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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Guidelines Development Process

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the Guidelines	Provide guidance to HIV care practitioners in the United States on the optimal use of antiretroviral (ARV) agents in pregnant women who are living with HIV for treatment of HIV infection and for prevention of perinatal transmission of HIV, as well as management of HIV-exposed infants.
Panel Members	The Panel is composed of approximately 30 voting members who have expertise in managing the care of pregnant women living with HIV (e.g., training in obstetrics/gynecology, infectious diseases, or women's health), pharmacology of ARV drugs during pregnancy, and interventions for prevention of perinatal transmission (e.g., specialized training in pediatric HIV infection), as well as community representatives with knowledge of HIV infection in pregnant women and interventions for prevention of perinatal transmission. The U.S. government representatives, appointed by their agencies, include at least one representative from each of the following Department of Health and Human Services agencies: the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration, and the National Institutes of Health (NIH). Members who do not represent U.S. government agencies are selected by Panel members after an open announcement to call for nominations. Each member serves on the Panel for a 3-year period, with an option for re-appointment. The Panel may also include liaison members from the Perinatal HIV Hotline, the American Academy of Pediatrics' Committee on Pediatric AIDS, and the American College of Obstetricians and Gynecologists. A list of all Panel members can be found in the Guidelines Panel Members section.
Financial Disclosures	All members of the Panel submit an annual written financial disclosure that reports any association with manufacturers of ARV drugs or diagnostics used for management of HIV infections. See Financial Disclosure for a list of the latest disclosures.
Users of the Guidelines	Providers of care to pregnant women who are living with HIV and to infants who have been exposed to HIV
Developer	The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding Source	Office of AIDS Research, NIH
Evidence for Recommendations	The recommendations in these guidelines are generally based on studies published in peer-reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data that was presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation Grading	See Table 2.
Method of Synthesizing Data	Each section of the guidelines is assigned to a small group of Panel members with expertise in the area of interest. A structured literature search is conducted by a technical assistance consultant and provided to the Panel working group. The members review and synthesize the available data and propose recommendations to the entire Panel. The Panel discusses all proposals during monthly teleconferences. Proposals are modified based on Panel discussions and then distributed, with ballots, to all Panel members for concurrence and additional comments. If there are substantive comments or votes against approval, the recommended changes and areas of disagreement are brought back to the full Panel (via email or teleconference) for additional review, discussion, and further modification to reach a final version that is acceptable to all Panel members. The recommendations in these final versions represent endorsement from a consensus of members and are included in the guidelines as official Panel recommendations.
Other Guidelines	These guidelines focus on pregnant women living with HIV and their infants. Other guidelines (all of which are available on the AIDS*info* website) outline the use of ARV agents in nonpregnant adults and adolescents with HIV; use of ARV agents in infants and children with HIV; treatment and prevention of opportunistic infections (OIs) in adults and adolescents with HIV, including pregnant women; treatment and prevention of OIs in children who have been exposed to HIV or who have HIV infection; and treatment of people who experience occupational or nonoccupational exposure to HIV. Preconception management for nonpregnant women of reproductive age is briefly discussed in this document. However, for a more detailed discussion of the issues surrounding the treatment of nonpregnant adults, the Working Group defers to the designated expertise offered by the Panels that have developed those guidelines.

Guidelines Development Process

Table 1. Outline of the Guidelines Development Process, cont'd

Topic	Comment
Update Plan	The Panel meets monthly by teleconference to review data that may require modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, new dosing formulations, and/or changes in dosing frequency), significant new safety or efficacy data, or other information that may have a significant impact on the clinical care of patients. In the event of significant new data that may affect patient safety, the Panel may issue a warning announcement and accompanying recommendations on the AIDS*info* website until the guidelines can be updated with appropriate changes.
Public Comments	A 2-week public comment period follows release of the updated guidelines on the AIDS*info* website. The Panel reviews these comments to determine whether additional revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at contactus@aidsinfo.nih.gov.

Table 2. Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement **B:** Moderate recommendation for the statement **C:** Optional recommendation for the statement	**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

Note: All recommendations in the following table are based on consensus expert opinion. More details can be found in the CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2016.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 1 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs							
EFV	COC: • No effect on EE concentrations • ↓ active metabolites of norgestimate LN AUC ↓ 83%; norelgestromin AUC ↓ 64%[31] • Etonogestrel (in COC) C_{24h} ↓ 61%[37] DMPA: • No effect on DMPA levels[28,30] Etonogestrel Implant: • Etonogestrel AUC ↓ 63% to 82%[46,48] LN Implant: • LN AUC ↓ 47%[42] • LN (emergency contraception) AUC ↓ 58%[26] Changes in ARV Levels and/or Effects on HIV *COC:* • No effect on EFV concentrations[31] • EFV C_{12h} ↓ 22%; was under therapeutic threshold in 3/16 subjects[37] *DMPA:* • No effect on HIV disease progression[28,49,50] • No effect on EFV concentrations[28]	COC: • No difference in pregnancy rates[47] • Pregnancy rate higher (13%) in women using COCs and EFV than COCs alone[45,51] • Progesterone >3 ng/mL (a surrogate for ovulation) in 3/16 women[52] • No ovulations[31] DMPA: • No increase in pregnancy rates[28,45,47,50] • Low progesterone[28,30,50] Etonogestrel Implant: • Pregnancy rate higher with EFV compared with no ART, but still lower than other hormonal methods of contraception[45] • Presumptive ovulation in 5%[48] LN Implant: • 12% pregnancy rate[38] • 15% pregnancy rate[42] • Pregnancy rate higher with EFV compared with no ART, but still lower than other hormonal methods of contraception[45]	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, some studies suggest higher pregnancy rate and ovulation rate and decreased progestin levels. EFV may decrease, but clinical significance unclear. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. Also, no effect on HIV disease progression or EFV levels. For implants, some studies suggest higher pregnancy rate and decreased hormone levels.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 2 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
EFV, continued	LN Implant: • No effect on HIV disease progression[42]	No increase in pregnancy rate[47]					
ETR	EE AUC ↑ 22%[53] NE: • No significant effect[53]	COC: • No ovulations[53]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, 1 study found no ovulations and no significant change in progestin levels. No evidence on POPs.
NVP	EE AUC ↓ 29%;[54] no change in EE AUC[55] NE AUC ↓ 18%[54] Etonogestrel (in COC) C_{24h} ↓ 22%[37] DMPA: • No significant change[28] LN Implant: • LN AUC ↑ 35%[42] Changes in ARV Levels and/or Effects on HIV *COC:* • No significant effect on NVP levels[52,54,56] *DMPA:* • No effect on HIV disease progression[28,49,50,57] *LN Implant:* • No effect on HIV disease progression[42,58]	COC: • No increase in pregnancy rate[45,47,51,59,60] • No ovulations[52,55,60] DMPA: • No increase in pregnancy rate[45,47,50,59] • No ovulations[28] Etonogestrel Implant: • No increase in pregnancy rate[45] LN Implant: • No increase in pregnancy rate[38,42,45,47,58]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed	For COCs, evidence does not show effects on pregnancy rate or ovulations. Evidence demonstrated small decrease in progestin levels. Also, no effect on NVP levels. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. Also, no effect on HIV disease progression. For implants, evidence does not show effects on pregnancy rate or HIV disease progression.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 3 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
NNRTIs, continued							
RPV	EE AUC ↑ 14%[36] NE: • No significant change[36] Changes in ARV Levels and/or Effects on HIV *COC:* • No change in RPV levels compared to historical controls[36]	COC: • No change in progesterone[36]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, evidence does not show effects on ovulation or progestin levels. Also, no change in RPV levels. No evidence on POPs.
RTV-Boosted PIs							
ATV/r	EE AUC ↓ 19%[61] Norgestimate AUC ↑ 85%[61] POP: • NE AUC ↑ 50%[62]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, increase in progestin levels seen in only 1 study. For POPs, increase in progestin levels seen in only 1 study. RTV inhibits CYP3A4, which may increase contraceptive hormone levels.
DRV/r	EE AUC ↓ 44%[63] NE AUC ↓ 14%[63]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, small decrease in progestin levels. No evidence on POPs.
FPV/r	EE AUC ↓ 37%[64] NE AUC ↓ 34%[64] No change in FPV/r levels[64]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, decrease in progestin levels. No evidence on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 4 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
LPV/r	EE AUC ↓ 55%[27] NE AUC ↓ 17% Patch: • EE AUC ↓ 45%[27] • Norelgestromin AUC ↑ 83%[27] DMPA: • DMPA AUC ↑ 46%[40] Etonogestrel Implant: • Etonogestrel AUC ↑ 52%[48] Changes in ARV Levels and/or Effects on HIV *Patch:* • LPV/r level ↓ 19%[27] *DMPA:* • No effect on HIV disease progression[40] • No change in LPV/r levels[40]	COC: • Increased pregnancy rate, but CIs overlap[45] Patch: • No ovulations[27] DMPA: • No pregnancies, no ovulations[40] • Increased pregnancy rate, but CIs overlap[45] Etonogestrel Implant: • No increase in pregnancy rate[45] LN Implant: • No increase in pregnancy rate.[38,45]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, nonsignificant increase in pregnancy rate. Small decrease in progestin level. For patch, no ovulations and progestin levels increased. For DMPA, evidence shows no effect on pregnancy rate or ovulations and progestin levels increased. For implants, evidence shows no effect on pregnancy rate and progestin levels increased.
SQV/r	↓ EE[65] Changes in ARV Levels and/or Effects on HIV *COC:* • No change in SQV/r levels[66]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No information on progestin levels for CHCs or POPs. RTV inhibits CYP3A4, which may increase contraceptive hormone levels. However, some PI/r cause decreases in progestin levels, so there are theoretical concerns about contraceptive effectiveness.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 5 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
RTV-Boosted PIs, continued							
TPV/r	EE AUC ↓ 48%[67] NE: • No significant change[67] Changes in ARV Levels and/or Effects on HIV: • No change in TPV levels[67]	N/A	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, no significant change in progestin levels but only from product label. No evidence on POPs. RTV inhibits CYP3A4, which may increase contraceptive hormone levels. However, some PI/r cause decreases in progestin levels, so there are theoretical concerns about contraceptive effectiveness.
COBI-Boosted PIs							
ATV/c	Drospirenone AUC ↑ 2.3-fold; EE AUC ↓ 22%[68]	N/A	**Contraindicated** with drospirenone-containing hormonal contraceptives due to potential for hyperkalemia. Consider alternative or additional contraceptive method.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	No evidence on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 6 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
COBI-Boosted PIs, continued							
DRV/c	Drospirenone AUC ↑ 1.6-fold; EE AUC ↓ 30%[68]	N/A	In combination with drospirenone-containing COCs, clinical monitoring is recommended due to the potential for hyperkalemia. Consider alternative or additional contraceptive method.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	Consider an alternative method, due to safety concerns.	No evidence on POPs.
PIs without RTV							
ATV	COC: • EE AUC ↑ 48%[69] • NE AUC ↑ 110%[69]	N/A	Prescribe oral contraceptive that contains no more than 30 mcg of EE, or recommend alternative contraceptive method.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, increased concentrations of estrogen and progestin, but only data available are from the product label. No evidence on POPs.
FPV	COC *APV:* • No change in EE AUC; C_{min} ↑ 32% • NE AUC ↑ 18%; C_{min} ↑ 45%[64] FPV with EE/Norethindrone: • APV AUC ↓ 22% and C_{min} 20%)[64]	N/A	Use alternative contraceptive method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Use of FPV alone with ethinyl estradiol/ norethindrone may lead to loss of virologic response. No evidence on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 7 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
PIs without RTV, continued							
IDV	COC: • EE AUC ↑ 22% • NE AUC ↑ 26%[70]	COC: • No pregnancies among women taking IDV and COCs[51]	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, small increases in EE and progestin have been observed, and 1 clinical study did not suggest any efficacy concerns. No evidence on POPs.
NFV	COC: • EE AUC ↓ 47% • NE AUC ↓ 18%[71] DMPA: • No change[28] NFV: • AUC ↓ 18%	COC: • 1 small study suggested that women using COCs and NFV may have had higher pregnancy rates than those using COCs alone[51] DMPA: • No pregnancies, no ovulations[28,50] • CD4 count/HIV RNA: no change[28,50]	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	No additional contraceptive protection is needed.	Can consider an alternative method (or a reliable method of barrier contraception) in addition to this method.	For COCs, a small decrease in progestin and a decrease in estrogen have been observed; 1 small clinical study suggests possible higher pregnancy rate with COC and NFV use. DMPA, PK, and clinical data demonstrate no change. However, NFV AUC slightly decreased. No evidence on POPs or implants.
CCR5 Antagonist							
MVC	COC: • No significant effect on EE or LN[72]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, no change in EE or progestin. No clinical data. No evidence on POPs.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (page 8 of 8)

ARV Drug	Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Clinical Studies	Dosing Recommendation/ Clinical Comment for COC/P/R	Dosing Recommendation/ Clinical Comment POPs	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants	Justification/ Evidence for Recommendation
Integrase Inhibitors							
BIC/FTC/ TAF	No significant drug interactions with EE or norgestimate.	N/A	No additional contraceptive protection is needed	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No clinical data.
DTG	COC: • No significant effect on norgestimate or EE • DTG AUC no change[41]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	COCs, no change in EE or progestin. No clinical data No evidence on POPs.
EVG/c	EVG/COBI *COC:* • Norgestimate AUC ↑ 126% EE AUC ↓ 25%[74]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	When administered as the 4-drug regimen EVG/COBI/FTC/TDF, increases in P and small decrease in EE were observed. No clinical data. No evidence on POPs.
RAL	COC: • EE no change • Norgestimate AUC ↑ 14%[73]	N/A	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	No additional contraceptive protection is needed.	For COCs, no change in EE and small increase in progestin. No clinical data. No evidence on POPs.

[a] Because the hormonal levels achieved with DMPA are substantially higher than are required for contraception, any small reduction in hormonal level due to ARVs is unlikely to reduce contraceptive effectiveness.

Key to Symbols:

↑ = increase ↓ = decrease

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CD4 = CD4 T lymphocyte; CHC = combination hormonal contraceptives; CI = confidence interval; C_{min} = minimum plasma concentration; COBI = cobicistat; COC/P/R =combined oral contraceptives/ patch/ring; CYP = cytochrome P450 3A4; DMPA = depot medroxyprogesterone acetate; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EE = ethinyl estradiol; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IDV = indinavir; LN =levonorgestrel; LPV/r

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives

= lopinavir/ritonavir; MVC = maraviroc; NE = norethindrone; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; P = progestin; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PK = pharmacokinetic; POP = progesterone-only oral contraceptive pills; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Tables 15a, 15b, and 15d.

Table 4. Clinical Trials of Pre-Exposure Prophylaxis

Trial	Study Population	Location	Intervention	Outcome	Comments
TDF2	1,219 sexually active adults; 55% male, 45% female; 94% unmarried; approximately 90% aged 21–29 years	Botswana	Daily oral TDF/FTC	63% protection	>30% did not complete study; cannot draw definitive conclusions for women and men separately.
PIP	4,758 serodiscordant heterosexual couples; 38% HIV-negative female partner, 62% HIV-negative male partner; 98% married; median age 33 years	Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, Zambia	Daily oral TDF or TDF/FTC	67% protection with TDF alone; 75% protection with TDF/FTC	Serodiscordant couples may be a distinct, unique population.
FEM-PrEP	1,951 heterosexual women aged 18–35 years and at high risk of infection	Kenya, South Africa, Tanzania	Daily oral TDF/FTC	Trial discontinued for futility in April 2011	Adherence assessment with monthly clinical samples to measure drug concentration is pending.
VOICE MTN-003	5,029 heterosexual women aged 18–45 years in areas with a high prevalence of HIV	Uganda, South Africa, Zimbabwe	Daily oral TDF or daily oral TDF/FTC or daily topical TFV gel	No study drug significantly reduced the risk of HIV acquisition. Estimates of effectiveness were <0 for TDF and TDF/FTC daily oral dosing (negative 48.8% and negative 4.2% TDF/FTC, respectively), and reduced risk of HIV infection of 14.7% for TFV gel.	Adherence to study drugs was low; TFV was detected in 30% of the oral TDF arm, 29% in the oral TDF/FTC arm, and 25% in the TFV gel arm.

