Pregnant People with HIV Who Have Never Received Antiretroviral Drugs (Antiretroviral-Naive)

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Panel's Recommendations
• For pregnant people who have never received antiretroviral therapy (ART), ART should be initiated as soon as possible, even before results of drug-resistance testing are available, as viral suppression earlier in pregnancy has been associated with lower risk of transmission (AI). When ART is initiated before the results of the drug-resistance assays are available, the antiretroviral (ARV) regimen should be modified, if necessary, based on the resistance assay results (AII). • ARV regimens that are *Preferred* for the treatment of pregnant people with HIV who have never received ARV drugs consist of the integrase strand transfer inhibitor (INSTI) dolutegravir (DTG) plus a dual-nucleoside reverse transcriptase inhibitor combination (see Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive; Early (Acute or Recent) HIV) (AIII). *Preferred* regimens include: o DTG plus (tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide [TAF]) plus (emtricitabine [FTC] or lamivudine [3TC]) *or* o DTG plus abacavir (ABC) plus 3TC – only for individuals who are HLA-B*5701 negative and without chronic hepatitis B virus (HBV) coinfection • ARV regimens that are *Preferred* for pregnant people with HIV with any prior use of long-acting injectable cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP) consist of the ritonavir-boosted protease inhibitor darunavir/ritonavir (DRV/r), rather than an INSTI (i.e., DTG), plus a dual-nucleoside reverse transcriptase inhibitor combination (see Pregnant People with HIV Who Have Previously Received Antiretroviral Medications but Are Not Currently on Antiretroviral Medications) (AIII). *Preferred* regimens include: o DRV/r plus (TDF or TAF) plus (FTC or 3TC) *or* o DRV/r plus ABC plus 3TC – only for individuals who are HLA-B*5701 negative and without chronic HBV coinfection • *Alternative* ARVs for the treatment of pregnant people with HIV who have never received ARV drugs are shown in Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive. • Choice of ART regimen should be based on results of resistance testing, concurrent medical conditions, and current recommendations for ART in pregnancy (AII). For additional information, see Recommendations for Use of Antiretroviral Drugs During Pregnancy: Overview.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional *Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Antiretroviral (ARV) regimens designated by the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission (the Panel) as *Preferred* regimens for pregnant people who have never received antiretroviral drugs (ARV naive) consist of the integrase strand transfer inhibitor (INSTI) dolutegravir (DTG) plus a dual–nucleoside reverse transcriptase inhibitor (NRTI) combination. *Preferred* regimens for the treatment of pregnant people who have never received ARV drugs include:

- DTG plus (tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide [TAF]) plus (emtricitabine [FTC] or lamivudine [3TC])

- DTG plus abacavir (ABC) plus 3TC – only for individuals who are HLA-B*5701 negative and without chronic hepatitis B virus (HBV) coinfection

The NRTI components are *Preferred* because they are recommended for nonpregnant adults and have several advantages, including reassuring pharmacokinetic (PK) data, extensive experience with use in pregnancy, once-daily dosing, and less toxicity than zidovudine plus 3TC.[1-3] Use of ABC requires testing for the HLA-B*5701 gene variant before initiating therapy. For this reason, providers may choose to use TDF or TAF rather than ABC to avoid delays in antiretroviral therapy (ART) initiation while awaiting HLA-B*5701 test results. In addition, ABC is not active against HBV; therefore, TDF and TAF with either 3TC or FTC—drugs that are active against hepatitis B virus—should be used for individuals with chronic HBV coinfection.

DTG is the *Preferred* INSTI for use in pregnancy because it has been studied extensively in pregnancy, is associated with high rates of viral suppression, fast rates of viral load decline, high tolerability, and a high genetic barrier to drug resistance.[4-6] For example, two randomized clinical trials that compared DTG plus two NRTIs to efavirenz (EFV) plus two NRTIs in ART-naive women who initiated therapy during pregnancy found that DTG-based ART produced more rapid viral suppression than EFV-based ART, with a greater proportion of women reaching an undetectable viral load (<50 copies/mL) at the time of delivery.[7,8] Higher rates of viral suppression did not translate into statistically significantly lower rates of observed vertical transmission with DTG compared with EFV; transmission rates were low with both regimens, and the studies were not powered to detect small differences.[8-10] Safety and efficacy data extending to 50 and 72 weeks postpartum supported use of DTG-based ART in pregnancy.[10,11] DTG is *Preferred* for use in pregnant people with early (acute or recent) HIV infection without prior use of long-acting injectable cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP) (see Early [Acute or Recent] HIV).

