HHS Recommendations for Use of Antiretroviral Drugs During Pregnancy: January 2023 Updates

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No conflicts of interest or relationships to disclose.

Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States

Developed by the HHS Panel on Treatment of
HIV During Pregnancy and Prevention of Perinatal Transmission—
A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

How to Cite the Perinatal Guidelines:

Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/perinatal. Accessed (insert date) [include page numbers, table number, etc., if applicable].

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

https://clinicalinfo.hiv.gov/en/guidelines

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Introductory Notes

- Will not cover changes to infant feeding (breastfeeding/chestfeeding) section today; please join on March 30 for special presentation by Dr. Judy Levison!
- Will not cover maternal HIV testing or infant testing and treatment
- Update adds significant focus on gender-neutral language, individualizing ART decisions, shared decision-making, patient autonomy, & gender-based violence

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What's New in the Guidelines
January 31, 2023

- PrEP use during periconception, antepartum, and postpartum periods
- Pregnancy counseling and care for persons with HIV of childbearing age and serodifferent couples trying to conceive
- Recommendations for use of ARVs during pregnancy
  - Pregnant people who have never received ART
  - People with HIV who are taking ART when they become pregnant
  - Pregnant people who have not achieved VL suppression on ART

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HIV PrEP During Periconception, Antepartum, & Postpartum Periods

- Discuss PrEP with all sexually active adults & adolescents without HIV
- Offer PrEP to those who request it or have specific indications
- TDF/FTC daily: only approved option with efficacy data for people with receptive vaginal HIV exposure plus safety data during pregnancy*
  - People who become pregnant while taking TDF/FTC can continue
- Injectable cabotegravir (CAB): approved for people with vaginal HIV exposure, but efficacy and safety during pregnancy unknown
  - If receiving CAB & become pregnant, shared decision-making

***See recent CAP016 RCT of TDF/FTC immediate vs deferred TDF/FTC PrEP during pregnancy and infant feeding: Moodley D, et al. Lancet HIV. 2023;10(3):e154-e163.**

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Long-acting, Injectable CAB PrEP & Pregnancy: Considerations

- Long half-life, so benefit of stopping when pregnant uncertain
- Structural similarities to other ARVs safe in pregnancy (e.g. DTG)
- If stop during pregnancy and HIV risk ongoing, offer alternative (e.g. TDF/FTC)
- HPTN 084: 29 pregnancies with CAB (13 live births); no congenital anomalies*

*HPTN 084: Delany-Moretlwe S, et al. Lancet 2022;399(10337):1779-1789.

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Key Point

Oral TDF/FTC daily still preferred PrEP option during conception and pregnancy due to more robust data for safety and efficacy during pregnancy than CAB

Prepregnancy Counseling for Persons of Childbearing Age with HIV

- Integrate family planning conversations into routine visits
  - Offer contraception if desired but review drug-drug interactions first
- Counsel about importance of ART adherence
  - "When fully suppressive ART is started before pregnancy and undetectable viral load is maintained…there is no risk of HIV transmission to the infant"
- Encourage individuals to disclose HIV status before pregnancy if safe; disclosure should not be required for assisting with conception
- Consider pregnancy-specific challenges to adherence

Reproductive Options for Serodifferent Couples

- Discuss reproductive options; the HIV status of one or both parents should not be a reason to withhold standard of care infertility treatment
- When people have different HIV status, condomless sex allows conception without transmission if the person with HIV sustains suppressed VL with ART
- When partners with different HIV status attempt conception, partner without HIV can choose to take PrEP if the partner with HIV has achieved VL suppression

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Choosing ART for Conception or Pregnancy

ART Scenario	Recommendations
Person of childbearing potential desires conception	When possible, initiate or change regimen with sufficient time to achieve VL suppression before attempting to conceive; ART choices for conception similar to for pregnant persons with HIV
Pregnant and ART-naïve	Initiate 3-drug ART with *Preferred* regimen; draw genotype(s) but do not need to wait for result to start
Pregnant and ART-experienced	Review: ART history, VL and resistance history, data for safety of current ART during pregnancy and changes in drug levels late in pregnancy, likely tolerability and drug interactions with regimen, disclosure of HIV status, risk of gender-based violence, preference, comfort with unknown risks

**For most PWH who become pregnant while tolerating ART with suppressed VL, regimen should be continued*

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HHS Perinatal Guidelines: Updated January 31, 2023
ART Options During Pregnancy

Category	Preferred	Alternative	Insufficient Data	Not recommended
NRTI	(TAF or TDF) + (FTC or 3TC), or ABC/3TC (if HLA-B*5701 neg)	AZT/3TC		
INSTI	Dolutegravir	Raltegravir (BID)	Bictegravir	Elvitegravir/cobicistat Cabotegravir/rilpivirine
Boosted PI	Darunavir (BID) + ritonavir (BID)	Atazanavir + ritonavir		Atazanavir/cobicistat Darunavir/cobicistat Lopinavir/ritonavir
NNRTI		Efavirenz, or Rilpivirine	Doravirine	Cabotegravir/rilpivirine