Adapted from: Kashuba et al., Pre-exposure prophylaxis for HIV prevention: how to predict success: Table Antiretroviral-based HIV prevention studies. *Lancet*. 2012;379(9835): 2409-2411.

Key to Acronyms: FTC = emtricitabine; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 1 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
European Collaborative Study and Swiss Mother and Child HIV Cohort Study; 1986–2000[1]	3,920/896	• Mono (573) • Multi-no PI (215) • Multi-PI (108)	• YES (compared with no ARV) • Multi: 1.82 (1.13–2.92) • Multi-PI: 2.60 (1.43–4.7)	• Increase in PTD if ARV was initiated before pregnancy versus in third trimester.
United States; 1990–1998[30]	3,266/2,123	• Mono (1,590) • Multi (396) • Multi-PI (137)	• NO (compared with mono) • Multi: 0.95 (0.60–1.48) • Multi-PI: 1.45 (0.81–2.50)	• 7 prospective clinical studies.
European Collaborative Study; 1986–2004[52]	4,372/2,033	• Mono (704) • Dual (254) • Multi (1,075)	• YES (compared with mono/dual) • Multi in pregnancy: 1.88 (1.34–2.65) • Multi pre-pregnancy: 2.05 (1.43–2.95)	• N/A

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 2 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
United States; 1990–2002[41]	2,543/Not given	Early (≤25 Weeks): • Mono (621) • ≥2 ARVs without PI or NNRTI (198) • Multi-NNRTI or Multi-PI (357) Late (≥32 Weeks): • Mono (932) • ≥2 ARVs without PI or NNRTI (258) • Multi-NNRTI or Multi-PI (588)	• NO (compared with mono) • No association between any ARV and preterm delivery	• PTD decreased with receipt of any ARV, ART that contained ZDV, and other ARV regimens compared with no ARV.
United States; 1990–2002[3]	1,337/999	• Mono (492) • Multi-no PI (373) • Multi-PI (134)	• YES (compared with Mono and Multi-no PI) • Multi-PI: 1.8 (1.1–3.03)	• Multi-PI reserved for those with advanced disease and those who experienced virologic failure while on other multi-ARV regimens.
Brazil, Argentina, Mexico, Bahamas; 2002–2005[38]	681/681	• Mono/Dual NRTI (94) • Multi-NNRTI (257) • Multi-PI (330)	• NO (compared with Mono/Dual-NRTI) • No association between any ARV regimen and PTD	• All patients were on ARV for ≥28 days during pregnancy. • Pre-eclampsia/ eclampsia, cesarean delivery, diabetes, and low BMI were associated with PTD.
Meta-Analysis, Europe and United States; 1986–2004[4]	11,224/Not given	• Multi-no PI (including Dual) or Multi-PI (2,556)	• YES (only comparing Multi-PI with Multi-no PI) • PI vs. Multi-no PI: 1.35 (1.08–1.70)	• 14 studies, 5 in PTD ARV comparison. • No overall increase in PTD with antepartum ARV. • PTD increased in those on ARV pre-pregnancy and in first trimester compared with later use.
Italy; 2001–2006[5]	419/366	• Multi-PI second trimester (97) • Multi-PI third trimester (146)	• YES • Multi-PI second trimester: 2.24 (1.22–4.12) • Multi-PI third trimester: 2.81 (1.46–5.39)	• Multivariate association also with HCV.
United States; 1989–2004[6]	8,793/6,228	• Mono (2,621) • Dual (1,044) • Multi-no PI (1,781) • Multi-PI (782)	• YES (compared with Dual) • Multi-PI: 1.21 (1.04–1.40)	• Lack of antepartum ARV also associated with PTD. • PTD and LBW decreased over time.

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 3 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
United Kingdom, Ireland; 1990–2005[7]	5,009/4,445	• Mono/Dual (1,061) • Multi-NNRTI or Multi-PI (3,384)	• YES (compared with Mono/Dual) • Multi-PI or Multi-NNRTI: 1.51 (1.19–1.93)	• Similar increased risk with Multi-PI or Multi-no PI. • No association with duration of ARV use.
Germany, Austria; 1995–2001[8]	183/183	• Mono (77) • Dual (31) • Multi-NNRTI (54) • Multi-PI (21)	• YES (compared with Mono) • Multi-PI: 3.40 (1.13–10.2)	N/A
United States; 2002–2007[25]	777/777	• Mono (6) • Dual (11) • Multi-no PI (202) • Multi-PI (558)	• NO (compared PI with all non-PI) • Multi-PI: 1.22 (0.70–2.12)	• All patients started ARV during pregnancy. • Study analyzed only spontaneous PTD.
Swiss Mother and Child HIV Cohort Study; 1985–2007[9]	1,180/941	• Mono (94) • Dual (53) • Multi-PI or Multi-no PI (409) • Multi-PI (385)	• YES (compared with no ARV) • Multi: 2.5 (1.4–4.3)	• No association of Mono/Dual with PTD compared with no ARV. • No confounding by duration of ARV or maternal risk factors.
Botswana; 2006–2008[10]	530/530	• Multi-NRTI, ABC plus ZDV plus 3TC (263) • Multi-PI, LPV/r plus ZDV plus 3TC (267)	• YES • Multi-PI vs. Multi-NRTI: 2.03 (1.26–3.27)	• Secondary analysis of data from randomized, controlled clinical trial of ARV begun at 26–34 weeks for prevention of perinatal transmission. • All CD4 cell counts >200 cells/mm^3
Botswana; 2007–2010[44]	4,347/3,659	• ARV, regimen unspecified (70) • Mono (2,473) • Multi (1,116), 91% Multi-NNRTI	• NO • No association between multi-ART and very PTD (<32 weeks' gestation)	• Observational; multi-ART before conception associated with very SGA and maternal hypertension during pregnancy.
Spain; 1986–2010[26]	519/371	• Mono/Dual NRTI (73) • All Multi (298) • Multi-PI (178)	• NO (compared with No ARV plus Mono/Dual) • Spontaneous PTD not associated with Multi ARV or Multi-PI before or during pregnancy	• PTD associated with Multi-ARV given in second half of pregnancy and with prior PTD.
Botswana; 2009–2011[11]	9,504/7,915	• Mono (4,625) • All Multi (3,290) • Multi-PI (312)	• YES (Multi-ARV before and during pregnancy compared with Mono): 1.2 (1.1–1.4) and 1.4 (1.2–1.8) • YES (Multi-PI compared with Multi-no PI before pregnancy): 2.0 (1.1–3.6)	• ART group classified by initiation before and during pregnancy.
France, ANRS French Perinatal Cohort; 1990–2009[12]	8,696/8,491	• Mono (950) • Dual (590) • Multi-PI (2,414)	• YES (Multi compared to Mono): 1.69 (1.38–2.07) • YES (before conception compared to during pregnancy): 1.31 (1.11–1.55)	• Patients on ART before and during pregnancy had increased rates of PTD.

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 4 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
United States; 2000–2011[43]	183/183	• Multi-PI (183)	• NO (no control group without ART) • Rate of PTD: 18.6%	• SGA rate: 31.2% • Patients on NNRTI-based ART less likely to have SGA: 0.28 (0.1–0.75).
United States; 2007–2010[13]	1,869/1,810	• Mono/Dual (138) • Multi-NRTI (193) • Multi-NNRTI (160) • Multi-PI (1,319)	• YES (compared with no ARV in first trimester) • Multi-PI in first trimester vs. none in first trimester • PTD 1.55 (1.16–2.07); spontaneous PTD 1.59 (1.10–2.30)	N/A
Latin America; 2002–2012[14]	1,512/1,446	• No ART or ART <28 days (66) • Mono/Dual (130) • Multi-no PI (409) • Multi-PI (907)	• YES (when on ARVs at conception): PTD 1.53 (1.11–2.09)	• ART for treatment rather than prophylaxis was associated with increased rates of LBW (<2,500 g) infants: 1.8 (1.26–2.56). • Multi-no PI associated with decreased risk of LBW (0.33 [0.14–0.74]) and stillbirth (0.11 [0.04–0.34]). • Multi-PI associated with decreased risk of stillbirth: 0.14 (0.05–0.34).
Uganda; 2009–2012[53]	356/356	• Multi-NNRTI, EFV (177) • Multi-PI, LPV/r (179)	• NO (no control group without ART)	• Trend in increased incidence of PTD among women starting ART 24–28-week GA was NS: aOR = 1.76 (0.96–3.23).
Italy; 1997–2013[54]	158/158	• Mono/Dual (27) • Multi-no PI (17) • Multi-PI (114)	• NO (no control group without ART)	• PTD rate was 17% for this cohort. • Trend towards association of PTD with longer duration of ART: 2.82 (0.35–8.09).
Canada; 1988–2011[15]	589/530	• No ART (59) • Mono (77) • Multi-no PI (166) • Multi-non-boosted PI (220) • Multi-boosted PI with RTV (144)	• YES (Multi-boosted PI compared to Multi-non-boosted PI): 2.01 (1.02–3.97) • NO (non-PI regimens compared to Multi-non-boosted PI): 0.81 (0.4–1.66)	• Highest risk of PTD was among women not taking ART compared to non-boosted PI group: 2.7 (1.2–6.09).

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 5 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
United Kingdom; 2007–2012[31]	493/493	• Multi-PI, LPV/r (306) • Multi-PI, ATV/r (187)	• NO (comparing 2 PI-based regimens): aOR = 1.87 (0.93–3.75)	• Rate of PTD was 13% among women who conceived on ART and 14% among women who started ART during pregnancy. • In a multivariate analysis, a history of PTD was associated with recurrent PTD: aOR = 5.23 (1.91–14.34).
Republic of the Congo; 2007–2012[39]	188/188	• Multi-no PI, EFV (31) • Multi-no PI, NVP (146)	• NO (comparing EFV 13% vs. NVP 10%)	• Rate of PTD was 11%, with no difference between study groups. • LBW increased in EFV group (33% vs. 16%, *P* = 0.04). • Stillbirth rate was 4% (8/188).
Tanzania; 2004–2011[16]	3,314/2,862	• No ART (452-excluded) • Mono (1,768) • Multi (1,094)	• YES (Multi before pregnancy vs. Mono): 1.24 (1.05–1.47) • Very PTD, YES (Multi before pregnancy vs. Mono):1.42 (1.02–1.99) • NO (Multi during pregnancy compared to Mono): 0.85 (0.7–1.02)	• Rate of PTD was 29%; women who conceived on ART were more likely to have PTD compared to women on ZDV monotherapy. • Pregnancy-induced hypertension associated with PTD: 1.25 (1.03–1.51).
67 Countries and US Territories, APR; 1989–2013[40]	14,684/14,684	• ARV with ZDV (12,780) • ARV without ZDV (1,904)	• NO (any ZDV-ARV vs. non-ZDV ARV exposure): 1.0 (0.9–1.2)	• PTD rate was 12%. • LBW rate was 16%; RR of LBW with ZDV ART vs. non-ZDV ART = 1.2 (1.0–1.3), *P* = 0.02. • Stillbirth rate: 1.5%, RR = 0.8 (0.5–1.1).
Texas, United States; 1984–2014[32]	1,004/792	• No ART (177) • Mono, Dual, or Multi-no PI (230) • Multi-PI (597)	• NO (no-PI ART vs. PI ART): 0.9 (0.5–1.5)	• Rate of PTD: 13% to 21%. • Rate of SGA: 19% to 23%, OR = 1.3 (0.8–1.9).

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 6 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
India, Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe, PROMISE Trial; 2011–2014[34]	3,490/3,096	• Mono (1,386) • All Multi (2,710) • Multi-PI with ZDV (1,385) • Multi-PI with TDF (325)	• YES (Multi ≥14 weeks vs. Mono)	• Rate of PTD: 21% on Multi-PI with ZDV ART compared to ZDV-Mono ($P < 0.001$). • Rate of very PTD: 6% in Multi-PI with TDF ART and 3% in Multi-PI with ZDV ART ($P = 0.04$). • LBW was more common in Multi-PI with ZDV ART compared to ZDV Mono (23% vs. 12%, $P < 0.001$) and in Multi-PI with TDF compared to ZDV Mono (17% vs. 9%, $P = 0.004$).
United States and Puerto Rico, SMARTT; 2007–2016[17]	1,864/1,658	• Multi (1,658)	• YES: (Multi-PI vs. No ART): 1.59 (1.1–2.3)	• PI-based ART exposure in first trimester was associated with increased risk of spontaneous PTD compared with no first-trimester ART.
South Africa; 2011–2014[24]	3,723/3,547	• Dual (974) • Multi (2,573)	• NO • Dual: 0.2 (0.08–0.5) • Multi: 0.3 (0.1–0.9)	• PTD rate regardless of ART: 22% to 23%. • LBW rate on ART: 9% to 15%. Risk of LBW: Dual 0.06 (0.02–0.2) and Multi 0.12 (0.04–0.4). • SGA rate on ART: 7% to 9%. Risk of SGA: Dual 0.37 (0.1 to 1.5) and Multi 0.3 (0.07 to 0.9). • Stillbirth rate on Dual (1.2%) and Multi (2.2%). Risk of stillbirth: Dual 0.08 (0.04–0.2) and Multi 0.2 (0.1–0.3).
Botswana; 2012–2014[18]	11,932/10,592	• Multi-PI (398) • Multi-NNRTI (4,597)	• YES • Multi-PI: 1.36 (1.06–1.75) • Multi-NNRTI: 1.14 (1.01–1.29)	• SGA rates were significantly higher in Multi PI ART (27.7% and 20.4%) and NVP-based ART (24.9% and 28.2%) compared to EFV-based ART (16.9%). • Stillbirth rates were higher in NVP-based ART: 2.31 (1.64–3.26).

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 7 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
19 Countries, 5 Continents; 2002–2013[35]	23,490 (meta-analysis of 10 studies)	• Mono, Dual, or Multi-no PI • Multi-PI	• YES • Multi-PI: 1.3 (1.04–1.6), I^2 = 47%	• 5 of 10 studies demonstrated increased risk of PTD with an aOR range of 1.2–4.14.
South Africa; 2011–2014[28]	1,461/1,159	• Dual (424) • Multi (735)	• YES • Multi: 1.65 (1.17-2.33) • ART before pregnancy: 1.72 (1.33-3.01)	• PTD rate was 25%. • Similar rates of PTD observed among women on ART before pregnancy and women starting ART during pregnancy.
Netherlands; 1997-2015[33]	2,184/1,392	• Multi (1,392) • PI-based and non-PI based ART	• NO • 1.39 (0.99–1.94); comparing women on ART before pregnancy to those who started ART during pregnancy	• PTD rate was 14.7%. • SGA rate was 23.8% overall; significantly higher in women taking ART before pregnancy (27.3%) vs. those starting ART during pregnancy (21.5%): aOR = 1.35 (1.0–1.9). • PI-based ART before pregnancy associated with SGA: 1.49 (1.1–2.1).
South Africa, SAPMTCTE; 2012–2013[20]	2,599/2,269	• Dual (873) • Multi (1,396)	• YES • 1.2 (1.0–1.5) compared to infants who were not exposed to HIV • 1.7 (1.1–2.5) in infants exposed to ART from conception	• PTD rate was 12.9%; women with HIV who were not on ARVs had higher rates of PTD than women without HIV. • LBW rate was 13.0%; HIV-exposed infants more likely to be LWB: 1.6 (1.3–1.9). • SGA rate was 16.9%; HIV-exposed infants more likely to have SGA: 1.3 (1.1–1.6).
Multiple Countries; 1993–2014[27]	37,877 (meta-analysis of 17 studies)	• Multi with TDF • Other ART without TDF	• NO • RR = 0.9 (0.81–0.99), I^2 = 59%; women on Multi with TDF had lower rates of PTD compared to women on other ART without TDF	• PTD rate over 4 studies was 20.3%. • Stillbirth rate over 3 studies was 4.4%; stillbirth rate was lower among TDF-exposed patients: 0.6 (0.43–0.84).