Ritonavir-boosted darunavir (DRV/r) is *Preferred* over an INSTI-based regimen for pregnant people with any prior CAB-LA use, pending results of genotypic resistance testing for INSTI mutations (see Early [Acute or Recent] HIV and Pregnant People with HIV Who Have Previously Received Antiretroviral Medications but Are Not Currently on Antiretroviral Medications). For pregnant people without prior CAB-LA use, DRV/r is now classified as an *Alternative* ARV drug for use in pregnancy. Its efficacy in pregnancy is well documented; in a recent large observational study, viral suppression with DRV/r was not statistically significantly different than viral suppression with DTG.[12] Importantly, however, although the use of once-daily dosing for DRV/r is approved for nonpregnant adults, PK data do not support once-daily dosing in pregnancy[13]; therefore, twice-daily dosing is recommended (see Darunavir).

The INSTI bictegravir (BIC) is now classified as an *Alternative* ARV drug for use in pregnancy because data about safety, PK, and efficacy in pregnancy are available but are more limited than data about drugs classified as *Preferred*. Detailed advantages and disadvantages of each of these *Preferred* medications in pregnancy, as well as of those in the *Alternative*, *Insufficient Data*, *Not Recommended*, and *Not Recommended Except in Special Circumstances* categories, are shown in Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive.

Recommendations for Regimens Other Than Combination (Three-Drug) ART

Although the Adult and Adolescent Antiretroviral Guidelines recommend some two-drug ARV regimens for nonpregnant ARV-naive people in certain clinical circumstances, two-drug ARV

regimens **are not recommended** for initiation of ART in ARV-naive pregnant people because of a lack of data in pregnancy.

ARV-Naive People Who Present in the Third Trimester

INSTIs have an important role when ART is initiated late in pregnancy, particularly for people who have high viral loads, because of the documented ability of DTG and raltegravir (RAL) to suppress viral load rapidly (a decrease of approximately 2 $\log_{10}$ copies/mL occurs by Week 2 of therapy with these drugs).[14-18]

In the Dolutegravir in Pregnant HIV Women and Their Neonates (DolPHIN 2) study, 268 ART-naive women in Uganda and South Africa were randomized to receive DTG plus two NRTIs or EFV plus two NRTIs at a minimum of 28 weeks gestational age (median: 31 weeks). At delivery, women in the DTG arm were significantly more likely to achieve viral loads of <50 copies/mL (74.1% vs. 42.7%; adjusted risk ratio 1.64 [1.31–2.06], $P < 0.0001$) than women in the EFV arm, with a faster time to reach viral loads <50 copies/ml (4.1 vs. 12.1 weeks).[7] The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) 1081 trial randomized 408 ART-naive women in South America, Africa, Thailand, and the United States who presented late in pregnancy (20 to <37 weeks gestation) to receive RAL plus two NRTIs or EFV plus two NRTIs. Among 307 women in the primary efficacy analysis, 84% in the EFV group and 94% in the RAL group achieved a viral load of <200 copies/mL at or near delivery (absolute difference 10%; 95% confidence interval, 3% to 18%; $P = 0.0015$); the difference primarily occurred among women enrolling later in pregnancy (interaction $P = 0.040$). The median time to achieve a viral load of <200 copies/mL was 8 days for women who received RAL-based ART and 15 days for women who received EFV-based ART. The decline in viral load was greater in the women who received RAL than in those who received EFV at 2, 4, and 6 weeks after initiation.[19]

RAL and DTG are likely to be similarly effective in reducing viral load rapidly for people who present in the third trimester. However, DTG is *Preferred* and RAL is *Alternative* when initiating ART in people who have never received ARV drugs, because RAL requires twice-daily dosing and has a lower barrier to development of drug resistance than DTG (see Adult and Adolescent Antiretroviral Guidelines). BIC is now an *Alternative* INSTI-based regimen when initiating ART during pregnancy, but data are not available for its use when initiating ART during the third trimester. Other INSTIs (i.e., elvitegravir [EVG] and cabotegravir [CAB]) are not recommended when initiating ART in pregnancy due to either concern for insufficient levels (EVG) or lack of data during pregnancy as initial treatment for ARV-naive adults or adolescents (CAB). For more information, see Table 6. What to Start: Initial Antiretroviral Regimens During Pregnancy for People Who Are Antiretroviral-Naive.

People who present after early (acute or recent) HIV infection at any time in pregnancy are discussed in Early (Acute or Recent) HIV.

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