Abbreviations: NRTI = nucleoside reverse transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; INSTI = integrase strand transfer inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; FTC = emtricitabine; 3TC = lamivudine; ABC = abacavir; AZT = zidovudine

Dolutegravir and Neural Tube Defects (NTDs)
Updated Data from Tsepamo Study

Exposure Group	NTD Prevalence Difference (%) (95% CI)
Dolutegravir (DTG) at conception vs. non-DTG at conception	0.06 (-0.03, 0.20)
DTG at conception vs. efavirenz at conception	0.09 (-0.00, 0.23)
DTG at conception vs. DTG started during pregnancy	0.10 (-0.03, 0.24)
DTG at conception vs. non-DTG started during pregnancy	0.08 (-0.04, 0.23)
DTG at conception vs. persons without HIV	0.09 (0.01, 0.23)

Source: Zash R, et al. IAS Conference 2021. Abstract 2562.

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TAF vs TDF in NRTI Backbone During Pregnancy

- When combined with DTG, efficacy and tolerability of TAF/FTC and TDF/FTC for treatment during pregnancy similar
- However, TAF/FTC associated with fewer adverse birth outcomes and less risk of insufficient weight gain during pregnancy
- Potential concerns about fetal bone and early-life growth abnormalities with TDF, although clinical findings reassuring to date

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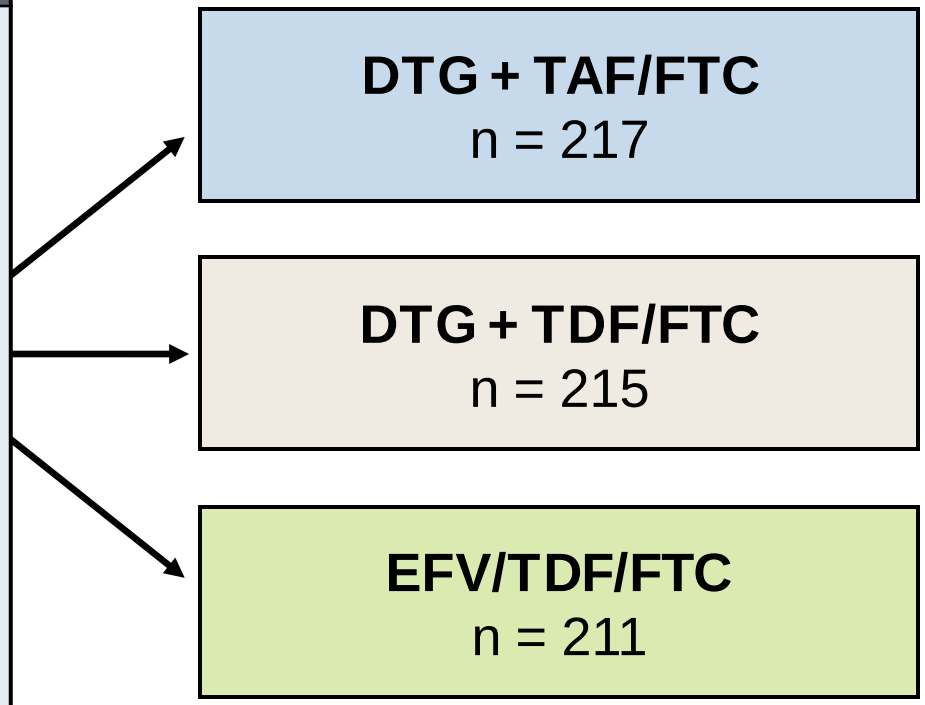
DTG + TAF/FTC or TDF/FTC vs EFV/TDF/FTC During Pregnancy