Table 5. Results of Studies Assessing the Association Between Antiretroviral Regimens and Preterm Delivery (page 8 of 8)

Study Location(s); Dates of Study	Total Number of Pregnancies/Total Number on ARV Drugs	Types of ARV Regimens Compared (Numbers)	Association Noted Between ARV Regimens and Preterm Delivery	Notes
United Kingdom/ Ireland; 2007–2015[55]	6,073/6,073	• Multi-PI (4,184) • Multi-NNRTI (1,889)	• YES • Multi-PI associated with PTD: 1.56 (1.19-2.04) • Multi-PI before conception with CD4 count <350 cells/mm^3, 1.99 (1.02–3.85) and 1.9 (1.01–3.57) and with CD4 count >350 cells/mm^3, 1.61 (1.07–2.43)	• PTD rate was 10.4%. • SGA rate was 20.4%.
South Africa; 2010–2015[29]	4,435/2,549	• Multi-NNRTI, EFV plus TDF plus FTC/3TC (1,481) • Multi-NNRTI, other EFV-based ART (187) • Multi-NNRTI, NVP-based ART (343) • ZDV (528)	• NO • NVP-based ART aOR = 0.66 (0.27–1.63) (NS) and other EFV-based ART (aOR 0.72; 95% CI, 0.24±2.12) vs. EFV plus TDF plus FTC/3TC.	• PTD rate was 10.4%. • SGA rate was 10.4%. • LBW rate was 9.6%.
North America; 2007–2013[19]	4,646/1,621	• Multi-PI, TDF plus FTC plus LPV/r, TDF plus FTC plus ATV/r, ZDV plus 3TC plus LPV/r (1,621)	• YES • TDF plus FTC plus ATV/r vs. ZDV plus 3TC plus LPV/r: aOR = 0.69 (0.51–0.94)	• PTD rate was 19%. • LBW rate was 19.6%.

Note: The data presented in the column Association Noted between ARV Regimens and Preterm Delivery represent the published results of the study in the corresponding row. Depending on the study designs, these are adjusted and unadjusted odds ratios and relative risks.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; aOR = adjusted odds ratio; ART = antiretroviral therapy; ARV = antiretroviral; ATV/r = atazanavir/ritonavir; BMI = body mass index; CD4 = CD4 T lymphocyte; dual = 2 ARV drugs; EFV = efavirenz; FTC = emtricitabine; GA = gestational age; HCV = hepatitis C virus; LBW = low birth weight; mono = single ARV drug; multi = 3 or more ARV drugs; multi-PI = combination ART with PI; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NS = nonsignificant; NVP = nevirapine; OR = odds ratio; PI = protease inhibitor; PROMISE = Promoting Maternal and Infant Survival Everywhere; PTD = preterm delivery; RR = relative risk; RTV = ritonavir; SAPMTCTE = South African Prevention of Mother-to-Child Transmission Evaluation; SGA = small for gestational age; SMARTT = Surveillance Monitoring for ART Toxicities; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

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

Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (page 1 of 4)

Note: For information about specific ARV drugs and dosing in pregnancy, see Table 6, Table 10, and the individual drug sections in Appendix B.

ART Regimen Component **Note:** ARV drugs and ARV regimens are listed alphabetically within drug classes and recommendation categories	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on an ART Regimen that has been Well Tolerated and Virologically Suppressive[a]	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[b]	New ART Regimen for Pregnant Women Whose Current ART is not Well Tolerated and/or is not Resulting in Virologic Suppression[b]	ART for Nonpregnant Women Who Are Trying to Conceive[b,c]
NRTIs[d,e]					
ABC	Preferred	Continue	Preferred	Preferred	Preferred
FTC	Preferred	Continue	Preferred	Preferred	Preferred
3TC	Preferred	Continue	Preferred	Preferred	Preferred
TDF	Preferred	Continue	Preferred	Preferred	Preferred
ZDV	Alternative	Continue	Alternative	Alternative	Alternative
TAF	Insufficient data[f]	Continue	Insufficient data	Insufficient data	Insufficient data
INSTIs Used in combination with a dual-NRTI backbone[e]					
DTG These are interim recommendations, pending the availability of additional data.[g]	Not recommended during the first trimester[g] Preferred after the first trimester	Consider continuation with counseling or switch during the first trimester[g] Continue if patient is in the second or third trimester	Not recommended during the first trimester[g] Preferred after the first trimester	Not recommended during the first trimester[g] Preferred after the first trimester	Not recommended[g]
RAL	Preferred	Continue	Preferred	Preferred	Preferred
BIC	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
EVG/COBI	Not recommended[h]	Consider switch, or continue with frequent viral load monitoring[h]	Not recommended[h]	Not recommended[h]	Not recommended[h]
PIs Used in combination with a dual-NRTI backbone[e]					
ATV/r	Preferred	Continue	Preferred	Preferred	Preferred
DRV/r	Preferred	Continue	Preferred	Preferred	Preferred
LPV/r	Alternative	Continue	Alternative	Alternative	Alternative
ATV/COBI	Not recommended[h]	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring[h]	Not recommended[h]	Not recommended[h]	Not recommended[h]
DRV/COBI	Not recommended[h]	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring[h]	Not recommended[h]	Not recommended[h]	Not recommended[h]

Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (page 2 of 4)

ART Regimen Component **Note:** ARV drugs and ARV regimens are listed alphabetically within drug classes and recommendation categories	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on an ART Regimen that has been Well Tolerated and Virologically Suppressive[a]	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[b]	New ART Regimen for Pregnant Women Whose Current ART is not Well Tolerated and/or is not Resulting in Virologic Suppression[b]	ART for Nonpregnant Women Who Are Trying to Conceive[b,c]
NNRTIs Used in combination with a dual-NRTI backbone[e]					
EFV	Alternative	Continue	Alternative	Alternative	Alternative
RPV[i]	Alternative[i]	Continue[i]	Alternative[i]	Alternative[i]	Alternative[i]
DOR	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
ETR	Not recommended	Continue	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]
NVP	Not recommended	Continue	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]
Entry and Fusion Inhibitors					
IBA	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
MVC	Not recommended	Continue	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]
T-20	Not recommended	Continue	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]	Not recommended, except in special circumstances[j]
FDC Regimens[e] The individual drug component that is most responsible for the overall recommendation is indicated in parentheses.					
ABC/DTG/3TC[g]	Not recommended during the first trimester Preferred after the first trimester (DTG[g])	Consider continuation with counseling or switch during the first trimester Continue if patient is in the second or third trimester (DTG[g])	Not recommended during the first trimester Preferred after the first trimester (DTG[g])	Not recommended during the first trimester Preferred after the first trimester (DTG[g])	Not recommended (DTG[g])
EFV/FTC/TDF	Alternative (EFV)	Continue	Alternative (EFV)	Alternative (EFV)	Alternative (EFV)
EFV/3TC/TDF	Alternative (EFV)	Continue	Alternative (EFV)	Alternative (EFV)	Alternative (EFV)
FTC/RPV/TDF	Alternative (RPV[i])	Continue (RPV[i])	Alternative (RPV[i])	Alternative (RPV[i])	Alternative (RPV[i])
BIC/FTC/TAF	Insufficient data (BIC, TAF)	Insufficient data (BIC)	Insufficient data (BIC, TAF)	Insufficient data (BIC, TAF)	Insufficient data (BIC, TAF)

Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (page 3 of 4)

ART Regimen Component **Note:** ARV drugs and ARV regimens are listed alphabetically within drug classes and recommendation categories	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on an ART Regimen that has been Well Tolerated and Virologically Suppressive[a]	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[b]	New ART Regimen for Pregnant Women Whose Current ART is not Well Tolerated and/or is not Resulting in Virologic Suppression[b]	ART for Nonpregnant Women Who Are Trying to Conceive[b,c]
DOR/3TC/TDF	Insufficient data (DOR)	Insufficient data (DOR)	Insufficient data (DOR)	Insufficient data (DOR)	Insufficient data (DOR)
FTC/RPV/TAF	Insufficient data (TAF[f])	Continue (RPV[i], TAF[f])	Insufficient data (TAF[f])	Insufficient data (TAF[f])	Insufficient data (TAF[f])
EVG/COBI/FTC/TDF	Not recommended (EVG/COBI[h])	Consider switch or continue with frequent viral load monitoring (EVG/COBI[h])	Not recommended (EVG/COBI[h])	Not recommended (EVG/COBI[h])	Not recommended (EVG/COBI[h])
EVG/COBI/FTC/TAF	Not recommended[h] (EVG/COBI[h])	Consider switch or continue with frequent viral load monitoring (EVG/COBI[h])	Not recommended (EVG/COBI[h])	Not recommended (EVG/COBI[h])	Not recommended (EVG/COBI[h])
DRV/COBI/FTC/TAF	Not recommended (DRV/COBI[h])	Consider switch or continue with frequent viral load monitoring (DRV/COBI[h])	Not recommended (DRV/COBI[h])	Not recommended (DRV/COBI[h])	Not recommended (DRV/COBI[h])
DTG/RPV As a complete regimen[k]	Not recommended[g,k]	Not recommended during the first trimester (DTG,[g] RPV[k]) If after the first trimester, switch or add additional agents (DTG[g]/RPV[k])	Not recommended[g,k]	Not recommended[g,k]	Not recommended[g,k]

[a] When changes in ARV regimens are being considered, women should be given information about the benefits and risks of switching ARV drugs so they can participate in decision making.

[b] **Do not initiate** ARV regimens with component that have documented resistance or suspected resistance based on prior ARV exposure.

[c] This guidance is intended for women who are trying to conceive. These recommendations are not intended for all women living with HIV who might become pregnant.

[d] ABC/3TC, TDF/FTC, and TDF/3TC are preferred two-NRTI backbones and ZDV/3TC is an alternative two-NRTI backbone for ART regimens.

[e] When using FDCs, refer to Table 10 and the drug sections in Appendix B for information about the dosing and safety of individual components of the FDC during pregnancy.

[f] Available data about the use of TAF in pregnancy support continuing it in pregnant women who are virally suppressed, although data are insufficient to recommend it when initiating ART in pregnancy.

[g] The following are interim recommendations pending additional data: DTG is a preferred INSTI for pregnant women after the first trimester, 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** the 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 women who become pregnant while taking DTG and who present to care during the first trimester, providers should counsel patients about the risk of neural tube defects and the risk of viral rebound (with associated risk for perinatal transmission) if changes are made to the ART regimen. For more information, see Interim Panel Recommendations Regarding the Use of Dolutegravir at the Time of Conception in Preconception Counseling and Care and Interim Panel Recommendations Regarding the Use of Dolutegravir in Pregnancy in Recommendations for the Use of Antiretroviral Drugs During Pregnancy.

Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant Women and Nonpregnant Women Who Are Trying to Conceive (page 4 of 4)

[h] DRV/COBI, EVG/COBI, and ATV/COBI **are not recommended** for use in pregnancy due to PK changes that pose a risk for low drug levels and viral rebound in the second and third trimesters. However, in pregnant women who present as virologically suppressed on these regimens, it is appropriate to consider continuing them with increased viral load monitoring. If there are concerns about switching, see Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy. Although PK data on ATV/COBI are not available yet, it is anticipated that the data will show pharmacokinetic changes that are similar to those observed with DRV/COBI and EVG/COBI.

[i] Although PK data indicate that RPV plasma concentration is reduced during the second and third trimester, the reduction is less than the reductions seen with EVG/COBI or DRV/COBI. Higher-than-standard doses have not been studied, so there are insufficient data to recommend a dose change in pregnancy. With standard dosing, viral load should be monitored more frequently.

[j] Although these drugs are not recommended for initial treatment in ART-naive pregnant women, there may be special circumstances in which treatment-experienced women may need to continue or initiate ETR, NVP, MVC, and T-20 in order to maintain or achieve viral suppression. There are limited safety and efficacy data about the use of ETR, MVC, and T-20 in pregnancy. NVP is not recommended for ART-naive women because it has a greater potential for adverse events than other NNRTIs, complex lead-in dosing, and low barrier to resistance; however, if a pregnant woman presents to care on a well-tolerated, NVP-containing regimen, it is likely that NVP will be safe and effective during pregnancy. See Table 6 and Nevirapine for more information.

[k] 2-drug ART regimens **are not recommended** for use in pregnancy.

The following drugs (that are not listed above) should not be used in pregnancy; if a woman becomes pregnant while taking these medications, she 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, 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 additional information about ARV drugs and ARV combinations that are not recommended for use in adults and refer to the table above and Table 6 for ARV regimens that are recommended for use in pregnancy.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV = darunavir; 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; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumerate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 8. Newborn Antiretroviral Management According to Risk of HIV Infection in the Newborn

Drug selection and dosing considerations are related to the age and gestational age of the newborn. Consultation is available through the National Perinatal HIV Hotline (888-448-8765).

Category	Description	Neonatal ARV Management
Low Risk of Perinatal HIV Transmission	• Mothers who received ART during pregnancy with sustained viral suppression near delivery and no concerns related to adherence	ZDV for 4 weeks
Higher Risk of Perinatal HIV Transmission[a,b]	• Mothers who received neither antepartum nor intrapartum ARV drugs • Mothers who received only intrapartum ARV drugs • Mothers who received antepartum and intrapartum ARV drugs but who have detectable viral load near delivery, particularly if delivery was vaginal • Mothers with acute or primary HIV infection during pregnancy or breastfeeding (in which case, the mother **should discontinue** breastfeeding).[c]	2-drug ARV prophylaxis (NICHD-HPTN 040/PACTG 1043 regimen) with 6 weeks ZDV and 3 doses of NVP (prophylactic dosage, with doses given within 48 hours of birth, 48 hours after first dose, and 96 hours after second dose) *or* Empiric HIV therapy using either ZDV, 3TC, and NVP (treatment dosage) *or* ZDV, 3TC, and RAL administered from birth to age 6 weeks.[d]
Presumed Newborn HIV Exposure	• Mothers with unknown HIV status who test HIV positive at delivery or postpartum or whose newborns have a positive HIV antibody test	ARV management as above (for higher risk of perinatal HIV transmission) Infant ARVs should be discontinued immediately if supplemental testing confirms that the mother does not have HIV.
Newborn with HIV[e]	• Positive newborn HIV virologic test/NAT	3-drug ARV regimen using treatment dosages

[a] See text for evidence supporting a 2-drug ARV prophylaxis regimen and empiric HIV therapy.

[b] See the Intrapartum Care section for guidance on indications for scheduled cesarean delivery and intrapartum IV ZDV to reduce the risk of perinatal HIV transmission for mothers with an elevated viral load at delivery.

[c] Most Panel members would opt to administer empiric HIV therapy to infants whose mothers had acute HIV during pregnancy because of the higher risk for *in utero* transmission. If acute HIV is diagnosed during breastfeeding, mother should stop breastfeeding.

[d] The optimal duration of empiric HIV therapy in newborns at higher risk of perinatal HIV transmission is unknown. Some Panel members opt to discontinue NVP, RAL, and/or 3TC when a birth NAT returns negative, while others would continue empiric HIV therapy for infants at highest risk of HIV acquisition for 6 weeks. In all cases, ZDV should be continued for 6 weeks. It is recommended that providers consult with an expert in pediatric HIV infection to determine therapy duration based on case-specific risk factors and interim HIV NAT results.

