Supplemental Online Content

Eke AC, Lockman S, Mofenson LM. Antiretroviral treatment of HIV/AIDS during pregnancy. *JAMA*. Published online April 3, 2023. doi:10.1001/jama.2023.5076

eTable. Preferred and Alternative Antiretroviral Drugs for Therapy During Pregnancy

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable. Preferred and Alternative Antiretroviral Drugs for Therapy During Pregnancy

ANTIRETROVIRAL MANAGEMENT FOR WOMEN WHO BECOME PREGNANT WHILE TAKING ART *People who are taking ART when pregnancy occurs and have undetectable viral load should generally continue their regimen (unless receiving one of a few antiretroviral[s] not recommended for in nonpregnant adults or for which pregnancy safety/efficacy concerns exist)*		
PREFERRED ANTIRETROVIRAL REGIMENS WHEN ART IS BEING INITIATED IN PREGNANCY *Clinical trial data in non-pregnant adults show viral efficacy and durability with acceptable toxicity/ease of use; pregnancy-specific pharmacokinetic data available to guide dosing; favorable risk-benefit balance for drug/combination compared to other drug options.*		
Drug and Dosing	**Pregnancy-Related Information**	**Selected Adverse Effects**
Dual nucleoside backbone:		
Zidovudine 300 mg + lamivudine 150 mg, given twice daily	• High placental transfer drugs to fetus. No evidence human teratogenicity (can rule out 1.5-fold increase overall birth defects, 2-fold increase more common cardiac/genitourinary defects, APR).	• Zidovudine associated with prenatal anemia. • Long term zidovudine use has been associated with mitochondrial toxicity, although this is generally rare.
Tenofovir alafenamide 25 mg + emtricitabine 200 OR lamivudine 300 mg, once daily	• Low placental transfer tenofovir alafenamide prodrug; high placental transfer tenofovir active drug and lamivudine and emtricitabine. • No evidence human teratogenicity (can rule out 2-fold increase overall birth defects, Antiretroviral Pregnancy Registry [APR]). • Combined with dolutegravir, fewer adverse birth outcomes than tenofovir disoproxil fumarate in one study. • Less renal/bone toxicity than tenofovir disoproxil fumarate.	• Combined with dolutegravir, associated with excessive weight gain in non-pregnant persons. • Higher gestational weight gain in pregnancy than with tenofovir disoproxil fumarate but remains below that in pregnant people without HIV.
Tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg OR lamivudine 300 mg, once daily	• Low placental transfer tenofovir disoproxil fumarate prodrug; high placental transfer tenofovir active drug and lamivudine and emtricitabine. • No evidence human teratogenicity (can rule out 1.5-fold increase overall birth defects, 2-fold increase more common cardiac/genitourinary defects, APR).	• Potential concern for maternal/fetal renal/bone toxicity (but no substantial clinical findings to date). • Insufficient weight gain during pregnancy especially when combined with efavirenz.

Drug and Dosing	Pregnancy-Related Information	Selected Adverse Effects
Abacavir 600 mg + lamivudine 300 mg, once daily	• High placental transfer drugs to fetus. • No evidence human teratogenicity (can rule out 1.5-fold increase overall birth defects, 2-fold increase more common cardiac/genitourinary defects, APR).	• HLA-B*5701 testing required before use because abacavir-based combinations may cause life-threatening hypersensitivity reaction in patients who test positive for the HLA-B*5701 allele. • Should not be used in persons with hepatitis B coinfection.
Third Antiretroviral Drug (combined with dual nucleoside backbone)		
Integrase inhibitor		
Dolutegravir 50 mg, once daily	• High rates viral suppression; rapid drop in viral load within days of initiating therapy. • High placental transfer to fetus. • No evidence human teratogenicity (can rule out 2-fold increase overall birth defects, APR); use at conception <u>not</u> associated with neural tube defects (see text).	• Sleep disturbance; rarely associated with depression and suicidal ideation. • Associated with excessive weight gain in non-pregnant persons (especially given with tenofovir alafenamide). • Higher gestational weight gain in pregnancy given with tenofovir alafenamide than with tenofovir disoproxil fumarate but remains below that in pregnant people without HIV.
Protease inhibitor		
Darunavir 600 mg + ritonavir 100 mg, given twice daily	• Must be combined with low-dose ritonavir boosting and should be given twice daily during pregnancy (due to pregnancy pharmacokinetics). • Low placental transfer to fetus. • No evidence human teratogenicity (can rule out 2-fold increase overall birth defects, APR).	• Protease inhibitors may slightly increase rate of preterm birth (less of a concern with contemporary protease inhibitors than older agents such as lopinavir/ritonavir).
<u>ALTERNATIVE DUAL NUCELOSIDE COMBINATIONS AND THIRD ANTIRETROVIRAL DRUGS WHEN ART IS BEING INITIATED IN PREGNANCY</u> *Clinical trial data in non-pregnant adults show viral efficacy and data in pregnant persons are generally favorable but may be more limited (generally more concerns related to pharmacokinetic, dosing, tolerability, formulation, administration or interactions than drugs in Preferred Category but acceptable for use in pregnancy).*		
Dual nucleoside backbone:		