IMPAACT2010/VESTED: Background

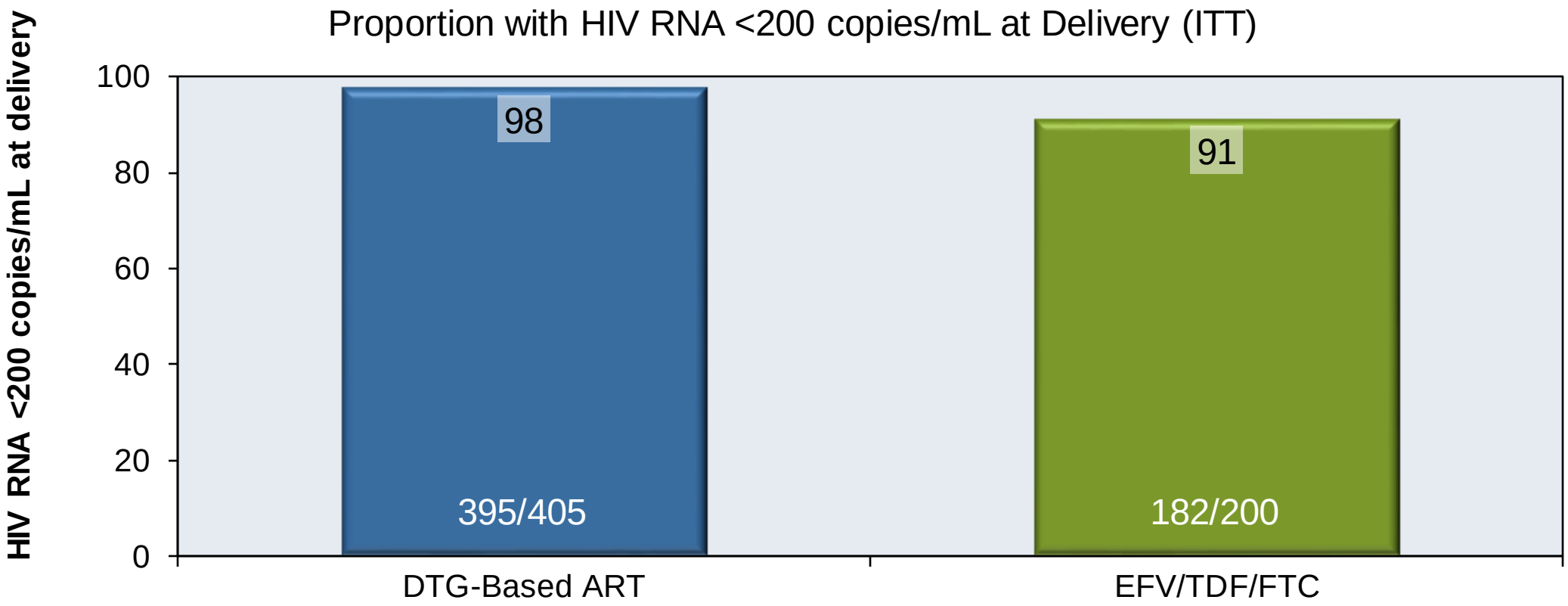
Study Design: IMPAACT2010/VESTED

- **Background**:
  - Randomized, open-label, international, phase III noninferiority trial (22 sites in 9 countries)
- **Enrollment Criteria:**
  - ART-naïve pregnant adults (<14 days ART during pregnancy permitted)
  - 14-28 weeks gestation
- **Endpoints:**
  - Primary: delivery HIV RNA <200 copies/mL
  - Secondary: adverse pregnancy outcomes, maternal and fetal adverse effects



Source: Lockman S, et al. Lancet. 2021;397(10281):1276-1292.

DTG + TAF/FTC or TDF/FTC vs EFV/TDF/FTC During Pregnancy
IMPAACT2010/VESTED: Results



Virologic suppression at delivery superior with DTG (p=0.005); time to viral suppression superior (p<0.001)
No difference in efficacy between the two different DTG groups

Source: Lockman S, et al. Lancet. 2021;397(10281):1276-1292.

DTG + TAF/FTC or TDF/FTC vs EFV/TDF/FTC During Pregnancy
IMPAACT2010/VESTED: Results

IMPAACT2010/VESTED: Adverse Pregnancy Outcomes			
Adverse Outcomes, %	**DTG + TAF/FTC** (n = 217)	**DTG + TDF/FTC** (n = 215)	**EFV/TDF/FTC** (n=211)
Any adverse outcome	24.1	32.9	32.7
Preterm delivery	5.8	9.4	12.1
Small for gestational age	16.3	22.5	20.5
Stillbirth	3.7	5.2	1.9

Adverse pregnancy outcomes significantly less frequent with DTG + TAF/FTC vs DTG + TDF/FTC and EFV/TDF/FTC ($p<0.05$)

Preterm delivery & neonatal death significantly less frequent with DTG + TAF/FTC vs EFV/TDF/FTC ($p<0.05$)

Source: Lockman S, et al. Lancet. 2021;397(10281):1276-1292.

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DTG + TAF/FTC or TDF/FTC vs EFV/TDF/FTC During Pregnancy
IMPAACT2010/VESTED: Results

IMPAACT2010/VESTED: Maternal Weight Gain			
Maternal Weight Gain	**DTG + FTC/TAF** (n = 217)	**DTG + FTC/TDF** (n = 215)	**EFV/FTC/TDF** (n=211)
Average weekly weight gain, kg	0.378*	0.319	0.291

More weight gain with DTG + FTC/TAF vs DTG + FTC/TDF (p=0.011) and vs EFV/FTC/TDF (p<0.05) – clinical significance unknown

Recommended weight gain in 2nd & 3rd trimester per IOM: 0.45 kg/week

Source: Lockman S, et al. Lancet. 2021;397(10281):1276-1292.