[e] Most Panel members do not recommend delaying the initiation of ART pending results of the confirmatory HIV NAT, given low likelihood of a false-positive HIV NAT.

Note: ARV drugs should be initiated as close to the time of birth as possible, preferably within 6 to 12 hours of delivery. See Table 9 for dosing specifics.

Key to Acronyms: 3TC = lamivudine; ART = antiretroviral therapy; ARV =antiretroviral; IV = intravenous; NAT = nucleic acid test; NVP = nevirapine; the Panel = Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; RAL = raltegravir; ZDV = zidovudine

Table 9. Antiretroviral Dosing Recommendations for Newborns (page 1 of 3)

Newborns at Low Risk of Perinatal HIV Transmission	
Recommended Regimen	**Recommended Duration**
• ZDV	• ZDV administered for 4 weeks
Newborns at Higher Risk of Perinatal HIV Transmission	
Recommended Regimen	**Recommended Duration**
• 2-drug ARV prophylaxis with ZDV and 3 doses of NVP (NICHD-HPTN 040/PACTG 1043 regimen), *or*	• ZDV administered for 6 weeks; 3 doses of NVP during the first week of life
• Empiric HIV therapy with ZDV/3TC/NVP, *or*	• ZDV administered for 6 weeks; 3TC and NVP administered for 2–6 weeks, up to 6 weeks of age[a]
• Empiric HIV therapy with ZDV/3TC/RAL	• ZDV administered for 6 weeks; 3TC and RAL administered for 2–6 weeks, up to 6 weeks of age[a]
Newborns with HIV Infection	
Recommended Regimen	**Recommended Duration**
• HIV therapy with ZDV/3TC/NVP, *or*	• Lifelong therapy
• HIV therapy with ZDV/3TC/RAL	• Lifelong therapy

<table>
<tr><th colspan="4">Indication</th></tr>
<tr><th>Drug</th><th>Low Risk Prophylaxis</th><th>Higher Risk Prophylaxis: 2-Drug</th><th>Higher Risk Prophylaxis: Empiric and HIV Therapy</th></tr>
<tr><td rowspan="3">ZDV

Note: For newborns unable to tolerate oral agents, the IV dose is 75% of the oral dose while maintaining the same dosing interval.</td><td colspan="2">≥35 Weeks Gestation at Birth:
• ZDV 4 mg/kg/dose orally twice daily

Simplified Weight-Band Dosing for Newborns ≥35 Weeks Gestation at Birth:
<table><tr><th>Weight Band (kg)</th><th>Volume (mL) ZDV 10 mg/mL Oral Syrup Twice Daily</th></tr><tr><td>2 to <3 kg</td><td>1 mL</td></tr><tr><td>3 to <4 kg</td><td>1.5 mL</td></tr><tr><td>4 to <5 kg</td><td>2 mL</td></tr></table></td><td>≥35 Weeks Gestation at Birth
Birth–4 Weeks:
• ZDV 4 mg/kg/dose orally twice daily
Age >4 Weeks:
• ZDV 12 mg/kg/dose orally twice daily

Simplified Weight-Band Dosing for Newborns Aged ≥35 Weeks Gestation from Birth to 4 Weeks:
<table><tr><th>Weight Band (kg)</th><th>Volume (mL) ZDV 10 mg/mL Oral Syrup Twice Daily</th></tr><tr><td>2 to <3 kg</td><td>1 mL</td></tr><tr><td>3 to <4 kg</td><td>1.5 mL</td></tr><tr><td>4 to <5 kg</td><td>2 mL</td></tr></table></td></tr>
<tr><td colspan="2">≥30 to <35 Weeks Gestation at Birth
Birth to Age 2 Weeks:
• ZDV 2 mg/kg/dose orally twice daily
Age 2 Weeks to 4–6 Weeks:
• ZDV 3 mg/kg/dose orally twice daily</td><td>≥30 to <35 Weeks Gestation at Birth
Birth to Age 2 Weeks:
• ZDV 2 mg/kg/dose orally twice daily
Age 2 Weeks to 6–8 Weeks:
• ZDV 3 mg/kg/dose orally twice daily
Age >6–8 Weeks:
• ZDV 12 mg/kg/dose orally twice daily</td></tr>
<tr><td colspan="2"><30 Weeks Gestation at Birth
Birth to Age 4–6 Weeks:
• ZDV 2 mg/kg/dose orally twice daily</td><td><30 Weeks Gestation at Birth
Birth to Age 4 Weeks:
• ZDV 2 mg/kg/dose orally twice daily
Age 4 to 8–10 Weeks:
• ZDV 3 mg/kg/dose orally twice daily
Aged >8–10 Weeks:
• ZDV 12 mg/kg/dose orally twice daily</td></tr>
</table>

Table 9. Antiretroviral Dosing Recommendations for Newborns (page 2 of 3)

Indication			
Drug	**Low Risk Prophylaxis**	**Higher Risk Prophylaxis: 2-Drug**	**Higher Risk Prophylaxis: Empiric and HIV Therapy**
3TC	N/A	N/A	≥32 Weeks Gestation at Birth *Birth to Age 4 Weeks:* • 3TC 2 mg/kg/dose orally twice daily *Age >4 Weeks:* • 3TC 4 mg/kg/dose orally twice daily
NVP	N/A	≥32 Weeks Gestation at Birth: • NVP in 3 doses given 1. Within 48 hours of birth, 2. 48 hours after the 1st dose, *and* 3. 96 hours after the 2nd dose Birth Weight 1.5 to 2 kg: • NVP 8 mg per dose orally. **Note:** No calculation is required for this dose; **this is the actual dose, not a mg/kg dose**. Birth Weight >2 kg: • NVP 12 mg per dose orally. **Note:** No calculation is required for this dose; **this is the actual dose, not a mg/kg dose**.	≥37 Weeks Gestation at Birth *Birth to Age 4 Weeks:* • NVP 6 mg/kg/dose orally twice daily[b] *Age >4 Weeks:* • NVP 200 mg/m^2 of BSA/dose orally twice daily 34 to <37 Weeks Gestation at Birth *Birth to Age 1 Week:* • NVP 4 mg/kg/dose orally twice daily *Age 1 to 4 Weeks:* • NVP 6 mg/kg/dose orally twice daily *Age >4 Weeks:* • NVP 200 mg/m^2 of BSA/dose orally twice daily **Note:** NVP dose adjustment at 4 weeks of age is optional for empiric HIV therapy.
RAL **Note:** If the mother has taken RAL 2–24 hours prior to delivery, the neonate's first dose of RAL should be delayed until 24–48 hours after birth; additional ARVs should be started as soon as possible.	N/A	N/A	≥37 Weeks Gestation at Birth and Weighing ≥2 kg[c] *Birth to Age 6 Weeks:*

Body Weight (kg)	**Volume (Dose) of Suspension, RAL 10 mg/mL, to be Administered**
Birth to 1 Week: Once Daily Dosing	**Approximately 1.5 mg/kg/dose**
2 to <3 kg	0.4 mL (4 mg) once daily
3 to <4 kg	0.5 mL (5 mg) once daily
4 to <5 kg	0.7 mL (7 mg) once daily
1 to 4 Weeks: Twice Daily Dosing	**Approximately 3 mg/kg/dose**
2 to <3 kg	0.8 mL (8 mg) twice daily
3 to <4 kg	1 mL (10 mg) twice daily
4 to <5 kg	1.5 mL (15 mg) twice daily
4 to 6 Weeks: Twice Daily Dosing	**Approximately 6 mg/kg/dose**
3 to <4 kg	2.5 mL (25 mg) twice daily
4 to <6 kg	3 mL (30 mg) twice daily

[a] The optimal duration of empiric HIV therapy in newborns at higher risk of perinatal HIV transmission is unknown. Some Panel members opt to discontinue NVP, RAL, and/or 3TC when birth NAT returns negative, while others would continue empiric HIV therapy for infants at the highest risk of HIV acquisition for 6 weeks. In all cases in which the newborn is at higher risk of HIV acquisition, ZDV should be continued for 6 weeks. Consultation with an expert in pediatric HIV to select a therapy duration based on case-specific risk factors and interim HIV NAT results is recommended.

Table 9. Antiretroviral Dosing Recommendations for Newborns (page 3 of 3)

[b] Investigational NVP treatment dose recommended by the Panel; FDA has not approved a dose of NVP for infants <1 month of age.

[c] RAL dosing is increased at 1 and 4 weeks of age because metabolism by UGT1A1 is low at birth and increases rapidly during the next 4 to 6 weeks of life. No dosing information is available for preterm or low birthweight infants.

Key to Acronyms: 3TC = lamivudine; ARV =antiretroviral; BSA = body surface area; FDA = Food and Drug Administration; IV = intravenous; N/A = no recommendation; NAT = nucleic acid test; NVP = nevirapine; the Panel = the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; RAL = raltegravir; UGT1A1 = uridine diphosphate glucotransferase; ZDV = zidovudine

Appendix B: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy

Table 10. Antiretroviral Drug Use in Pregnant Women with HIV: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 1 of 21)