Drug and Dosing	Pregnancy-Related Information	Selected Adverse Effects
Zidovudine 300 mg + lamivudine 150 mg, given twice daily	• High placental transfer drugs to fetus. • No evidence human teratogenicity (can rule out 1.5-fold increase overall birth defects, 2-fold increase more common cardiac/genitourinary defects, APR).	• Zidovudine associated with prenatal anemia. • Long term zidovudine use has been associated with mitochondrial toxicity, although this is generally rare.
Third Antiretroviral Drug (combined with dual nucleoside backbone)		
Integrase inhibitor		
Raltegravir 400 mg, given twice daily	• Rapid drop in viral load within days of initiating therapy. • Must be given twice daily during pregnancy. • High placental transfer to fetus. • No evidence human teratogenicity (can rule out 2-fold increase overall birth defects, APR).	• Weight gain and a slightly increased risk of liver dysfunction. • Lower genetic barrier to resistance compared to other integrase-strand inhibitors.
Protease inhibitor		
Atazanavir 300 mg + ritonavir 100 mg, once daily	• Must be combined with low-dose ritonavir boosting in pregnancy. • Low placental transfer to fetus • Increase dose in $2^{nd}/3^{rd}$ trimesters, in treatment-experienced patients. • No evidence human teratogenicity (can rule out 1.5-fold increase overall birth defects, 2-fold increase more common cardiac/genitourinary defects, APR).	• Protease inhibitors may slightly increase rate of preterm birth (less of a concern with contemporary protease inhibitors than older agents such as lopinavir/ritonavir). • Associated with maternal indirect hyperbilirubinemia; effect of *in utero* exposure in infant indirect bilirubin levels unclear (non-pathologic increase neonatal bilirubin observed in some studies). • Some studies show low language and social-emotional scores in children exposed to atazanavir *in utero*.
Non-nucleoside reverse transcriptase inhibitor		
Efavirenz 600 mg, once daily	• Moderate placental transfer • Demonstrated to be safer than lopinavir/ritonavir or nevirapine-based therapy at conception. • No evidence human teratogenicity (can rule out 1.5-fold increase overall birth defects, 2-fold increase more common cardiac/genitourinary defects, APR).	• Rash, neuropsychiatric disorders, hepatic toxicity have been reported, including in pregnancy. • Higher rate adverse pregnancy outcomes and lower gestational weight gain when given with tenofovir disoproxil fumarate/emtricitabine compared to dolutegravir/tenofovir alafenamide/emtricitabine ART.

Rilpivirine 25 mg, once daily	• Should not be used if HIV viral load is >100,000 copies/mL. • Pharmacokinetics highly variable in pregnancy (levels 20-50% lower in pregnancy than postpartum; most women exceed therapeutic exposure). • More frequent viral load monitoring recommended. • Moderate to high placental transfer • No evidence human teratogenicity (can rule out 2-fold increase overall birth defects, APR).	• Rash, neuropsychiatric disorders, hepatic toxicity have been reported.