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Clinical Scenarios and Recommendations

ART When Person Becomes Pregnant	Recommendations for the ART Regimen
Taking a *Preferred* 3-drug ART regimen for pregnancy, suppressed, tolerating it well	Continue
Taking an *Alternative* 3-drug ART regimen for pregnancy, suppressed, tolerating it well	Counsel about options; reasonable to continue or switch to *Preferred* option
Taking a regimen that is *Not Recommended* for pregnancy due to toxicity or poor efficacy (stavudine, indinavir, didanosine, nelfinavir, etc.)	Switch regimen
Taking any regimen and VL >200 to 1,000 copies/mL	Evaluate adherence carefully, obtain resistance testing, switch ART based on results

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Clinical Scenarios and Recommendations

ART When Person Becomes Pregnant (Assume VL Suppressed, Tolerating)	Recommendations for the ART Regimen
3-drug regimen with insufficient data (BIC/TAF/FTC or DOR with 2 NRTIs)	Counsel about insufficient data; continue with frequent VL monitoring* *or* switch
Cobicistat-boosted regimen (EVG/cobi/TAF/FTC, DRV/cobi, or ATV/cobi)	Counsel about risks of decreased drug levels late in pregnancy; continue with frequent VL monitoring* *or* switch
Oral 2-drug regimen (DTG/3TC, DTG/RPV)	Counsel about insufficient efficacy data in pregnancy; continue with frequent VL monitoring* *or* switch
Receiving IM CAB/RPV every 1 or 2 months	Counsel about insufficient safety & efficacy data in pregnancy; continue with frequent VL monitoring* *or* switch

*Frequent VL monitoring = every 1-2 months

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Clinical Scenarios and Recommendations

Early HIV (Acute, Recent) During Pregnancy	Recommendations for ART
Acute or recent HIV infection & no past IM CAB PrEP exposure	Obtain genotype resistance assay; preferred empiric regimen: DTG + (TAF or TDF) with (FTC or 3TC)
Acute or recent HIV infection & past IM CAB PrEP exposure	Obtain genotype resistance assay (with integrase genotype); preferred empiric regimen: darunavir* + ritonavir + (TAF or TDF) with (FTC or 3TC)

*Reminder: darunavir with ritonavir both dosed BID for pregnancy & requires food; PIs may increase risk of preterm birth

Speaker note: these recommendations can apply to anyone newly diagnosed with HIV during pregnancy, especially late in pregnancy

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Key Point

Dolutegravir with (TAF or TDF) and (FTC or 3TC) is generally the preferred regimen during any trimester of pregnancy. Exceptions include if integrase resistance concern, tolerability issues, or preference for other regimen in setting of suppressed viral load with no strong reason to change.

Recommended HIV Laboratory Monitoring During Pregnancy

Lab Test	Entry Into Antenatal Care	2-4 Weeks After ART Initiation or Modification	Monthly	Every 3 Months During Pregnancy	At Approximately 36 Weeks Gestation or Within 4 Weeks of Delivery
HIV RNA	✔	✔	✔ (until non-detectable)	✔ (at least every 3 months)	✔ (to inform mode of delivery, infant prophylaxis)
CD4	✔			✔ (if on ART <2 years, CD4 <300, missed ART doses, detectable VL)	

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Drug Resistance Testing & Pregnancy

- Resistance testing (genotype and, if indicated, phenotype) should be performed for pregnant persons with HIV if HIV RNA level **>200 to 1,000 copies/mL**

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New Language on Amniocentesis

- Amniocentesis, if clinically indicated, may be performed on pregnant people with HIV after patient-centered counseling about the risks, benefits, and alternatives
- The pregnant person should be receiving an effective ARV regimen and, ideally, have HIV RNA levels that are undetectable
- If a pregnant person with detectable HIV RNA levels requires amniocentesis, consultation with an expert should be considered

Intrapartum Care for People with HIV (No Changes)

- Continue antepartum ART on schedule during labor and before C-section
- If **HIV RNA >1,000 copies/mL** or unknown near time of delivery (within 4 weeks) or known or suspected missed doses since last HIV RNA or not yet taking ART:
  - Administer intrapartum IV AZT
  - Schedule C-section at 38 weeks

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Key Point

Adherence support and viral load monitoring during pregnancy and near delivery are critical to care for pregnant persons with HIV and to eliminating risk for transmission.

Reminders

- Develop delivery plan early
- Antiretroviral pregnancy registry (APR): http://www.apregistry.com/
- Join us March 30 for special guest & discussion of infant feeding!

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