Note: When using FDCs, refer to other sections in Appendix B and Table 10 for information about the dosing and safety of individual drug components of the FDC during pregnancy.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
NRTIs NRTIs are recommended for use as part of combination regimens, usually including 2 NRTIs with either an NNRTI or 1 or more PIs. Use of single or dual NRTIs alone is not recommended for treatment of HIV infection. See text for discussion of potential maternal and infant mitochondrial toxicity.				
Abacavir (ABC) *Ziagen* (ABC/3TC) *Epzicom* (ABC/DTG/3TC) *Triumeq* (ABC/3TC/ZDV) *Trizivir* **Note:** Generic available for some formulations.	ABC (Ziagen)[d] *Tablet:* • 300 mg *Solution:* • 20 mg/mL ABC/3TC (Epzicom):[d] • ABC 600 mg plus 3TC 300 mg tablet ABC/DTG/3TC (Triumeq): • ABC 600 mg plus 3TC 300 mg plus DTG 50 mg tablet ABC/3TC/ZDV (Trizivir):[d] • ABC 300 mg plus 3TC 150 mg plus ZDV 300 mg tablet	Standard Adult Doses *ABC (Ziagen):* • ABC 300 mg twice daily or ABC 600 mg once daily, without regard to food *ABC/3TC (Epzicom):* • 1 tablet once daily without regard to food *ABC/DTG/3TC (Triumeq):* • 1 tablet daily without regard to food *ABC/3TC/ZDV (Trizivir):* • 1 tablet twice daily without regard to food Dosing in Pregnancy: • No change in dose indicated. PK in Pregnancy: • PK not significantly altered in pregnancy. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, ZDV, DTG).	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). HSRs occur in approximately 5% to 8% of nonpregnant individuals. A small percentage of reactions are fatal, and these fatal reactions are usually associated with re-challenge. Rate of reactions during pregnancy is unknown. Testing for HLA-B*5701 identifies patients at risk of reactions and should be done and documented as negative before starting ABC. Patients should be educated regarding symptoms of HSR.	December 7, 2018
Didanosine (ddI) *Videx* *Videx EC* **Note:** Generic available for some formulations	ddI (Videx) *Buffered Tablets (Non-EC):* • No longer available *Solution:* • 10 mg/mL oral solution Videx EC (EC Beadlets) Capsules: • 125 mg • 200 mg • 250 mg • 400 mg Delayed-Release Capsules:[d] • 200 mg • 250 mg • 400 mg	Standard Adult Doses *Body Weight ≥60 kg:* • ddI 400 mg once daily *With TDF:* • ddI 250 mg once daily; take 1/2 hour before or 2 hours after a meal. *Body Weight <60 kg:* • ddI 250 mg once daily *With TDF:* • ddI 200 mg once daily; take 1/2 hour before or 2 hours after a meal. **Note:** Preferred dosing with oral solution is twice daily (total daily dose divided into 2 doses). Take 1/2 hour before or 2 hours after a meal. Dosing in Pregnancy: • No change in dose indicated.	ddI **is not recommended** for pregnant women. Low-moderate placental transfer to fetus.[b] ddI **should not be used** with d4T. Lactic acidosis, sometimes fatal, has been reported in pregnant women receiving ddI and d4T together.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 2 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Didanosine, continued		PK in Pregnancy: • PK is not significantly altered in pregnancy.		
Emtricitabine (FTC) *Emtriva* (FTC/EFV/TDF) *Atripla* (FTC/BIC/TAF) *Biktarvy* (FTC/RPV/TDF) *Complera* (FTC/TAF) *Descovy* (FTC/EVG/COBI/TAF) *Genvoya* (FTC/RPV/TAF) *Odefsey* (FTC/EVG/COBI/TDF) *Stribild* (FTC/DRV/COBI/TAF) *Symtuza* (FTC/TDF) *Truvada*	FTC (Emtriva) *Capsule:* • 200 mg *Oral Solution:* • 10 mg/mL FTC/EFV/TDF (Atripla): • FTC 200 mg plus EFV 600 mg plus TDF 300 mg tablet FTC/BIC/TAF (Biktarvy): • FTC 200 mg plus BIC 50 mg plus TAF 25 mg tablet FTC/RPV/TDF (Complera): • FTC 200 mg plus RPV 25 mg plus TDF 300 mg tablet FTC/TAF (Descovy): • FTC 200 mg plus TAF 25 mg tablet FTC/EVG/COBI/TAF (Genvoya): • FTC 200 mg plus EVG 150 mg plus COBI 150 mg plus TAF 10 mg tablet FTC/RPV/TAF (Odefsey): • FTC 200 mg plus RPV 25 mg plus TAF 25 mg tablet FTC/EVG/COBI/TDF (Stribild): • FTC 200 mg plus EVG 150 mg plus COBI 150 mg plus TDF 300 mg tablet FTC/DRV/COBI/TAF (Symtuza): • FTC 200 mg plus DRV 800 mg plus COBI 150 mg plus TAF 10 mg tablet FTC/TDF (Truvada): • FTC 200 mg plus TDF 300 mg tablet	Standard Adult Doses *FTC (Emtriva)* *Capsule:* • EVG 200 mg once daily without regard to food *Oral Solution:* • EVG 240 mg (24 mL) once daily without regard to food *FTC/EFV/TDF (Atripla):* • 1 tablet once daily at or before bedtime • Take on an empty stomach to reduce side effects. *FFTC/BIC/TAF (Biktarvy):* • 1 tablet once daily with or without food *FTC/RPV/TDF (Complera):* • 1 tablet once daily with food *FTC/TAF (Descovy):* • 1 tablet once daily with or without food *FTC/EVG/COBI/TAF (Genvoya):* • 1 tablet once daily with food *FTC/RPV/TAF (Odefsey):* • 1 tablet once daily with food *FTC/EVG/COBI/TDF (Stribild):* • 1 tablet once daily with food *FTC/DRV/COBI/TAF (Symtuza):* • 1 tablet once daily with food *FTC/TDF (Truvada):* • 1 tablet once daily without regard to food Dosing in Pregnancy: • No change in FTC dose indicated. PK in Pregnancy: • PK of FTC is not significantly altered in pregnancy. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., TDF, TAF, EFV, RPV, DRV, EVG, BIC, COBI)	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). If patient is HBV-coinfected, it is possible that a HBV flare may occur if the drug is stopped; see HIV/Hepatitis B Virus Coinfection.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 3 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Lamivudine (3TC) *Epivir* (3TC/TDF) *Cimduo* (3TC/ZDV) *Combivir* (3TC/DOR/TDF) *Delstrigo* (3TC/ABC) *Epzicom* (3TC/EFV/TDF) *Symfi* (3TC/EFV/TDF) *Symfi Lo* (3TC/TDF) *Temixys* (3TC/ABC/DTG) *Triumeq* (3TC/ABC/ZDV) *Trizivir* **Note:** Generic available for some formulations	3TC (Epivir)[d] *Tablets:* • 150 mg • 300 mg *Oral Solution:* • 10 mg/mL 3TC/TDF (Cimduo): • 3TC 300 mg plus TDF 300 mg tablet 3TC/ZDV (Combivir):[d] • 3TC 150 mg plus ZDV 300 mg tablet 3TC/DOR/TDF (Delstrigo): • 3TC 300 mg plus DOR 100 mg plus TDF 300 mg tablet 3TC/ABC (Epzicom):[d] • 3TC 300 mg plus ABC 600 mg tablet 3TC/EFV/TDF (Symfi): • 3TC 300 mg plus EFV 600 mg plus TDF 300 mg tablet 3TC/EFV/TDF (Symfi Lo): • 3TC 300 mg plus EFV 400 mg plus TDF 300 mg tablet 3TC/TDF (Temixys): • 3TC 300 mg plus TDF 300 mg tablet 3TC/ABC/DTG (Triumeq): • 3TC 300 mg plus ABC 600 mg plus DTG 50 mg tablet 3TC/ABC/ZDV (Trizivir):[d] • 3TC 150 mg plus ABC 300 mg plus ZDV 300 mg tablet	Standard Adult Doses *3TC (Epivir):* • 3TC 150 mg twice daily or 300 mg once daily, without regard to food *3TC/TDF (Cimduo):* • 1 tablet once daily without regard to food *3TC/ZDV (Combivir):* • 1 tablet twice daily without regard to food *3TC/DOR/TDF (Delstrigo):* • 1 tablet once daily without regard to food *3TC/ABC (Epzicom):* • 1 tablet once daily without regard to food *3TC/EFV/TDF (Symfi or Symfi Lo):* • 1 tablet once daily on an empty stomach and preferably at bedtime *3TC/ABC/DTG (Triumeq):* • 1 tablet once daily without regard to food *3TC/TDF (Temixys):* • 1 tablet once daily without regard to food *3TC/ABC/ZDV (Trizivir):* • 1 tablet twice daily without regard to food PK in Pregnancy: • PK not significantly altered in pregnancy. Dosing in Pregnancy: • No change in dose indicated. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., ABC, DOR, DTG, EFV, TDF, ZDV).	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). If patient has HIV/HBV coinfection, it is possible that an HBV flare may occur if the drug is stopped; see HIV/Hepatitis B Virus Coinfection. **Note:** 3TC products developed specifically for treatment of HBV (e.g., Epivir-HBV) contain a lower dose of 3TC that **is not appropriate** for treatment of HIV.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 4 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Stavudine (d4T) *Zerit* **Note:** Generic products are available for all formulations.	d4T (Zerit) *Capsules:* • 15 mg • 20 mg • 30 mg • 40 mg *Oral Solution:* • 1 mg/mL following reconstitution **Note:** Extended-release capsule formulation (Zerit XR) has been discontinued by the manufacturer.	Standard Adult Doses[e] *Body Weight ≥60 kg:* • 40 mg twice daily without regard to meals *Body Weight <60 kg:* • 30 mg twice daily without regard to meals Dosing in Pregnancy: • No change in dose indicated. PK in Pregnancy: • PK not significantly altered in pregnancy.	d4T **is not recommended** for pregnant women. High placental transfer.[b] No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects). Lactic acidosis, sometimes fatal, has been reported in pregn aant women receiving ddI and d4T together.	December 7, 2018
Tenofovir Alafenamide (TAF) *Vemlidy* (TAF/BIC/FTC) *Biktarvy* (TAF/FTC) *Descovy* (TAF/EVG/COBI/FTC) *Genvoya* (TAF/FTC/RPV) *Odefsey* (TAF/DRV/COBI/FTC) *Symtuza* **Note:** Generic available for some formulations.	TAF (Vemlidy)[d] *Tablet:* • 25 mg TAF/BIC/FTC (Biktarvy): • TAF 25 mg plus BIC 50 mg plus FTC 200 mg tablet TAF/FTC (Descovy): • TAF 25 mg plus FTC 200 mg tablet TAF/EVG/COBI/FTC (Genvoya): • TAF 10 mg plus EVG 150 mg plus COBI 150 mg plus FTC 200 mg tablet TAF/FTC/RPV (Odefsey): • TAF 25 mg plus FTC 200 mg plus RPV 25 mg tablet TAF/DRV/COBI/FTC (Symtuza): • TAF 10 mg plus DRV 800 mg plus COBI 150 mg plus FTC 200 mg tablet	Standard Adult Dose *TAF (Vemlidy):* • 1 tablet once daily with food *TAF/BIC/FTC (Biktarvy):* • 1 tablet once daily with or without food *TAF/FTC (Descovy):* • 1 tablet once daily with or without food • Same dose (TAF 25 mg) can be used with or without pharmaco-enhancers. *TAF/EVG/COBI/FTC (Genvoya):* • 1 tablet once daily with food *TAF/FTC/RPV (Odefsey):* • 1 tablet once daily with food *TAF/DRV/COBI/FTC (Symtuza):* • 1 tablet once daily with food PK in Pregnancy: • Plasma PK not significantly altered in pregnancy.	Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats. Renal function should be monitored because of potential for renal toxicity.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 5 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Tenofovir Alafenamide, continued		Dosing in Pregnancy: • No change in dose indicated. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., BIC, COBI. DRV, EVG, FTC, RPV).		
Tenofovir Disoproxil Fumarate (TDF) *Viread* (TDF/EFV/FTC) *Atripla* (TDF/3TC) *Cimduo* (TDF/FTC/RPV) *Complera* (TDF/DOR/3TC) *Delstrigo* (TDF/EVG/COBI / FTC) *Stribild* (TDF/EFV/3TC) *Symfi* (TDF/EFV/3TC) *Symfi Lo* (TDF/3TC) *Temixys* (TDF/FTC) *Truvada* **Note:** Generic available for some formulations	TDF (Viread) *Tablet:*[d] • 300 mg *Powder:* • 40 mg/1 g oral powder TDF/EFV/FTC (Atripla): • TDF 300 mg plus EFV 600 mg plus FTC 200 mg tablet TDF/3TC (Cimduo): • TDF 300 mg plus 3TC 300 mg tablet TDF/FTC/RPV (Complera): • TDF 300 mg plus FTC 200 mg plus RPV 25 mg tablet TDF/DOR/3TC (Delstrigo): • TDF 300 mg plus DOR 100 mg plus 3TC 300 mg tablet TDF/EVG/COBI /FTC (Stribild): • TDF 300 mg plus EVG 150 mg plus COBI 150 mg plus FTC 200 mg tablet TDF/EFV/3TC (Symfi): • TDF 300 mg plus EFV 600 mg plus 3TC 300 mg tablet TDF/EFV/3TC (Symfi Lo): • TDF 300 mg plus EFV 400 mg plus 3TC 300 mg tablet	Standard Adult Doses *TDF (Viread)* *Tablet:* • TDF 300 mg once daily without regard to food *Powder:* • TDF 8 mg/kg (up to a maximum of TDF 300 mg). Take with food. *TDF/EFV/FTC (Atripla):* • 1 tablet once daily at or before bedtime. Take on an empty stomach to reduce side effects. *TDF/3TC (Cimduo):* • 1 tablet once daily without regard to food *TDF/FTC/RPV (Complera):* • 1 tablet once daily with food *TDF/DOR/3TC (Delstrigo):* • 1 tablet once daily without regard to food. *TDF/EVG/COBI/FTC (Stribild):* • 1 tablet once daily with food *TDF/EFV/3TC (Symfi or Symfi Lo):* • 1 tablet once daily on an empty stomach and preferably at bedtime *TDF/3TC (Temixys):* • 1 tablet once daily without regard to food	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Studies in monkeys (at doses approximately 2-fold higher than those for human therapeutic use) show decreased fetal growth and reduction in fetal bone porosity within 2 months of starting maternal therapy. Human studies demonstrate no consistent link to low birth weight, but data are conflicting about potential effects on growth outcomes later in infancy. If patient is HBV coinfected, it is possible that an HBV flare may occur if TDF is stopped; see HIV/Hepatitis B Virus Coinfection. Renal function should be monitored because of potential for renal toxicity.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 6 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Tenofovir Disoproxil Fumarate, continued	TDF/3TC (Temixys): • TDF 300 mg plus 3TC 300 mg tablet TDF/FTC (Truvada): • TDF 300 mg plus FTC 200 mg tablet	*TDF/FTC (Truvada):* • 1 tablet once daily without regard to food PK in Pregnancy: • AUC is lower in third trimester than postpartum, but trough levels are adequate. Dosing in Pregnancy: • No change in dose is indicated. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, COBI, DOR, EFV, EVG, FTC, RPV)		
Zidovudine (ZDV) *Retrovir* (ZDV/3TC) *Combivir* (ZDV/ABC/3TC) *Trizivir* **Note:** Generic available for all formulations.	ZDV (Retrovir) *Capsule:* • 100 mg *Tablet:* • 300 mg *Oral Solution:* • 10 mg/mL *Intravenous Solution:* • 10 mg/mL ZDV/3TC (Combivir): • ZDV 300 mg plus 3TC 150 mg tablet ZDV/ABC/3TC (Trizivir): • ZDV 300 mg plus 3TC 150 mg plus ABC 300 mg tablet	Standard Adult Dose *ZDV (Retrovir):* • ZDV 300 mg BID or ZDV 200 mg TID without regard to food *Active Labor:* • ZDV 2 mg/kg IV loading dose, followed by ZDV 1 mg/kg/hour continuous infusion from beginning of active labor until delivery *Combivir:* • 1 tablet twice daily without regard to food *Trizivir:* • 1 tablet twice daily without regard to food Dosing in Pregnancy: • No change in dose is indicated. PK in Pregnancy: • PK is not significantly altered in pregnancy. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., ABC, 3TC)	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects).	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 7 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
NNRTI NNRTIs are recommended for use in combination regimens with 2 NRTI drugs. Hypersensitivity reactions, including hepatic toxicity and rash, more common in women; unclear if increased in pregnancy.				
Doravirine (DOR) *Pifeltro* (DOR/3TC/TDF) *Delstrigo*	DOR (Pifeltro): • 100 mg tablet DOR/3TC/TDF (Delstrigo): • DOR 100 mg plus 3TC 300 mg plus TDF 300 mg tablet	Standard Adult Dose *DOR (Pifeltro):* • 100 mg once daily with or without food *DOR/3TC/TDF (Delstrigo):* • 1 tablet once daily with or without food PK in Pregnancy: • No PK studies in human pregnancy. Dosing in Pregnancy: • Insufficient data to make dosing recommendation. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, TDF)	No human data are available on placental transfer of DOR, but animal studies suggest that DOR crosses the placenta. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.	December 7, 2018
Efavirenz (EFV) *Sustiva* (EFV/FTC/TDF) *Atripla* (EFV/3TC/TDF) *Symfi* (EFV/3TC/TDF) *Symfi Lo* **Note:** Generic available for some formulations.	EFV (Sustiva)[d] *Capsules:* • 50 mg • 200 mg *Tablet:* • 600 mg EFV/FTC/TDF (Atripla): • EFV 600 mg plus FTC 200 mg tablet TDF 300 mg plus EFV/3TC/TDF (Symfi): • EFV 600 mg plus 3TC 300 mg plus TDF 300 mg tablet EFV/3TC/TDF (Symfi Lo): • EFV 400 mg plus 3TC 300 mg plus TDF 300 mg tablet	Standard Adult Doses *EFV (Sustiva):* • EFV 600 mg once daily at or before bedtime, on an empty stomach to reduce side effects *EFV/FTC/TDF (Atripla):* • 1 tablet once daily at or before bedtime, on an empty stomach to reduce side effects *EFV/3TC/TDF (Symfi or Symfi Lo):* • 1 tablet once daily on an empty stomach and preferably at bedtime PK in Pregnancy: • AUC is decreased during the third trimester compared with postpartum, but nearly all third-trimester participants exceeded target exposure. Dosing in Pregnancy: • No change in dose is indicated.	Moderate placental transfer to fetus.[b] The FDA advises women to avoid becoming pregnant while taking EFV and advises health care providers to avoid administration during the first trimester of pregnancy, as fetal harm may occur. Although the limited data on first-trimester EFV exposure cannot rule out a 2-fold or 3-fold increased incidence of a rare outcome such as NTDs, the available data from a meta-analysis of >2,000 births suggest that there is no large increase in the risk of neural tube defects with first-trimester exposure (e.g., a 10-fold increase to a rate of 1%). As a result, the current Perinatal Guidelines do not restrict the use of EFV in pregnant women or in women who are planning to become pregnant. This is consistent with both the British HIV Association and WHO guidelines for use of ARV drugs in pregnancy.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 8 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Efavirenz, continued		• For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, FTC, TDF)	EFV should be continued in pregnant women who are on a virologically suppressive, EFV-based regimen, because ARV drug changes during pregnancy may be associated with loss of viral control and an increased risk of perinatal transmission (see Pregnant Women Living with HIV Who are Currently Receiving Antiretroviral Therapy).	
Etravirine (ETR) *Intelence*	ETR (Intelence) *Tablets:* • 25 mg • 100 mg • 200 mg For patients unable to swallow tablets whole, the tablets may be dispersed in a glass of water.	Standard Adult Dose *ETR (Intelence):* • 200 mg twice daily with food PK in Pregnancy: • PK data in pregnancy (n = 26) suggest that etravirine exposure during pregnancy increases 1.2-fold to 1.6-fold. Dosing in Pregnancy: • No change in dose indicated.	Variable placental transfer, usually in the moderate to high categories, ranging from 0.19–4.25 (data from 19 mother-infant pairs).[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.	December 7, 2018
Nevirapine (NVP) *Viramune Viramune XR (Extended Release)* **Note:** Generic available for some formulations	NVP (Viramune) *Tablets:* • 200 mg[d] *Oral Suspension:* • 50 mg/5 mL Viramune XR Tablets: • 100 mg • 400 mg[d]	Standard Adult Dose: • 200 mg once-daily Viramune (immediate release) for 14 days (lead-in period); thereafter, 200 mg twice daily or 400 mg (Viramune XR tablet) once daily, without regard to food. • Repeat lead-in period if therapy is discontinued for >7 days. • In patients who develop mild-to-moderate rash without constitutional symptoms during lead-in period, continue lead-in dosing until rash resolves, but administer for ≤28 days total. PK in Pregnancy: • PK of immediate release tablets is not significantly altered in pregnancy.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects and 2-fold increase in cardiovascular and genitourinary defects. Increased risk of symptomatic, often rash-associated, and potentially fatal liver toxicity among women with CD4 cell counts ≥250/mm^3 when first initiating therapy; pregnancy does not appear to increase risk. NVP should be initiated in pregnant women with CD4 cell counts ≥250 cells/mm^3 only when benefit clearly outweighs risk because of potential increased risk of	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 9 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Nevirapine, continued		• No data are available on extended release formulations in pregnancy. Dosing in Pregnancy: • No change in dose indicated.	life-threatening hepatotoxicity in women with high CD4 cell counts. Elevated transaminase levels at baseline may increase the risk of NVP toxicity. Women who become pregnant while taking NVP-containing regimens and who are tolerating their regimens well can continue therapy, regardless of CD4 cell count.	
Rilpivirine (RPV) *Edurant* (RPV/FTC/TDF) *Complera* (RPV/DTG) *Juluca* (RPV/FTC/TAF) *Odefsey*	RPV (Edurant) *Tablets:* • 25 mg RPV/FTC/TDF (Complera): • RPV 25 mg plus FTC 200 mg plus TDF 300 mg tablet RPV/DTG (Juluca): • RPV 25 mg plus DTG 50 mg tablet RPV/FTC/TAF (Odefsey): • RPV 25 mg plus FTC 200 mg plus TAF 25 mg tablet	Standard Adult Dose *RPV (Edurant):* • RPV 25 mg once daily with food *RPV/FTC/TDF (Complera):* • 1 tablet once daily with food *RPV/DTG (Juluca):* • 1 tablet once daily with food *RPV/FTC/TAF (Odefsey):* • 1 tablet once daily with food PK in Pregnancy: • RPV PK highly variable during pregnancy. RPV AUC and trough concentration reduced 20% to 50% lower in pregnancy than postpartum. While most pregnant women exceeded target exposure, those with detectable viral loads had lower RPV troughs. Dosing in Pregnancy: • While RPV plasma concentration is reduced during pregnancy, higher-than-standard doses have not been studied. Insufficient data are available to recommend a dosing change in pregnancy. With standard dosing, viral loads should be monitored more frequently. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., DTG, FTC, TAF, TDF).	Moderate to high placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects). 2-drug regimens (e.g., RPV/DTG FDC) **are not recommended** in pregnancy.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 10 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
PIs PIs are recommended for use in combination regimens with 2 NRTI drugs. Hyperglycemia, new onset or exacerbation of diabetes mellitus, and diabetic ketoacidosis reported with PI use; unclear if pregnancy increases risk. Conflicting data regarding preterm delivery in women receiving PIs (see Combination Antiretroviral Drug Regimens and Pregnancy Outcomes).				
Atazanavir (ATV) *Reyataz* **Note:** Generic available for some formulations. **Note:** ATV must be combined with low-dose RTV boosting in pregnancy. (ATV/COBI) *Evotaz*	ATV (Reyataz) *Capsules*: • 100 mg (generic product only) • 150 mg[d] • 200 mg[d] • 300 mg[d] *Oral Powder:* • 50 mg packet ATV/COBI (Evotaz): • ATV 300 mg plus COBI 150 mg tablet	Standard Adult Doses *ARV-Naive Patients* *Without RTV Boosting:* • ATV 400 mg once daily with food; ATV without RTV boosting **is not recommended** when used with TDF, H2-receptor antagonists, PPIs, or during pregnancy. *With RTV Boosting:* • ATV 300 mg plus RTV 100 mg once daily with food • When combined with EFV in ARV-naive patients: ATV 400 mg plus RTV 100 mg once daily with food *ARV-Experienced Patients:* • ATV 300 mg plus RTV 100 mg once daily with food • Do not use with PPIs or EFV *If Combined with an H2-Receptor Antagonist:* ATV 300 mg plus RTV 100 mg once daily with food *If Combined with an H2-Receptor Antagonist and TDF:* • ATV 400 mg plus RTV 100 mg once daily with food Powder Formulation: • Oral powder is taken with RTV once daily with food at the same recommended adult dose as the capsules. ATV/COBI (Evotaz): • 1 tablet once daily with food PK in Pregnancy *ATV (Reyataz):* • ATV concentrations reduced during pregnancy; further reduced when given concomitantly with TDF or H2-receptor antagonist. *ATV/COBI (Evotaz):* • No PK studies in human pregnancy. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., COBI).	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Must be given as low-dose RTV-boosted regimen in pregnancy. Effect of *in utero* ATV exposure on infant indirect bilirubin levels is unclear. Nonpathologic elevations of neonatal hyperbilirubinemia have been observed in some, but not all, clinical trials to date. Oral powder (but *not* capsules) contains phenylalanine, which can be harmful to patients with phenylketonuria. ATV/COBI **is not recommended** for use in pregnancy. For women who become pregnant while taking ATV/COBI, consider switching to a more effective, recommended regimen. If an ATV/COBI regimen is continued, doses should be administered with food; viral load should be monitored frequently.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 11 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Atazanavir, continued		Dosing in Pregnancy *ATV (Reyataz):* • Use of unboosted ATV **is not recommended** during pregnancy. • Use of ATV **is not recommended** for ARV-experienced pregnant women taking TDF *and* an H2-receptor antagonist. • Use of an increased dose (ATV 400 mg plus RTV 100 mg once daily with food) during the second and third trimesters results in plasma ATV concentrations equivalent to those seen in nonpregnant adults on standard dosing. Although some experts recommend increased ATV dosing in all women during the second and third trimesters, the package insert recommends increased ATV dosing only for ARV-experienced pregnant women in the second and third trimesters who are also receiving either TDF or an H2-receptor antagonist. *ATV/COBI (Evotaz):* • Insufficient data to make dosing recommendation in pregnancy (see Cobicistat section).		
Darunavir (DRV) *Prezista* **Note:** Must be combined with low-dose RTV or COBI boosting. (DRV/COBI) *Prezcobix* (DRV/COBI/FTC/TAF) *Symtuza*	DRV (Prezista): *Tablet:* • 75 mg • 150 mg • 600 mg • 800 mg *Oral Suspension:* • 100 mg/mL DRV/COBI (Prezcobix): • DRV 800 mg plus COBI 150 mg tablet DRV/COBI/FTC/TAF (Symtuza): • DRV 800 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg tablet	**Standard Adult Doses** ARV-Naive Patients: • DRV 800 mg plus RTV 100 mg once daily with food • DRV 800 mg plus COBI 150 mg once daily with food ARV-Experienced Patients: *If Patient Has No DRV Resistance Mutations:* • DRV 800 mg plus RTV 100 mg once daily with food • DRV 800 mg plus COBI 150 mg once daily with food *If Any DRV Resistance Mutations Are Present:* • DRV 600 mg plus RTV 100 mg twice daily with food *DRV/COBI (Prezcobix):* • 1 tablet once daily with food *DRV/COBI/FTC/TAF (Symtuza):* • 1 tablet once daily with food Dosing in Pregnancy: • The Panel **does not recommend** once-daily dosing with DRV/r during pregnancy or the use of DRV/c during pregnancy. Twice-daily DRV/r dosing (DRV 600 mg plus RTV 100 mg with food) is	Low placental transfer to fetus.[b] No evidence of teratogenicity in mice, rats, or rabbits. No evidence of human teratogenicity. Must be boosted with low-dose RTV. The Panel **does not recommend** once-daily dosing with DRV/COBI during pregnancy or the use of DRV/COBI during pregnancy. If a DRV/c regimen is continued during pregnancy, viral load should be monitored frequently.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 12 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Darunavir, continued		recommended for all pregnant women. Increased twice-daily DRV dose (DRV 800 mg plus RTV 100 mg with food) during pregnancy does not result in an increase in darunavir exposure and **is not recommended**. PK in Pregnancy: • Decreased exposure in pregnancy with use of DRV/r. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., COBI, FTC, TAF)		
Fosamprenavir (FPV) *Lexiva (a prodrug of amprenavir)* **Note:** Must be combined with low-dose RTV boosting in pregnancy.	FPV (Lexiva) *Tablets:* • 700 mg *Oral Suspension:* • 50 mg/mL	Standard Adult Doses *FPV (Lexiva)* *ARV-Naive Patients:* • FPV 1400 mg twice daily without food, *or* • FPV 1400 mg plus RTV 100 or 200 mg once daily without food, *or* • FPV 700 mg plus RTV 100 mg twice daily without food *PI-Experienced Patients:* • Once-daily dosing **is not recommended** • FPV 700 mg plus RTV 100 mg twice daily without food *Coadministered with EFV:* • FPV 700 mg plus RTV 100 mg twice daily without food; *or* • FPV 1400 mg plus RTV 300 mg once daily without food PK in Pregnancy: • With RTV boosting, AUC is reduced during the third trimester. However, exposure is greater during the third trimester with boosting than in nonpregnant adults without boosting, and trough concentrations achieved during the third trimester were adequate for patients without PI resistance mutations. Dosing in Pregnancy: • Use of unboosted FPV or once-daily FPV with RTV boosting **is not recommended** during pregnancy. No change is indicated in standard boosted twice-daily dose (FPV 700 mg plus RTV 100 mg twice daily without food).	FPV **should not** be used during pregnancy. Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. Increased fetal loss in rabbits, but no increase in defects in rats and rabbits.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 13 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Indinavir (IDV) *Crixivan* **Note:** Must be combined with low-dose RTV boosting in pregnancy	IDV (Crixivan) *Capsules:* • 200 mg • 400 mg	Standard Adult Dose *Without RTV Boosting:* • IDV 800 mg every 8 hours, taken 1 hour before or 2 hours after meals; may be taken with skim milk or a low-fat meal. *With RTV Boosting:* • IDV 800 mg plus RTV 100 mg twice daily without regard to meals PK in Pregnancy: • IDV exposure markedly reduced when administered without RTV boosting during pregnancy. IDV exposure is low with IDV 400 mg/RTV 100 mg dosing during pregnancy; no PK data available on alternative boosted dosing regimens in pregnancy. Dosing in Pregnancy: • Use of unboosted IDV **is not recommended** during pregnancy.	Minimal placental transfer to fetus.[b] No evidence of human teratogenicity in cases reported to the Antiretroviral Pregnancy Registry (can rule out 2-fold increase in overall birth defects). Must be given as low-dose, RTV-boosted regimen in pregnancy. Theoretical concern regarding increased indirect bilirubin levels, which may exacerbate physiologic hyperbilirubinemia in neonates. Minimal placental passage mitigates this concern. Given the available alternative ARVs, IDV **is not recommended** for treatment of pregnant women in the United States.	December 7, 2018
Lopinavir/ Ritonavir (LPV/r) *Kaletra*	LPV/r (Kaletra) *Tablets (Coformulated):* • LPV/r 200 mg/50 mg • LPV/r 100 mg/25 mg *Oral Solution:* • LPV/r 400 mg/100 mg/5 mL	Standard Adult Dose: • LPV/r 400 mg/100 mg twice daily, *or* • LPV/r 800 mg/200 mg once daily *Tablets:* • Take without regard to food. *Oral Solution:* • Take with food. With EFV or NVP (PI-Naive or PI-Experienced Patients): • LPV/r 500 mg/125 mg tablets twice daily without regard to meals (use a combination of 2 LPV 200-mg plus RTV 50-mg tablets and 1 LPV 100-mg plus RTV 25-mg tablet), *or* • LPV/r 520 mg/130 mg oral solution (6.5 mL) twice daily with food	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Oral solution contains 42% alcohol and 15% propylene glycol and is not recommended for use in pregnancy. Once-daily LPV/r dosing **is not recommended** during pregnancy.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 14 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Lopinavir/ Ritonavir, continued		PK in Pregnancy: • With twice-daily dosing, LPV exposure is reduced in pregnant women receiving standard adult doses; increasing the dose by 50% results in exposure equivalent to that seen in nonpregnant adults receiving standard doses. • No PK data are available for once-daily dosing in pregnancy. Dosing in Pregnancy: • Once-daily dosing **is not recommended** during pregnancy. • Some experts recommend that an increased dose (i.e., LPV/r 600 mg/150 mg twice daily without regard to meals or LPV/r 500 mg/125 mg twice daily without regard to meals) should be used in the second and third trimesters, especially in PI-experienced pregnant women and women who start treatment during pregnancy with a baseline viral load >50 copies/mL. If standard dosing is used, monitor virologic response and, if available, LPV drug levels.		
Nelfinavir (NFV) *Viracept*	NFV (Viracept): *Tablets:* • 250 mg • 625 mg (tablets can be dissolved in a small amount of water) *Powder for Oral Suspension:* • 50 mg/g	Standard Adult Dose: • NFV 1250 mg twice daily, *or* • NFV 750 mg 3 times daily with food PK in Pregnancy: • Lower NFV exposure was observed during the third trimester than postpartum in women receiving NFV 1250 mg twice daily; however, adequate drug levels are generally achieved during pregnancy, although levels are variable in late pregnancy. Dosing in Pregnancy: • NFV 750 mg 3 times daily with food **is not recommended** during pregnancy. No change in standard dose (NFV 1250 mg twice daily with food) indicated.	NFV **should not** be used during pregnancy. Minimal to low placental transfer to fetus.[b] No evidence of human teratogenicity; can rule out 1.5-fold increase in overall birth defects and 2-fold increase in risk of cardiovascular and genitourinary birth defects. Contains aspartame; should not be used in individuals with phenylketonuria.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 15 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Saquinavir (SQV) *Invirase* **Note:** Must be combined with low-dose RTV for PK boosting	SQV (Invirase) *Tablet:* • 500 mg *Capsule:* • 200 mg	Standard Adult Dose: • SQV 1000 mg plus RTV 100 mg twice a day with food or within 2 hours after a meal PK in Pregnancy: • Based on limited data, SQV exposure may be reduced in pregnancy, but this effect is not sufficient to warrant a dose change. Dosing in Pregnancy: • No change in dose indicated.	SQV **should not be used** during pregnancy. **Contraindicated** in patients with pre-existing cardiac conduction system disease. Baseline ECG recommended before starting, because PR and/or QT interval prolongations have been observed. Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. Must be boosted with low-dose RTV.	December 7, 2018
Tipranavir (TPV) *Aptivus* **Note:** Must be combined with RTV for PK boosting	TPV (Aptivus) *Capsules:* • 250 mg *Oral Solution:* • 100 mg/mL	Standard Adult Dose: • TPV/r 500 mg/200 mg twice daily *With RTV Tablets:* • Take with food. *With RTV Capsules or Solution:* • Take without regard to food; however, administering with food may help make the dose more tolerable. Dosing in Pregnancy: • Insufficient data to make dosing recommendation PK in Pregnancy: • Limited PK data in human pregnancy	TPV **should not be used** during pregnancy. Moderate placental transfer to fetus reported in 1 patient.[b] Insufficient data to assess teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. Must be given as low-dose, RTV-boosted regimen.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 16 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Entry Inhibitors				
Enfuvirtide (T-20) *Fuzeon*	T-20 (Fuzeon) *Injectible:* • Supplied as lyophilized powder. Each vial contains 108 mg of T-20; reconstitute with 1 mL of sterile water for injection for SQ delivery of approximately 90 mg/1 mL.	T-20 is indicated for advanced HIV disease and must be used in combination with other ARV drugs to which the patient's virus is susceptible, as determined by resistance testing. Standard Adult Dose: • T-20 90 mg (1 mL) twice daily without regard to meals PK in Pregnancy: • No PK data in human pregnancy. Dosing in Pregnancy: • Insufficient data to make dosing recommendation.	Minimal to low placental transfer to fetus.[b] No data on human teratogenicity.	December 7, 2018
Ibalizumab (IBA) *Trogarzo*	IBA (Trogarzo) *Solution:* • Solution for IV infusion is available in single-dose vials	Standard Adult Dose *IBA (Trogarzo):* • IBA 2000-mg loading dose, followed by IBA 800-mg maintenance doses administered every 2 weeks Dosing in Pregnancy: • Insufficient data are available to make dosing recommendation. PK in Pregnancy: • No PK studies have been reported in human pregnancy.	No data are available, but placental transfer of IBA, a monoclonal antibody, is possible. Insufficient data are available to assess for teratogenicity in humans.	December 7, 2018
Maraviroc (MVC) *Selzentry*	MVC (Selzentry) *Tablets:* • 150 mg • 300 mg	Standard Adult Dose: • MVC 300 mg twice daily with or without food • MVC should only be used for patients with CCR5-tropic virus (and no X4-tropic virus). Dose Adjustments: • Increase to MVC 600 mg BID when used with potent CYP3A inducers: EFV, ETR, and rifampin. • Decrease to MVC 150 mg BID when used with CYP3A inhibitors: all PIs except TPV/r, itraconazole.	No evidence of teratogenicity in rats or rabbits; insufficient data to assess for teratogenicity in humans. MVC placental passage category should be moderate.[b]	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 17 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Maraviroc, continued		PK in Pregnancy: • A PK study in human pregnancy demonstrated a 20% to 30% overall decrease in AUC, but C_{trough} exceeded the recommended minimal concentration of 50 ng/mL. Dosing in Pregnancy: • Standard adult dosing adjusted for concomitant ARV use appears appropriate.		
Integrase Inhibitors				
Bictegravir/ Emtricitabine/ Tenofovir Alafenamide (BIC/FTC/TAF) *Biktarvy* **Note:** BIC is not available as a single-entity formulation.	BIC/FTC/TAF (Biktarvy): • BIC 50 mg plus FTC 200 mg plus TAF 25 mg tablet	Standard Adult Dose *BIC/FTC/TAF (Biktarvy):* • 1 tablet once daily with or without food Dosing in Pregnancy: • There is insufficient data to make a dosing recommendation. PK in Pregnancy: • No PK studies have been reported in human pregnancy. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., FTC, TAF).	No data are available on placental transfer of BIC. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. To maximize BIC absorption, doses should not be administered within 2 hours of ingestion of any preparation containing minerals such as iron or calcium, including prenatal vitamins.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 18 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Dolutegravir (DTG) *Tivicay* (DTG/RPV) *Juluca* (DTG/ABC/3TC) *Triumeq*	DTG (Tivicay) *Tablet:* • DTG 50 mg tablet DTG/RPV (Juluca): • DTG 50 mg plus RPV 25 mg tablet DTG/ABC/3TC (Triumeq): • DTG 50 mg plus ABC 600 mg plus 3TC 300 mg tablet	Standard Adult Doses *In ARV-Naive or ARV-Experienced (but Integrase Inhibitor-Naive) Patients* *DTG (Tivicay):* • 1 tablet once daily, without regard to food *DTG/RPV (Juluca):* • 1 tablet once daily with food *DTG/ABC/3TC (Triumeq):* • 1 tablet once daily, without regard to food *ARV-Naive or ARV-Experienced (but Integrase Inhibitor-Naive) if Given with EFV, FPV/r, TPV/r, or Rifampin; or Integrase Inhibitor-Experienced* *DTG (Tivicay):* • 1 tablet twice daily, without regard to food PK in Pregnancy: • AUC may be decreased during the third trimester compared with postpartum, but good viral suppression observed in third-trimester recipients. Dosing in Pregnancy: • No change in dose indicated. • For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., ABC, 3TC, RPV)	High placental transfer to fetus.[b] No evidence of teratogenicity in mice, rats, or rabbits. Preliminary data suggest a possible increased risk of NTDs in infants born to women who initiated DTG prior to pregnancy and were receiving it at the time of conception. Dolutegravir **should not be initiated** during the first trimester of pregnancy (less than 14 weeks [up to 13 6/7 weeks] gestational age by LMP.) For more information see Interim Guidance about the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy . To maximize DTG absorption, doses should not be administered within 2 hours of ingestion of any preparation containing minerals such as iron or calcium, including prenatal vitamins.	December 7, 2018
Elvitegravir (EVG) *Vitekta* **Note:** As of October 2017, Vitekta (i.e., EVG as a single-entity formulation) is no longer available (EVG/COBI/FTC/TAF) *Genvoya* (EVG/COBI/FTC/TDF) *Stribild*	EVG/COBI/FTC/TAF (Genvoya): • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg tablet EVG/COBI/FTC/TDF (Stribild): • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TDF 300 mg tablet	Standard Adult Dose (Genvoya and Stribild): • 1 tablet once daily with food Dosing in Pregnancy: • Insufficient data to make dosing recommendation PK in Pregnancy: • PK studies in women who received EVG/c demonstrated significant reduction in EVG plasma exposure during pregnancy.	Evidence of high placental transfer of EVG and low transfer of COBI.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. EVG/COBI **is not recommended** for use in pregnancy. For women who become pregnant while taking EVG/c, consider switching to a more effective, recommended regimen. If an EVG/COBI regimen is continued, doses should not be administered within 2	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 19 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Elvitegravir, continued			hours of ingestion of any preparation containing minerals such as iron or calcium, including prenatal vitamins.	
Raltegravir (RAL) *Isentress* *Isentress HD*	RAL (Isentress) *Film-Coated Tablets:* • 400 mg *Chewable Tablets:* • 25 mg • 100 mg RAL (Isentress HD) *Film-Coated Tablets:* • 600 mg	Standard Adult Doses: • RAL 400-mg, film-coated tablets twice daily without regard to food • Two RAL 600-mg, film-coated tablets (1200 mg) once daily for ARV-naive patients or patients who are already virologically suppressed on an initial regimen of RAL 400 mg twice daily without regard to food • Chewable and oral suspension doses are not interchangeable with either film-coated tablets or each other *With Rifampin:* • Two RAL 400-mg, film-coated tablets (800 mg) twice daily without regard to food PK in Pregnancy: • Decreased drug concentrations in third trimester not of sufficient magnitude to warrant a change in dosing. Dosing in Pregnancy: • No change in dose is indicated. • Once-daily dosing (i.e., two RAL 600-mg, film-coated tablets) **should not be used** in pregnant women until more information is available.	High placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Case report of markedly elevated liver transaminases with RAL use in late pregnancy. Severe, potentially life-threatening, and fatal skin and HSRs have been reported in nonpregnant adults. Chewable tablets contain phenylalanine. To maximize RAL absorption, doses should not be administered within 2 hours of ingestion of any preparation containing minerals such as iron or calcium, including prenatal vitamins.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 20 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Cobicistat (COBI) *Tybost* (ATV/COBI) *Evotaz* (EVG/COBI/FTC/TAF) *Genvoya* (DRV/COBI) *Prezcobix* (EVG/COBI/FTC/TDF) *Stribild* (DRV/COBI/FTC/TAF) *Symtuza*	COBI (Tybost) *Tablet:* • COBI 150 mg ATV/COBI (Evotaz): • ATV/COBI 300 mg/50 mg tablet EVG/COBI/FTC/TAF (Genvoya): • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg tablet DRV/COBI (Prezcobix): • DRV/COBI 800 mg/150 mg tablet EVG/COBI/FTC/TDF (Stribild): • EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TDF 300 mg tablet DRV/COBI/FTC/TAF (Symtuza): • DRV 800 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg tablet	Standard Adult Doses *COBI (Tybost):* • As an alternative PK booster with ATV or DRV: 1 tablet (150 mg) once daily with food *ATV/COBI (Evotaz):* • 1 tablet once daily with food *EVG/COBI/FTC/TAF (Genvoya):* • 1 tablet once daily with food *DRV/COBI (Prezcobix):* • 1 tablet once daily with food *EVG/COBI/FTC/TDF (Stribild):* • 1 tablet once daily with food *DRV/COBI/FTC/TAF (Symtuza):* • 1 tablet once daily with food PK in Pregnancy: • Based on limited data, COBI exposure and pharmaco-enhancing effect on DRV and EVG are markedly reduced in pregnancy. • No data are available on the pharmaco-enhancing effect of COBI on ATV. • When coadministered with COBI, TAF exposure is not significantly different between pregnancy and the postpartum period. Dosing in Pregnancy: • While COBI exposure is markedly reduced during pregnancy, higher than standard doses have not been studied. The Panel recommends RTV as the preferred pharmaco-enhancer for PIs and INSTIs during pregnancy until more data are available on COBI activity during pregnancy. • For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., FTC, TAF, TDF, ATV, DRV, EVG).	Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits. Use of COBI-boosted ATV, DRV, or EVG **is not recommended** in pregnancy.	December 7, 2018

Table 10. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy[a] (page 21 of 21)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Use in Pregnancy	Last Reviewed
Ritonavir (RTV) *Norvir*	RTV (Norvir) *Capsules:* • 100 mg *Tablets:* • 100 mg *Oral Solution:* • 80 mg/mL *Powder:* • 100 mg/sachet	Standard Adult Dose as PK Booster for Other PIs: • RTV 100–400 mg per day in 1–2 divided doses (refer to other PIs for specific dosing recommendations.) *Tablet:* • Take with food. *Capsule or Oral Solution:* • To improve tolerability, take with food if possible. PK in Pregnancy: • Lower levels seen during pregnancy than during postpartum. Dosing in Pregnancy: • No dosage adjustment necessary when used as booster.	Low placental transfer to fetus.[b] No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects). Should only be used as low-dose booster for other PIs. Oral solution contains 43% alcohol and is therefore not recommended during pregnancy, because there is no known safe level of alcohol exposure during pregnancy.	December 7, 2018

[a] Individual ARV drug dosages may need to be adjusted in patients with renal or hepatic insufficiency (for details, see the Adult and Adolescent Guidelines, Appendix B, Table 8).

[b] Placental transfer categories are determined by mean or median cord blood/maternal delivery plasma drug ratio:

High: >0.6 **Moderate:** 0.3–0.6 **Low:** <0.3

[c] Only indicated for use in chronic HBV virus infection in adults.

[d] Generic formulation available

[e] WHO recommends maximum dose of 30 mg twice daily regardless of weight.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CD4 = CD4 T lymphocyte; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV = darunavir; 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; HBV = hepatitis b virus; HSR = hypersensitivity reaction; 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; SQ = subcutaneous; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TID = 3 times a day; TPV = tipranavir; TPV/r = tipranavir/ritonavir; WHO = World Health Organization; ZDV = zidovudine

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 1 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
PACTG 076; United States, France;[1] Formula feeding	ZDV vs. placebo	Long (from 14 weeks) IV IP	Long (6 weeks); infant only	Perinatal transmission at 18 months was 8.3% in ZDV arm vs. 25.5% in placebo arm (68% efficacy).
CDC Short-Course ZDV Trial; Thailand;[12] Formula feeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	None	Perinatal transmission at 6 months was 9.4% in ZDV arm vs. 18.9% in placebo arm (50% efficacy).
DITRAME (ANRS 049a) Trial; Ivory Coast, Burkina Faso;[11,39] Breastfeeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	Short (1 week); mother only	Perinatal transmission at 6 months was 18.0% in ZDV arm vs. 27.5% in placebo arm (38% efficacy). Perinatal transmission at 15 months was 21.5% in ZDV arm vs. 30.6% in placebo arm (30% efficacy). Perinatal transmission was 22.5% in ZDV arm vs. 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy).
CDC Short-Course ZDV Trial; Ivory Coast;[10,11] Breastfeeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	None	Perinatal transmission at 3 months was 16.5% in ZDV arm vs. 26.1% in placebo arm (37% efficacy). Perinatal transmission was 22.5% in ZDV arm vs. 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy).
PETRA Trial; South Africa, Tanzania, Uganda;[5] Breastfeeding and formula feeding	AP/IP/PP ZDV plus 3TC vs. IP/PP ZDV plus 3TC vs. IP-only ZDV plus 3TC vs. Placebo	Short (from 36 weeks) Oral IP	Short (1 week); mother and infant	Perinatal transmission at 6 weeks was 5.7% for AP/IP/PP ZDV plus 3TC, 8.9% for IP/PP ZDV plus 3TC, 14.2% for IP-only ZDV plus 3TC, and 15.3% for placebo (efficacy compared with placebo: 63%, 42%, and 0%, respectively). Perinatal transmission at 18 months was 14.9% for AP/IP/PP ZDV plus 3TC, 18.1% for IP/PP ZDV plus 3TC, 20.0% for IP-only ZDV plus 3TC, and 22.2% for placebo (efficacy compared with placebo: 34%, 18%, and 0%, respectively).

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 2 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
HIVNET 012 Trial; Uganda;[4] Breastfeeding	SD NVP vs. ZDV	No AP ARV drugs Oral IP: • SD NVP vs. oral ZDV	SD NVP within 72 hours of birth; infant only vs. ZDV for 1 week; infant only	Perinatal transmission at 6–8 weeks was 11.8% in NVP arm vs. 20.0% in ZDV arm (42% efficacy) and 15.7% in NVP arm vs. 25.8% in ZDV arm at 18 months (41% efficacy).
SAINT Trial; South Africa;[6] Breastfeeding and formula feeding	SD NVP vs. ZDV plus 3TC	No AP ARV drugs Oral IP: • SD NVP vs. ZDV plus 3TC	SD NVP within 48 hours of birth; mother and infant vs. ZDV plus 3TC for 1 week; mother and infant	Perinatal transmission at 8 weeks was 12.3% in SD NVP arm vs. 9.3% in ZDV plus 3TC arm (difference not statistically significant, $P = 0.11$).
PHPT-1; Thailand;[13] Formula feeding	4 ZDV regimens with different durations of AP and infant PP administration; no placebo	Long (from 28 weeks) or short (from 36 weeks) Oral IP	Long (6 weeks) or short (3 days); infant only	Perinatal transmission rate was 10.5% in the short-short arm. This arm was stopped at interim analysis. Perinatal transmission at 6 months was 6.5% in long-long arm vs. 4.7% in long-short arm and 8.6% in short-long arm (no statistical difference). *In utero* transmission was significantly higher with short vs. long maternal therapy regimens (5.1% vs. 1.6%).
PACTG 316 Trial; Bahamas, Belgium, Brazil, France, Germany, Italy, Spain, Sweden, Switzerland, United Kingdom, United States;[21] Formula feeding	SD NVP vs. placebo among women already receiving ZDV alone (23%) or ZDV plus other ARV drugs (77% combination therapy)	Nonstudy ARV regimen Oral IP: • Placebo vs. SD NVP plus IV ZDV	Placebo vs. SD NVP within 72 hours of birth plus nonstudy ARV drugs (ZDV); infant only	77% of women received dual- or triple-combination ARV regimens during pregnancy. Trial stopped early because of very low perinatal transmission in both arms: 1.4% in SD NVP arm vs. 1.6% in placebo arm (53% of perinatal transmission was *in utero*).
PHPT-2; Thailand;[40] Formula feeding	ZDV alone vs. ZDV plus maternal and infant SD NVP vs. ZDV plus maternal SD NVP	ZDV from 28 weeks Oral IP: • ZDV alone, *or* • ZDV plus SD NVP	ZDV for 1 week with or without SD NVP; infant only	ZDV-alone arm was stopped because the rate of perinatal transmission was higher in this arm than in the ZDV/NVP arm (6.3% vs. 1.1%, respectively). In arms in which the mother received SD NVP, the perinatal transmission rate did not differ significantly whether the infant received SD NVP or not (2.0% vs. 2.8%, respectively).
DITRAME Plus (ANRS 1201.0) Trial; Ivory Coast;[15] Breastfeeding and formula feeding	Open label, ZDV plus SD NVP	ZDV from 36 weeks Oral IP: • ZDV plus SD NVP	SD NVP plus ZDV for 1 week; infant only	Perinatal transmission at 6 weeks was 6.5% (95% CI, 3.9% to 9.1%); perinatal transmission for historical control group receiving short ZDV (98% of whom were breastfed) was 12.8%.
DITRAME Plus (ANRS 1201.1) Trial; Ivory Coast;[15] Breastfeeding and formula feeding	Open label, ZDV plus 3TC plus SD NVP	ZDV plus 3TC from 32 weeks (stopped at 3 days PP) Oral IP: • ZDV plus 3TC plus SD NVP	SD NVP plus ZDV for 1 week; infant only	Perinatal transmission at 6 weeks was 4.7% (95% CI, 2.4% to 7.0%); perinatal transmission for historical control group receiving short ZDV (98% of whom were breastfed) was 12.8%.

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 3 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
NVAZ Trial; Malawi;[7] Breastfeeding	Neonatal SD NVP vs. SD NVP plus ZDV	No AP or IP ARV drugs	SD NVP with or without ZDV for 1 week; infant only	Perinatal transmission at 6–8 weeks was 15.3% in SD NVP plus ZDV arm vs. 20.9% in SD NVP-only arm. Perinatal transmission rates at 6–8 weeks among infants without HIV at birth were 7.7% and 12.1%, respectively (36% efficacy).
Postnatal NVP plus ZDV Trial; Malawi;[8] Breastfeeding	Neonatal SD NVP vs. SD NVP plus ZDV	No AP ARV Oral IP: • SD NVP	SD NVP with or without ZDV for 1 week; infant only	Perinatal transmission at 6–8 weeks was 16.3% in NVP plus ZDV arm vs. 14.1% in SD NVP-only arm (difference not statistically significant). Perinatal transmission rates at 6–8 weeks among infants without HIV at birth were 6.5% and 16.9%, respectively.
Post-Exposure Infant Prophylaxis; South Africa;[9] Breastfeeding and formula feeding	Neonatal SD NVP vs. ZDV for 6 weeks	No AP or IP ARV drugs	SD NVP vs. ZDV for 6 weeks	For formula-fed infants only, perinatal transmission at 6 weeks was 14.3% in SD NVP arm vs. 14.1% in ZDV arm (not significant, $P = 0.30$). For breastfed infants only, perinatal transmission was 12.2% in SD NVP arm vs. 19.6% in ZDV arm ($P = 0.03$).
Mashi; Botswana;[41,42] Breastfeeding and formula feeding	Initial: • Short-course ZDV with/without maternal and infant SD NVP and with/without breastfeeding Revised: • Short-course ZDV plus infant SD NVP with/without maternal SD NVP and with/without breastfeeding; women with CD4 counts <200 cells/mm^3 received combination therapy.	First Randomization: • ZDV from 34 weeks Oral IP: • ZDV plus either SD NVP or placebo	Second Randomization: • Breastfeeding plus ZDV (infant) 6 months plus SD NVP; infant only, vs. • Formula feeding plus ZDV (infant) 4 weeks plus SD NVP; infant only	Initial Design: • In formula-feeding arm, perinatal transmission at 1 month was 2.4% in maternal and infant SD NVP arm vs. 8.3% in placebo arm ($P = 0.05$). • In breastfeeding plus infant ZDV arm, perinatal transmission at 1 month was 8.4% in SD NVP arm vs. 4.1% in placebo arm (difference not statistically significant). Revised Design: • Perinatal transmission at 1 month was 4.3% in maternal plus infant SD NVP arm vs. 3.7% in maternal placebo plus infant SD NVP arm (no significant difference; no interaction with mode of infant feeding). Perinatal transmission at 7 months was 9.1% in breastfeeding plus ZDV arm vs. 5.6% in formula-feeding arm; mortality at 7 months was 4.9% in breastfeeding plus ZDV arm vs. 9.3% in formula-feeding arm; HIV-free survival at 18 months was 15.6% in the breastfeeding plus ZDV arm vs. 14.2% in the formula-feeding arm.
SWEN; Uganda, Ethiopia, India;[24] Breastfeeding	SD NVP vs. NVP for 6 weeks	No AP ARV drugs Oral IP: • SD NVP	Infant SD NVP vs. NVP for 6 weeks	Postnatal Infection in Infants Without HIV at Birth: • Perinatal transmission at 6 weeks was 5.3% in SD NVP arm vs. 2.5% in extended NVP arm (risk ratio 0.54, $P = 0.009$). • Perinatal transmission at 6 months was 9.0% in SD NVP arm vs. 6.9% in extended NVP arm (risk ratio 0.80, $P = 0.16$). HIV-free survival was significantly lower in extended NVP arm at both 6 weeks and 6 months of age.

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 4 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
PEPI-Malawi Trial; Malawi;[23] Breastfeeding	SD NVP plus ZDV for 1 week (control) vs. 2 extended infant regimens (NVP or NVP/ZDV) for 14 weeks	No AP ARV drugs Oral IP: • SD NVP (if mother presents in time)	Infant SD NVP plus ZDV for 1 week (control) vs. Control plus NVP for 14 weeks vs. Control plus NVP/ZDV for 14 weeks	Postnatal Infection in Infants Without HIV at Birth: • Perinatal transmission at 6 weeks was 5.1% in control arm vs. 1.7% in extended NVP arm (67% efficacy) and 1.6% in extended NVP/ZDV arm (69% efficacy). • Perinatal transmission at 9 months was 10.6% in control arm vs. 5.2% in extended NVP arm (51% efficacy) and 6.4% in extended NVP/ZDV arm (40% efficacy). No significant difference in perinatal transmission between the extended prophylaxis arms; however, more hematologic toxicity with NVP/ZDV.
MITRA; Tanzania;[26] Breastfeeding	Infant 3TC for 6 months (observational)	ZDV/3TC from 36 weeks through labor	Maternal ZDV/3TC for 1 week; infant 3TC for 6 months	Perinatal transmission at 6 months was 4.9% (postnatal perinatal transmission between 6 weeks and 6 months was 1.2%).
Kisumu Breastfeeding Study; Kenya;[29] Breastfeeding	Maternal triple-drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4 count >250 cells/mm^3) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4 count >250 cells/mm^3) for 6 months, infant SD NVP	Perinatal transmission at 6 months was 5.0% (postnatal perinatal transmission between 7 days and 6 months was 2.6%).
MITRA-PLUS; Tanzania;[25] Breastfeeding	Maternal triple-drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4 count >200 cells/mm^3) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4 count >200 cells/mm^3) for 6 months, infant ZDV/3TC for 1 week	Perinatal transmission at 6 months was 5.0% (postnatal perinatal transmission between 6 weeks and 6 months was 0.9%), not significantly different from 6-month infant prophylaxis in MITRA.
Kesho Bora; Multi-African;[28] Breastfeeding primarily	AP ZDV/SD NVP with no postnatal prophylaxis vs. Maternal triple-drug prophylaxis in women with CD4 counts 200–500 cells/mm^3	Arm 1: • ZDV/3TC/LPV/r Arm 2: • ZDV plus SD NVP From 28 weeks through labor	Arm 1: • Maternal ZDV/3TC/LPV/r for 6 months, infant SD NVP plus ZDV for 1 week Arm 2: • Maternal ZDV/3TC for 1 week (no further postnatal prophylaxis), infant SD NVP plus ZDV for 1 week (no further postnatal prophylaxis)	Perinatal transmission at birth was 1.8% with maternal triple-drug prophylaxis (Arm 1) vs. 2.5% with ZDV/SD NVP (Arm 2), not significantly different. In women with CD4 counts 350–500 cells/mm^3, perinatal transmission at birth was 1.7% in both arms. Perinatal transmission at 12 months was 5.4% with maternal triple-drug prophylaxis (Arm 1) vs. 9.5% with ZDV/SD NVP (with no further postnatal prophylaxis after 1 week) (Arm 2) (P = 0.029).
Mma Bana; Botswana;[2] Breastfeeding	Compared 2 maternal triple-drug prophylaxis regimens in women with CD4 counts >200 cells/mm^3	Arm 1: • ZDV/3TC/ABC Arm 2: • ZDV/3TC/LPV/r From 26 weeks through labor	Arm 1: • Maternal ZDV/3TC/ABC for 6 months, infant SD NVP plus ZDV for 4 weeks Arm 2: • Maternal ZDV/3TC/LPV/r for 6 months, infant SD NVP plus ZDV for 4 weeks	Perinatal transmission at 6 months overall was 1.3%: 2.1% in ZDV/3TC/ABC Arm 1 vs. 0.4% in ZDV/3TC/LPV/r Arm 2 (P = 0.53).

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 5 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
BAN; Malawi;[27,43] **Breastfeeding**	Postpartum maternal triple-drug prophylaxis vs. infant NVP in women with CD4 counts ≥250 cells/mm^3	No AP drugs IP Regimens *Arm 1 (Control):* • ZDV/3TC plus SD NVP *Arm 2:* • ZDV/3TC plus SD NVP *Arm 3:* • ZDV/3TC plus SD NVP	Arm 1 (Control): • Maternal ZDV/3TC for 1 week; infant SD NVP plus ZDV/3TC for 1 week Arm 2: • Control as above, then maternal ZDV/3TC/LPV/r for 6 months Arm 3: • Control as above, then infant NVP for 6 months	Postnatal Infection in Infants Without HIV at 2 Weeks: • Perinatal transmission at 28 weeks was 5.7% in control Arm 1, 2.9% in maternal triple-drug prophylaxis Arm 2 (P = 0.009 vs. control), and 1.7% in infant NVP Arm 3 (P < 0.001 vs. control). • Perinatal transmission at 48 weeks was 7.0% in control Arm 1, 4.0% in maternal triple-drug prophylaxis Arm 2 (P = 0.0273 vs. control), and 4% in infant NVP Arm 3 (P = 0.0027 vs. control). No significant difference between maternal triple-drug prophylaxis (Arm 2) and infant NVP (Arm 3) (P = 0.12 at 28 weeks and P = 0.426 at 48 weeks).
HPTN 046; South Africa, Tanzania, Uganda, Zimbabwe;[38,44] **Breastfeeding**	Postpartum prophylaxis to prevent breast milk transmission of HIV with 6 weeks of infant NVP vs. 6 months of infant NVP	AP drugs allowed if required for maternal health	All infants received daily NVP from birth through age 6 weeks. Arm 1: • Daily infant NVP from 6 weeks through 6 months Arm 2: • Daily infant placebo from 6 weeks through 6 months	In infants without HIV at age 6 weeks, the 6-month infant HIV infection rate was 1.1% (0.3% to 1.8%) in the extended NVP arm vs. 2.4% (1.3% to 3.6%) in the placebo arm (P = 0.048). 18-month postnatal infection rates were 2.2% (1.1% to 3.3%) in the extended NVP arm vs. 3.1% (1.9% to 4.4%) in the placebo arm (P = 0.28). HIV infection and mortality rates did not differ between arms at any age through 18 months. At infant randomization at age 6 weeks, 29% of mothers in each arm were receiving a triple-drug ARV regimen for the treatment of HIV. For mothers receiving triple-drug ARV regimens at the time of randomization, in infants without HIV at age 6 weeks, the 6-month infant HIV infection rate was 0.2% and not statistically different from the rates seen in the extended NVP arm (0.5%) and placebo arm (0%). For mothers with CD4 counts >350 cells/mm^3 who were not receiving triple-drug ARV regimens, in infants without HIV at age 6 weeks, the 6-month infant HIV infection rate was 0.7% (0% to 1.5%) in the extended NVP arm vs. 2.8% (1.3% to 4.4%) in the placebo arm (P = 0.014).

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 6 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
NICHD-HPTN 040/ PACTG 1043 Trial; Brazil, Argentina, South Africa, United States;[45] Formula feeding	Infant prophylaxis with 6 weeks of ZDV vs. 6 weeks of infant ZDV plus 3 doses of NVP in first week of life vs. 6 weeks of infant ZDV plus 2 weeks 3TC/NFV	No AP drugs If mother presented early enough, IV ZDV during labor through delivery	Arm 1 (Control): • Infant ZDV for 6 weeks Arm 2: • Control as above plus NVP, with first dose within 48 hours of birth, second dose 48 hours later, and third dose 96 hours after second dose Arm 3: • Control as above, plus 3TC and NFV from birth through age 2 weeks	IP HIV transmission among infants with negative HIV test at birth: 4.8% (3.2% to 7.1%) with ZDV (Arm 1) vs. 2.2% (1.2% to 3.9%) with ZDV plus NVP (Arm 2) (P = 0.046 compared with Arm 1) vs. 2.4% (1.4% to 4.3%) with ZDV plus 3TC/NFV (Arm 3) (P = 0.046 compared with Arm 1). Overall HIV transmission rates, including *in utero* infection: 11.0% (8.7% to 14.0%) with ZDV (Arm 1) vs. 7.1% (5.2% to 9.6%) with ZDV plus NVP (Arm 2) (P = 0.035 compared with Arm 1) vs. 7.4% (5.4% to 9.9%) with ZDV plus 3TC/NFV (Arm 3) (P = 0.035 compared with Arm 1). Grade 3 or 4 neutropenia more frequent in ZDV/3TC/NFV Arm 3 (70 infants) than in ZDV-alone Arm 1 (33 infants) or ZDV/NVP Arm 2 (32 infants) (P < 0.001).
ANRS 12174 Trial; Burkina Faso, South Africa, Uganda, Zambia;[30,31] Breastfeeding	Compared 2 infant ARV prophylaxis regimens during breastfeeding; infants tested PCR-negative at birth and were born to mothers with CD4 counts >350 cells/mm^3	As per standard of care	Arm 1: • Daily infant LPV/r from 1 week through 50 weeks of age Arm 2: • Daily infant 3TC from 1 week through 50 weeks of age	Postnatal Infection in Infants Without HIV at Birth: • Postnatal transmission at age 50 weeks was 1.4% (0.70–2.76) in Arm 1 vs. 1.5% (0.80–2.91) in Arm 2 (P = 0.83). • HIV-free survival was 96.5% (84.6–97.7) in Arm 1 vs. 96.3% (94.4–97.5) in Arm 2 (P = 0.85).
PROMOTE; Uganda;[46] Breastfeeding	Compared 2 triple-ARV regimens; no CD4 restriction	Arm 1: • ZDV/3TC/LPV/r Arm 2: • ZDV/3TC/EFV • ARVs started at 12–28 weeks' gestation and continued through labor	Randomized regimen continued postpartum through 1 year of breastfeeding	HIV-free survival was 92.9% in the LPV/r arm vs. 97.2% in the EFV arm (P = 0.10). Only 2 of 374 liveborn infants acquired infection, both in the LPV/r arm.
PROMISE; India, Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe;[18] Breastfeeding and formula feeding (antepartum component)	Compared ZDV prophylaxis and 2 ART regimens during pregnancy among women at >14 weeks' gestation and with CD4 counts ≥350 cells/mm^3	Arm 1: • ZDV during pregnancy plus SD NVP plus TDF plus FTC at delivery Arm 2: • ZDV plus 3TC plus LPV/r Arm 3: • TDF plus FTC plus LPV/r	Arm 1: • TDF/FTC tail continued for 6–14 days postpartum Arms 2 and 3: • ART regimen continued for 6–14 days postpartum Infants received once-daily NVP for 6 weeks.	Infant HIV Infection Rates by Age 14 Days *Arm 1:* • 1.8% (25/1,386) *Arm 2:* • 0.5% (7/1,385) *Arm 3:* • 0.6% (2/325) Combined ART arms vs. ZDV arm difference in perinatal transmission risk: -1.3% (95% CI, -2.1% to -0.4%)

Supplemental Table 1. Results of Major Studies on Antiretroviral Interventions to Prevent Perinatal HIV Transmission (page 7 of 7)

Study Name; Location(s); Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum Interventions	Postpartum Interventions	Perinatal Transmission Rate and Efficacy
PROMISE; India, Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe;[18] Breastfeeding (postpartum component)	Compared infant NVP and maternal ART during breastfeeding among infants born to women with CD4 counts ≥350 cells/mm^3	This was a postpartum study. intervention only. Eligible women included women enrolled in PROMISE antepartum (see above) and women who received no ARV drugs during pregnancy.	Arm 1: • Mothers received TDF plus FTC plus LPV/r Arm 2: • Once-daily infant NVP Regimens were continued until 42 days after last breastmilk exposure or age 18 months, whichever came first.	Infant Infection Rates: *Arm 1:* • 0.57% (7/1,219) *Arm 2:* • 0.58% (7/1,211) Rates of Infant HIV-1–Free Survival at 24 Months *Arm 1:* • 97.1% *Arm 2:* • 97.7%

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; AP = antepartum; ARV = antiretroviral; ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; CI = confidence interval; EFV = efavirenz; FTC = emtricitabine; IP = intrapartum; IV = intravenous; LPV/r = lopinavir/ritonavir; NFV = nelfinavir; NVP = nevirapine; PCR = polymerase chain reaction; PP = postpartum; SD = single-dose; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine