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

Tables

May 24, 2010 Release

The in-text tables from the May 24, 2010 release of the ***Perinatal Guidelines*** have been compiled in this document to facilitate downloading. Each table is identical in numbering and content to those found in the guidelines document. References within these tables may be found in the appropriate section of the guidelines document, when applicable.

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the guidelines	Provide guidance to HIV care practitioners on the optimal use of antiretroviral agents in pregnant women for treatment of HIV infection and for prevention of mother-to-child transmission (MTCT) of HIV in the United States.
Panel members	The Panel is composed of approximately 30 voting members who have expertise in management of pregnant HIV-infected women (e.g., training in either obstetrics/gynecology or women's health) and interventions to prevent MTCT (e.g., pediatric specialists in HIV infection), as well as community representatives with knowledge of HIV infection in pregnant women and interventions to prevent MTCT. The U.S. government representatives, appointed by their agency, include at least one representative from each of the following HHS agencies: Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), and the National Institutes of Health (NIH). Members who do not represent the U.S. government agencies are selected after an open announcement to call for nominations. Each member serves on the Panel for a 3-year period, with an option for reappointment. A list of current Panel members can be found on Page iv of this document.
Financial disclosure	All members of the Panel submit a written financial disclosure annually. A list of the latest disclosures can be found in Appendix A of this document.
Users of the guidelines	Providers of care to HIV-infected pregnant women and to HIV-exposed infants
Funding source	Office of AIDS Research, NIH
Evidence collection	The recommendations are generally based on studies published in peer-reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.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. The members synthesize the available data and propose a recommendation to the Panel. All proposals are discussed at monthly teleconferences and then are voted on by the Panel members before being endorsed as official recommendations.

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Other guidelines	These guidelines focus on HIV-infected pregnant women and their infants. Separate guidelines outline the use of antiretroviral therapy in nonpregnant HIV-infected adults and adolescents, HIV-infected children, and those who experience occupational or nonoccupational exposure to HIV. These guidelines are also available at the AIDS*info* Web site (**http://www.aidsinfo.nih.gov**). There is brief discussion of preconception management for nonpregnant women of reproductive age in this document. However, for more detailed discussion on issues of treatment of nonpregnant adults, the Working Group defers to the designated expertise offered by Panels that have developed those guidelines.
Update plan	The Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, dosing formulations, or frequency), new significant safety or efficacy data, or other information that may have a significant impact on the clinical care of patients. For cases in which significant new data become available that may affect patient safety, a warning announcement with the Panel's recommendations may be made on the AIDS*info* Web site until appropriate changes can be made in the guidelines document. Updated guidelines are available at the AIDS*info* Web site (**http://www.aidsinfo.nih.gov**).
Public comments	After release of an update on the AIDS*Info* Web site, the public is given a 2-week period to submit comments to the Panel. These comments are reviewed, and a determination is made as to whether revisions are indicated. The public is also able to 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

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission

Study Location(s) Mode of Infant Feeding	Antiretroviral Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission Rate and Efficacy
PACTG 076 United States, France *[1]* Formula feeding	ZDV vs placebo	Long (from 14 weeks) Intravenous IP	Long (6 weeks), infant only	• MTCT at 18 months was 8.3% in ZDV arm vs 25.5% in placebo arm (68% efficacy).
CDC short-course ZDV trial Thailand *[22]* Formula feeding	ZDV vs placebo	Short (from 36 weeks) Oral IP	None	• MTCT at 6 months was 9.4% in ZDV arm vs 18.9% in placebo arm (50% efficacy).
DITRAME (ANRS 049a) trial Côte d'Ivoire, Burkina Faso *[21, 58]* Breastfeeding	ZDV vs placebo	Short (from 36 weeks) Oral IP	Short (1 week), mother only	• MTCT was 18.0% in ZDV arm vs 27.5% in placebo arm at 6 months (38% efficacy) and 21.5% vs 30.6% at 15 months (30% efficacy). • MTCT 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 Côte d'Ivoire *[20-21]* Breastfeeding	ZDV vs placebo	Short (from 36 weeks) Oral IP	None	• MTCT was 16.5% in ZDV arm vs 26.1% in placebo arm at 3 months (37% efficacy). • MTCT was 22.5% in ZDV arm vs 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy).

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission

PETRA trial South Africa, Tanzania, and Uganda *[14]* Breastfeeding and formula feeding	AP/IP/PP ZDV + 3TC vs IP/PP ZDV + 3TC vs IP-only ZDV + 3TC vs placebo	Short (from 36 weeks) Oral IP	Short (1 week), mother and infant	• MTCT was 5.7% at 6 weeks for AP/IP/PP ZDV + 3TC, 8.9% for IP/PP ZDV + 3TC, 14.2% for IP-only ZDV + 3TC, and 15.3% for placebo (efficacy compared to placebo: 63%, 42%, and 0%, respectively). • MTCT was 14.9% at 18 months for AP/IP/PP ZDV + 3TC, 18.1% for IP/PP ZDV + 3TC, 20.0% for IP-only ZDV + 3TC, and 22.2% for placebo (efficacy compared to placebo: 34%, 18%, and 0%, respectively).
HIVNET 012 trial Uganda *[13]* Breastfeeding	sdNVP vs ZDV	No AP ARV Oral IP: sdNVP vs oral ZDV	sdNVP within 72 hours of birth (infant only) vs ZDV (1 week), infant only	• MTCT was 11.8% in NVP arm vs 20.0% in ZDV arm at 6 to 8 weeks (42% efficacy); 15.7% in NVP arm vs 25.8% in ZDV arm at 18 months (41% efficacy).
SAINT trial South Africa *[16]* Breastfeeding and formula feeding	sdNVP vs ZDV + 3TC	No AP ARV Oral IP: sdNVP vs ZDV + 3TC	sdNVP within 48 hours of birth (mother and infant) vs ZDV + 3TC (1 week), mother and infant	• MTCT was 12.3% in sdNVP arm vs 9.3% in ZDV + 3TC arm at 8 weeks (difference not statistically significant, p=0.11).
Perinatal HIV Prevention Trial (PHPT-1) Thailand *[23]* Formula feeding	Four ZDV regimens with different durations of AP and infant PP administration, no placebo	Long (from 28 weeks), short (from 36 weeks) Oral IP	Long (6 weeks), short (3 days), infant only	• Short-short arm stopped at interim analysis (10.5%). MTCT was 6.5% in long-long arm vs 4.7% in long-short arm and 8.6% in short-long arm at 6 months (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 *[7]* Formula feeding	sdNVP vs placebo among women already receiving ZDV alone (23%) or ZDV + other ARV drugs (77% combination therapy)	Nonstudy ARV regimen Oral IP: placebo vs sdNVP + intravenous ZDV	Placebo vs sdNVP within 72 hours of birth + nonstudy ARV drugs (ZDV), infant only	• 77% of women received dual or triple combination ARV regimens during pregnancy. • Trial stopped early due to very low MTCT in both arms: 1.4% in sdNVP arm vs 1.6% in placebo arm (53% of MTCT was *in utero*).

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission

Perinatal HIV Prevention Trial (PHPT-2) Thailand *[27]* Formula feeding	ZDV alone vs ZDV + maternal and infant sdNVP vs ZDV + maternal sdNVP	ZDV from 28 weeks Oral IP: ZDV alone or ZDV + sdNVP	ZDV for 1 week with or without sdNVP, infant only	• ZDV-alone arm was stopped due to higher MTCT than the NVP–NVP arm (6.3% vs 1.1%). In arms in which the mother received sdNVP, MTCT rate did not differ significantly between the infant receiving or not receiving sdNVP (2.0% vs 2.8%).
DITRAME Plus (ANRS 1201.0) trial Abidjan, Côte d'Ivoire *[24]* Breastfeeding and formula feeding	Open label, ZDV + sdNVP	ZDV from 36 weeks Oral IP: ZDV plus sdNVP	sdNVP + ZDV for 1 week, infant only	• MTCT was 6.5% (95% CI 3.9%–9.1%) at 6 weeks; MTCT for historical control group receiving short ZDV (98% breastfed) was 12.8%.
DITRAME Plus (ANRS 1201.1) trial Abidjan, Côte d'Ivoire *[24]* Breastfeeding and formula feeding	Open label, ZDV + 3TC + sdNVP	ZDV + 3TC from 32 weeks (stopped at 3 days PP) Oral IP: ZDV + 3TC + sdNVP	sdNVP + ZDV for 1 week, infant only	• MTCT was 4.7% (95% CI 2.4%–7.0%) at 6 weeks; MTCT for historical control group receiving short ZDV (98% breastfed) was 12.8%.
NVAZ trial Malawi *[17]* Breastfeeding	Neonatal sdNVP vs sdNVP + ZDV	No AP or IP ARV (latecomers)	sdNVP with or without ZDV for 1 week, infant only	• MTCT was 15.3% in sdNVP + ZDV arm and 20.9% in sdNVP-only arm at 6 to 8 weeks. MTCT rate at 6 to 8 weeks among infants who were HIV uninfected at birth was 7.7% and 12.1%, respectively (36% efficacy).
Postnatal NVP + ZDV trial Malawi *[18]* Breastfeeding	Neonatal sdNVP vs sdNVP + ZDV	No AP ARV Oral IP: sdNVP	sdNVP with or without ZDV for 1 week, infant only	• MTCT was 16.3% in NVP + ZDV arm and 14.1% in sdNVP-only arm at 6 to 8 weeks (difference not statistically significant). MTCT rate at 6 to 8 weeks among infants who were HIV uninfected at birth was 6.5% and 16.9%, respectively.
Post-exposure Infant Prophylaxis South Africa *[19]* Breastfeeding and formula feeding	Neonatal sdNVP vs ZDV for 6 weeks	No AP or IP ARV	sdNVP vs ZDV for 6 weeks	• For formula-fed infants only, MTCT was 14.3% in sdNVP arm vs14.1% in ZDV arm at 6 weeks (not significant, p=0.30). For breastfed infants only, MTCT was 12.2% in sdNVP arm and 19.6% in ZDV arm (p=0.03).

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission

Mashi Botswana *[28, 59]* Breastfeeding and formula feeding	Initial: short-course ZDV with/without maternal and infant sdNVP and with/without breastfeeding Revised: short-course ZDV + infant sdNVP with/without maternal sdNVP and with/without breastfeeding; women with CD4 <200 receive combination therapy	1st randomization ZDV from 34 weeks Oral IP: ZDV + either sdNVP vs placebo	2nd randomization Breastfeeding + ZDV (infant) 6 months + sd NVP, infant only vs Formula feeding + ZDV (infant) 4 weeks + sdNVP, infant only	• Initial design: In formula-feeding arm, MTCT at 1 month was 2.4% in maternal and infant sdNVP arm and 8.3% in placebo arm (p=0.05). In breastfeeding + infant ZDV arm, MTCT at 1 month was 8.4% in sdNVP arm and 4.1% in placebo arm (difference not statistically significant). • Revised design: MTCT at 1 month was 4.3% in maternal + infant sdNVP arm and 3.7% in maternal placebo + infant sdNVP arm (no significant difference; no interaction with mode of infant feeding). • MTCT at 7 months was 9.1% in breastfeeding + ZDV arm and 5.6% in formula feeding arm; mortality at 7 months was 4.9% in breastfeeding + ZDV arm vs 9.3% in formula feeding arm; HIV-free survival at 18 months was 15.6% breastfeeding + ZDV arm vs 14.2% formula feeding arm.
SWEN Uganda, Ethiopia, India *[30]* Breastfeeding	sdNVP vs NVP for 6 weeks	No AP ARV Oral IP: sdNVP	Infant sdNVP vs NVP for 6 weeks	• Postnatal infection in infants uninfected at birth: - MTCT at 6 weeks was 5.3% in sdNVP arm vs 2.5% in extended NVP arm (risk ratio 0.54, p=0.009). - MTCT at 6 months was 9.0% in sdNVP arm vs 6.9% in extended NVP arm (risk ratio 0.80, p=0.16). • HIV-free survival significantly lower in extended NVP arm at both 6 weeks and 6 months

PEPI-Malawi Trial Malawi *[29]* Breastfeeding	sdNVP + ZDV for 1 week (control) vs two extended infant regimens (NVP or NVP/ZDV) for 14 weeks	No AP ARV Oral IP: sdNVP (if mother presents in time)	Infant sdNVP + ZDV for 1 week (control) vs control + NVP for 14 weeks vs control + NVP/ZDV for 14 weeks	• Postnatal infection in infants uninfected at birth: - MTCT at 6 weeks was 5.1% in control vs 1.7% in extended NVP (67% efficacy) and 1.6% in extended NVP/ZDV arms (69% efficacy). - MTCT at 9 months was 10.6% in control vs 5.2% in extended NVP (51% efficacy) and 6.4% in extended NVP/ZDV arms (40% efficacy). • No significant difference in MTCT between the extended prophylaxis arms; however, more hematologic toxicity with NVP/ZDV
MITRA Tanzania *[36]* 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	• MTCT at 6 months was 4.9% (postnatal MTCT between 6 weeks and 6 months was 1.2%).
Kisumu Breastfeeding Study (KiBS) Kenya *[31]* Breastfeeding	Maternal triple drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4 >250) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4 >250) for 6 months; infant sdNVP	• MTCT at 6 months was 5.0% (postnatal MTCT between 7 days and 6 months was 2.6%).
MITRA-PLUS Tanzania *[33]* Breastfeeding	Maternal triple drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4 >200) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4 >200) for 6 months; infant ZDV/3TC for 1 week	• MTCT at 6 months was 5.0% (postnatal MTCT between 6 weeks and 6 months was 0.9%), not significantly different from 6 months infant prophylaxis in MITRA.

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission

Kesho Bora Multi-African *[35]* Breastfeeding primarily	Antepartum ZDV/ sdNVP with no postnatal prophylaxis vs maternal triple drug prophylaxis in women with CD4 between 200 and 500	Arm 1: ZDV/3TC/LPV/r Arm 2: ZDV + sdNVP From 28 weeks through labor	Arm 1: Maternal ZDV/3TC/LPV/r for 6 months; infant sdNVP + ZDV for 1 week Arm 2: Maternal ZDV/3TC for 1 week (no further postnatal prophylaxis); infant sdNVP + ZDV for 1 week (no further postnatal prophylaxis)	• MTCT at birth was 1.8% with maternal triple drug prophylaxis Arm 1 and 2.2% with ZDV/sdNVP Arm 2, not significantly different. • MTCT at 12 months was 5.5% with maternal triple drug prophylaxis Arm 1 and 9.5% with ZDV/sdNVP (with no further postnatal prophylaxis after 1 week) Arm 2 (p=0.04).
Mma Bana Botswana *[34]* Breastfeeding	Maternal triple drug prophylaxis (compares 2 regimens) in women with CD4 >200	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 sdNVP + ZDV for 4 weeks Arm 2: Maternal ZDV/3TC/LPV/r for 6 months; infant sdNVP + ZDV for 4 weeks	• MTCT at 6 months overall was 1.3%: 2.1% in ZDV/3TC/ABC Arm 1 and 0.4% in ZDV/3TC/LPV/r Arm 2 (p=0.53).
BAN Malawi *[32]* Breastfeeding	Postpartum maternal triple drug prophylaxis vs infant NVP in women with CD4 ≥250	No AP drugs IP regimens: Arm 1 (control): ZDV/3TC + sdNVP Arm 2: ZDV/3TC + sdNVP Arm 3: ZDV/3TC + sdNVP	Arm 1 (control): Maternal ZDV/3TC for 1 week; infant sdNVP + 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 uninfected at 2 weeks: - MTCT at 28 weeks was 5.7% in control Arm 1; 2.9% in maternal triple drug prophylaxis Arm 2 (p=0.009 vs control); 1.7% in infant NVP Arm 3 (<0.001 vs control). • No significant difference between maternal triple drug prophylaxis Arm 2 and infant NVP Arm 3 (p=0.12).

Key to Abbreviations: 3TC: lamivudine; ABC: abacavir; AP: antepartum; ARV: antiretroviral; CDC: Centers for Disease Control and Prevention; IP: intrapartum; LPV/r: lopinavir/ritonavir; MTCT: mother-to-child transmission; NFV: nelfinavir; NVP: nevirapine; PP: postpartum; sd: single-dose; ZDV: zidovudine

Table 4. Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy (See *Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy* for more detail on drugs.)

Antiretroviral Generic name (Abbreviation)/ Trade name	FDA Pregnancy Category *	Placental Passage Newborn: Mother Drug Ratio	Long-term Animal Carcinogenicity Studies	Animal Teratogenicity Studies
Nucleoside and nucleotide analogue reverse transcriptase inhibitors				
Abacavir (ABC)/ Ziagen	C	Yes (rats)	Positive (malignant and non-malignant tumors of liver and thyroid in female rats and preputial and clitoral glands in mice and rats at 6–32x human exposure)	Positive (rodent anasarca and skeletal malformations at 1,000 mg/kg [35x human exposure] during organogenesis; not seen at 8.5x human exposure in rabbits)
Didanosine (ddI)/ Videx	B	Yes (humans) 0.5	Negative (no tumors in lifetime rodent study at 0.7–3x maximum human exposure)	Negative (at 12x and 14.2x human exposure in rabbits and rats, respectively)
Emtricitabine (FTC)/ Emtriva	B	Yes (mice and rabbits) 0.4–0.5	Negative (no tumors in lifetime rodent study at 26–31x human exposure)	Negative (at 60x, 60x, and 120x human exposure in rats, mice, and rabbits, respectively)
Lamivudine (3TC)/ Epivir	C	Yes (humans) ~1.0	Negative (no tumors in lifetime rodent study at 10–58x human exposure)	Negative (at 35x human exposure in rats and rabbits; however, embryolethality seen in rabbits at 1x human exposure)
Stavudine (d4T)/ Zerit	C	Yes (rhesus monkeys) 0.76	Positive (in mice and rats at very high dose exposure; liver and bladder tumors [rats only] at 250x and 732x human exposure in mice and rats, respectively)	Negative (at 399x [rats] and 183x [rabbits] human exposure, although sternal bone ossification decreased and rat neonatal mortality increased at 399x human exposure in rats)
Tenofovir DF (TDF)/ Viread	B	Yes (humans) 0.95–0.99	Positive (hepatic adenomas in female mice only at 16x human exposure)	Negative (at 14x and 19x human exposure in rats and rabbits, respectively)
Zidovudine (AZT, ZDV)/ Retrovir	C	Yes (humans) 0.85	Positive (nonmetastasizing vaginal epithelial tumors at 3x and 24x human exposure in mice and rats, respectively)	Positive (increased fetal malformations associated with maternal toxicity at 300x human exposure in rats. Increased fetal resorptions at 66–226x and 12–87x human exposure in rats and rabbits, respectively, with no developmental abnormalities)
Non-nucleoside reverse transcriptase inhibitors				
Efavirenz (EFV)/ Sustiva	D	Yes (cynomolgus monkeys, rats, rabbits) ~1.0	Positive (hepatocellular adenomas and carcinomas and pulmonary alveolar/bronchiolar adenomas in female mice at 1.7x human exposure; no increases in tumors in rats at 0.2x human exposure)	Positive (anencephaly, anophthalmia, microophthalmia, and cleft palate in cynomolgus monkey at exposures comparable to human exposure; no reproductive toxicities in pregnant rabbits at 0.5–1x human exposure)

Table 4. Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy

Antiretroviral Generic name (Abbreviation)/ Trade name	FDA Pregnancy Category *	Placental Passage Newborn: Mother Drug Ratio	Long-term Animal Carcinogenicity Studies	Animal Teratogenicity Studies
Non-nucleoside reverse transcriptase inhibitors (cont)				
Etravirine (ETR)/ Intelence	B	Unknown	Positive (hepatocellular adenomas and carcinomas in female mice at 0.6x human exposure; no findings in rats at 0.2–0.7x human exposure)	Negative (in rats and rabbits at exposures comparable to human exposures)
Nevirapine (NVP)/ Viramune	B	Yes (humans) ~1.0	Positive (hepatocellular adenomas and carcinomas in mice and rats at less than human exposure)	Negative (in rats and rabbits at 1–1.5x human exposure; however, decreased fetal body weight in rats at 1.5x human exposure)
Protease inhibitors				
Atazanavir (ATV)/ Reyataz	B	Minimal/variable (humans)	Positive (benign hepatocellular adenomas in female mice at 7.2x human exposure)	Negative (at 2x and 1x human exposure in rats and rabbits, respectively)
Darunavir (DRV)/ Prezista	C	Unknown	Positive (hepatic adenomas, carcinomas [male mice], thyroid neoplasms [rats only] at 0.1–0.3x and 0.7–1x human exposure in mice and rats, respectively)	Negative (at 0.5x and 0.05x human exposure in rats/mice and rabbits, respectively)
Fosamprenavir (f-APV)/ Lexiva)	C	Unknown	Positive (hepatic adenomas and carcinomas [mice and rats]; thyroid adenomas, interstitial cell hyperplasia, and uterine endometrial adenocarcinoma [rats only] at 0.1–0.7x and 0.3–1.4x human exposure in mice and rats, respectively	Negative (at 0.8x and 2x human exposure in rabbits and rats respectively; increased incidence of abortions in rabbits at 0.8x human exposure)
Indinavir (IDV)/ Crixivan	C	Minimal (humans)	Positive (thyroid adenomas in male rats at 1.3x human exposure)	Negative (however supernumerary ribs in rats at exposures less than or slightly greater than human exposure)
Lopinavir + Ritonavir (LPV/r)/ Kaletra)	C	Yes (humans) 0.20±0.13	Positive (hepatic adenomas and carcinomas at 1.6–2.2x and 0.5x human exposure in mice and rats, respectively)	Positive (no effects in rabbits and dogs at ~1x human exposure; decreased fetal viability and body weight, delayed skeletal ossification and increase in skeletal variations in rats at maternally toxic doses [at 0.7x and 1.8x human exposure for lopinavir and ritonavir, respectively])
Nelfinavir (NFV)/ Viracept	B	Minimal/variable (humans)	Positive (thyroid follicular adenomas and carcinomas at 1–3x human exposure in rats)	Negative (in rats at human exposure and in rabbits at significantly lower than human exposure)

Table 4. Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy

Antiretroviral Generic name (Abbreviation)/ Trade name	FDA Pregnancy Category *	Placental passage Newborn: Mother Drug Ratio	Long-term Animal Carcinogenicity Studies	Animal Teratogenicity Studies
Protease inhibitors (cont)				
Ritonavir (RTV)/ Norvir	B	Minimal (humans)	Positive (hepatic adenomas and carcinomas in male mice at 0.3x human exposure)	Positive (early resorptions, decreased fetal body weight, ossification delays, and developmental variations in rats at maternally toxic dose [~0.3x human exposure]; cryptorchidism in rats at 0.22x human exposure)
Saquinavir (SQV) Invirase	B	Minimal (humans)	Negative (at 0.29x and 0.65x human exposure [coadministration with ritonavir] in rats and mice, respectively)	Negative (at 0.29x and 0.21x human exposure [coadministration with ritonavir] in rats and rabbits, respectively)
Tipranavir (TPV)/ Aptivus	C	Unknown	Positive (hepatic adenomas and carcinomas in mice at less than human exposure; thyroid follicular cell adenoma in female rats at exposures comparable to human exposure)	Negative (decreased ossification and pup weights in rats at 0.8x human exposure)
Entry inhibitors				
Enfuvirtide (T-20)/ Fuzeon	B	None (based on very limited human data)	Not conducted	Negative
Maraviroc (MVC)/ Selzentry	B	Unknown	Negative (in transgenic mice and rats at 11x human exposure)	Negative (at 20x and 5x human exposure in rats and rabbits, respectively)
Integrase inhibitors				
Raltegravir (RAL)/ Isentress	C	Yes (rats, rabbits) † Rats: 1.5–2.5 Rabbits: 0.02	In progress	Negative (however, supernumerary ribs in rats at 3x human exposure)

* Food and Drug Administration Pregnancy Categories:
A - Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and no evidence exists of risk during later trimesters).
B - Animal reproduction studies fail to demonstrate a risk to the fetus, and adequate but well-controlled studies of pregnant women have not been conducted.
C - Safety in human pregnancy has not been determined; animal studies are either positive for fetal risk or have not been conducted, and the drug should not be used unless the potential benefit outweighs the potential risk to the fetus.
D - Positive evidence of human fetal risk that is based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of the drug among pregnant women might be acceptable despite its potential risks.
X - Studies among animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit.

† Values obtained from fetal (not newborn) blood samples. See text under "Placental and breast milk passage" in section on Raltegravir (Isentress) in ***Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy***.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy

(See also "Supplement: Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy" for additional toxicity data and "Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents" for detailed guidelines regarding treatment options.)

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
NRTIs/ NtRTIs		See text for discussion of potential maternal and infant mitochondrial toxicity.	NRTIs are recommended for use as part of combination regimens, usually including two NRTIs with either an NNRTI or one or more PIs. Use of single or dual NRTIs alone is not recommended for treatment of HIV infection. (Zidovudine alone may be considered for prophylaxis of perinatal transmission in pregnant women with HIV RNA <1,000 copies/mL.)
Recommended Agents			
Lamivudine*	Pharmacokinetics not significantly altered in pregnancy; no change in dose indicated *[1]*.	No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects) *[2]*. Well-tolerated, short-term safety demonstrated for mother and infant. If hepatitis B coinfected, possible hepatitis B flare if drug stopped postpartum (see **Special Considerations: Hepatitis B Virus Coinfection**).	Because of extensive experience with lamivudine in pregnancy in combination with zidovudine, lamivudine plus zidovudine is the recommended dual NRTI backbone for pregnant women.
Zidovudine*	Pharmacokinetics not significantly altered in pregnancy; no change in dose indicated *[3]*.	No evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects) *[2]*. Well-tolerated, short-term safety demonstrated for mother and infant.	Preferred NRTI for use in combination antiretroviral regimens in pregnancy based on efficacy studies and extensive experience. Zidovudine should be included in the antenatal antiretroviral regimen unless there is severe toxicity, stavudine use, documented resistance, or the woman is already on a fully suppressive regimen.
Alternate Agents			
Abacavir*	Pharmacokinetics not significantly altered in pregnancy; no change in dose indicated.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Hypersensitivity reactions occur in ~5%–8% of nonpregnant persons; fatal reactions occur in a much smaller percentage of persons and are usually associated with rechallenge. Rate of hypersensitivity reactions in pregnancy is unknown. Testing for HLA-B*5701 identifies patients at risk of reactions *[4-5]* and should be done and documented as negative before starting abacavir. Patient should be educated regarding symptoms of hypersensitivity reaction.	Alternate NRTI for dual nucleoside backbone of combination regimens. See footnote regarding use in triple NRTI regimen. #
Didanosine	Pharmacokinetics not significantly altered in pregnancy; no change in dose indicated *[6]*.	Cases of lactic acidosis, some fatal, have been reported in pregnant women receiving didanosine and stavudine together *[7-8]*.	Alternate NRTI for dual nucleoside backbone of combination regimens. Didanosine should be used with stavudine only if no other alternatives are available.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Alternate Agents (continued)			
Emtricitabine†	Pharmacokinetic study shows slightly lower levels in third trimester compared to postpartum *[9]*. No clear need to increase dose.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*.	Alternate NRTI for dual nucleoside backbone of combination regimens.
Stavudine	Pharmacokinetics not significantly altered in pregnancy; no change in dose indicated *[10]*.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Cases of lactic acidosis, some fatal, have been reported in pregnant women receiving didanosine and stavudine together *[7-8]*.	Alternate NRTI for dual nucleoside backbone of combination regimens. Stavudine should be used with didanosine only if no other alternatives are available. Do not use with zidovudine due to potential for antagonism.
Use in Special Circumstances			
Tenofovir†	Limited studies in human pregnancy; data indicate AUC lower in third trimester than postpartum but trough levels similar.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Studies in monkeys at doses approximately 2-fold higher than dosage for human therapeutic use show decreased fetal growth and reduction in fetal bone porosity within 2 months of starting maternal therapy *[11]*. Clinical studies in humans (particularly children) show bone demineralization with chronic use; clinical significance unknown *[12-13]*. Significant placental passage in humans (cord:maternal blood ratio 0.6–0.99). If hepatitis B coinfected, possible hepatitis B flare if drug stopped postpartum (see **Special Considerations: Hepatitis B Virus Coinfection**).	Because of limited data on use in human pregnancy and concern regarding potential fetal bone effects, tenofovir should be used as a component of a maternal combination regimen only after careful consideration of other alternatives. Because of potential for renal toxicity, renal function should be monitored.
NNRTIs		Hypersensitivity reactions, including hepatic toxicity, and rash more common in women; unclear if increased in pregnancy.	NNRTIs are recommended for use in combination regimens with 2 NRTI drugs.
Recommended Agents			
Nevirapine	Pharmacokinetics not significantly altered in pregnancy; no change in dose indicated *[14-15]*.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Increased risk of symptomatic, often rash-associated, and potentially fatal liver toxicity among women with CD4 counts >250/mm^3 when first initiating therapy *[16-17]*; unclear if pregnancy increases risk.	Nevirapine should be initiated in pregnant women with CD4 counts >250 cells/mm^3 only if benefit clearly outweighs risk, due to the increased risk of potentially life-threatening hepatotoxicity in women with high CD4 counts. Women who enter pregnancy on nevirapine regimens and are tolerating them well may continue therapy, regardless of CD4 count.

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Use in Special Circumstances			
Efavirenz†	Small study in 13 breastfeeding women in Rwanda of 600 mg once daily; postpartum peak levels during lactation were 61% higher than previously reported in HIV-infected nonpregnant individuals at that dose *[18]*.	FDA Pregnancy Class D; significant malformations (anencephaly, anophthalmia, cleft palate) were observed in 3 (15%) of 20 infants born to cynomolgus monkeys receiving efavirenz during the first trimester at a dose giving plasma levels comparable to systemic human therapeutic exposure. There are 6 retrospective case reports and 1 prospective case report of neural tube defects in humans with first-trimester exposure *[2, 19-20]*; relative risk unclear.	Use of efavirenz should be avoided in the first trimester. Use after the first trimester can be considered if, after consideration of other alternatives, this is the best choice for a specific woman. If efavirenz is to be continued postpartum, adequate contraception must be assured. Women of childbearing potential must be counseled regarding the teratogenic potential of efavirenz and avoidance of pregnancy while on the drug. Because of the known failure rates even with contraception, alternate antiretroviral regimens should be strongly considered in women of childbearing potential.
Insufficient Data to Recommend Use			
Etravirine	No pharmacokinetic studies in human pregnancy.	No experience in human pregnancy.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy.
Protease Inhibitors (PIs)		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 text).	PIs are recommended for use in combination regimens with 2 NRTI drugs.
Recommended Agents			
Lopinavir/ ritonavir	Pharmacokinetic studies of the new lopinavir/ ritonavir tablet formulation are under way, but data are not yet available.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Well-tolerated, short-term safety demonstrated in Phase I/II studies.	Pharmacokinetic studies of the new tablet formulation are under way but are not yet conclusive as to the optimal dose in pregnancy. Some experts would administer standard dosing (2 tablets twice daily) throughout pregnancy and monitor virologic response and lopinavir drug levels, if available. Other experts, extrapolating from the capsule formulation pharmacokinetic data, would increase the dose of the tablet formulation during the third trimester (from 2 tablets to 3 tablets twice daily), returning to standard dosing postpartum. Once-daily lopinavir/ritonavir dosing is not recommended during pregnancy because there are no data to address whether drug levels are adequate with such administration.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Alternate Agents			
Atazanavir (recommended to be combined with low-dose ritonavir boosting)	Two of three intensive pharmacokinetic studies of atazanavir with ritonavir boosting during pregnancy suggest that standard dosing results in decreased plasma concentrations compared to nonpregnant adults *[21-23]*. Atazanavir concentrations further reduced ~25% with concomitant tenofovir use *[23]*.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Transplacental passage is low, with cord blood concentration averaging 10%–16% of the maternal delivery atazanavir concentration *[21, 23]*. Theoretical concern re: increased indirect bilirubin levels exacerbating physiologic hyperbilirubinemia in the neonate not observed in clinical trials to date *[21-24]*.	Alternative PI for use in combination regimens in pregnancy. Should give as low-dose ritonavir-boosted regimen, may use once-daily dosing. In treatment-naïve patients unable to tolerate ritonavir, 400 mg once-daily dosing without ritonavir boosting may be considered, although there are no data describing atazanavir concentrations or efficacy under these circumstances. If coadministered with tenofovir, atazanavir must be given with low-dose ritonavir boosting.
Indinavir (combined with low-dose ritonavir boosting)	Two studies including 18 women receiving indinavir 800 mg three times daily showed markedly lower levels during pregnancy compared to postpartum, although suppression of HIV RNA was seen *[25-26]*. In a study of ritonavir-boosted indinavir (400 mg indinavir/100 mg ritonavir twice daily), 82% of women met the target trough level *[27]*.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Theoretical concern re: increased indirect bilirubin levels, which may exacerbate physiologic hyperbilirubinemia in the neonate, but minimal placental passage. Use of unboosted indinavir during pregnancy is not recommended.	Alternate PI for use in combination regimens in pregnancy. Must give as low-dose ritonavir-boosted regimen.
Nelfinavir	Adequate drug levels are achieved in pregnant women with nelfinavir 1,250 mg given twice daily, although levels are variable in late pregnancy *[28-30]*. In a study of pregnant women in their second and third trimester dosed at 1,250 mg given twice daily, women in the third trimester had lower concentration of nelfinavir than women in the second trimester *[30]*. In a study of the new 625-mg tablet formulation dosed at 1,250 mg twice daily, lower AUC and peak levels were observed during the third trimester of pregnancy than postpartum *[31]*.	No evidence of human teratogenicity (can rule out 2-fold increase in overall birth defects) *[2]*. Well-tolerated, short-term safety demonstrated for mother and infant.	Given pharmacokinetic data and extensive experience with use in pregnancy, nelfinavir is an alternative PI for combination regimens in pregnant women receiving combination antiretroviral drugs only for perinatal prophylaxis. In clinical trials of initial therapy in nonpregnant adults, nelfinavir-based regimens had a lower rate of viral response compared to lopinavir-ritonavir or efavirenz-based regimens but similar viral response to atazanavir- or nevirapine-based regimens.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Alternate Agents (continued)			
Ritonavir	Phase I/II study in pregnancy showed lower levels during pregnancy compared to postpartum *[2, 32]*.	Limited experience at full dose in human pregnancy; has been used as low-dose ritonavir boosting with other PIs.	Given low levels in pregnant women when used alone, recommended for use in combination with second PI as low-dose ritonavir "boost" to increase levels of second PI.
Saquinavir HGC (combined with low-dose ritonavir boosting)	Limited pharmacokinetic data on saquinavir HGC and the new 500-mg tablet formulation suggest that 1,000 mg saquinavir HGC/100 mg ritonavir given twice daily achieves adequate saquinavir drug levels in pregnant women *[33]*.	Well-tolerated, short-term safety demonstrated for mother and infant for saquinavir in combination with low-dose ritonavir.	There are only limited pharmacokinetic data on saquinavir HGC and the new tablet formulation in pregnancy. Ritonavir-boosted saquinavir HGC or saquinavir tablets are alternative PIs for combination regimens in pregnancy and are alternative initial antiretroviral recommendations for nonpregnant adults. Must give as low-dose ritonavir-boosted regimen.
Insufficient Data to Recommend Use			
Darunavir (combined with low-dose ritonavir boosting)	No pharmacokinetic studies in human pregnancy.	No experience in human pregnancy.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy. Must give as low-dose ritonavir-boosted regimen.
Fosamprenavir (recommended to be combined with low-dose ritonavir boosting)	No pharmacokinetic studies in human pregnancy.	Limited experience in human pregnancy.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy. Recommended to be given as low-dose ritonavir-boosted regimen.
Tipranavir (combined with low-dose ritonavir boosting)	No pharmacokinetic studies in human pregnancy.	No experience in human pregnancy.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy. Must give as low-dose ritonavir-boosted regimen.
Entry Inhibitors			
Insufficient Data to Recommend Use			
Enfuvirtide	No pharmacokinetic studies in human pregnancy.	Minimal data in human pregnancy *[34]*.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy.
Maraviroc	No pharmacokinetic studies in human pregnancy.	No experience in human pregnancy.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy.

Table 5. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Integrase Inhibitors			
Insufficient Data to Recommend Use			
Raltegravir	No pharmacokinetic studies in human pregnancy.	No experience in human pregnancy.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy.

Abbreviations: AUC: area under the curve; HGC: hard gel capsule; NRTI: nucleoside reverse transcriptase inhibitor; NtRTI: nucleotide reverse transcriptase inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; PI: protease inhibitor.

* Zidovudine and lamivudine are included as a fixed-dose combination in Combivir; zidovudine, lamivudine, and abacavir are included as a fixed-dose combination in Trizivir; lamivudine and abacavir are included as a fixed-dose combination in Epzicom.

† Emtricitabine and tenofovir are included as a fixed-dose combination in Truvada; emtricitabine, tenofovir, and efavirenz are included as a fixed-dose combination in Atripla.

\# Triple NRTI regimens including abacavir have been less potent virologically compared to PI-based combination antiretroviral drug regimens. Triple NRTI regimens should be used only when an NNRTI- or PI-based combination regimen cannot be used (e.g., due to significant drug interactions).

Table 6. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal Transmission of HIV-1 in the United States

Clinical Scenario	Recommendations
Nonpregnant HIV-infected woman of childbearing potential who has indications for initiating antiretroviral therapy	• Initiate combination antiretroviral drug therapy as per adult treatment guidelines. • Avoid drugs with teratogenic potential (e.g., efavirenz) if the woman is trying to conceive or is not using adequate contraception. Exclude pregnancy before starting treatment with efavirenz.
HIV-infected woman on combination antiretroviral drug therapy who becomes pregnant	**Woman:** • In general, if woman requires treatment, antiretroviral drugs should not be stopped during the first trimester or during pregnancy. • Continue current combination antiretroviral therapy regimen if successfully suppressing viremia; however, avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (e.g., combination stavudine/didanosine) throughout the pregnancy. • Perform HIV antiretroviral drug resistance testing if the woman has detectable viremia on therapy. • Continue combination antiretroviral therapy regimen during intrapartum period (zidovudine given as continuous infusion[1] during labor while other antiretroviral agents are continued orally) and postpartum. • Schedule cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant:** • Start zidovudine as soon as possible after birth and administer for 6 weeks.[2]
HIV-infected pregnant woman who is antiretroviral naïve and has indications for antiretroviral therapy	**Woman:** • Perform HIV antiretroviral drug resistance testing prior to initiating combination antiretroviral drug therapy and repeat after initiating therapy if viral suppression is suboptimal. • Initiate combination antiretroviral regimen. - Avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (e.g., combination stavudine/didanosine). - Use zidovudine as a component of the antiretroviral regimen when feasible. - Use nevirapine as a component of the antiretroviral regimen only if the woman has CD4 count ≤250 cells/mm^3. If the woman has CD4 count >250 cells/mm^3, use nevirapine as a component of therapy only if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • If woman requires immediate initiation of therapy for her own health, initiate treatment as soon as possible, including in the first trimester. • Continue combination antiretroviral therapy regimen during intrapartum period (zidovudine given as continuous infusion[1] during labor while other antiretroviral agents are continued orally) and postpartum. • Schedule cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant:** • Start zidovudine as soon as possible after birth and administer for 6 weeks.[2]

Table 6. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal Transmission of HIV-1 in the United States

Clinical Scenario	Recommendations
HIV-infected pregnant woman who is antiretroviral naïve and does not require treatment for her own health	**Woman:** • Perform HIV antiretroviral drug resistance testing prior to initiating combination antiretroviral drug therapy and repeat after initiation of therapy if viral suppression is suboptimal. • Prescribe a combination antiretroviral drug prophylaxis regimen (i.e., at least 3 drugs) for prophylaxis of perinatal transmission. - Consider delaying initiation of antiretroviral prophylaxis until after first trimester is completed. - Avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (e.g., combination stavudine/didanosine). - Use zidovudine as a component of the antiretroviral regimen when feasible. - If the woman has CD4 count >250 cells/mm^3 use nevirapine as a component of therapy only if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • Although use of zidovudine prophylaxis alone is controversial, consider if woman has plasma HIV RNA level <1,000 copies/mL on no therapy. • Continue antiretroviral prophylaxis regimen during intrapartum period (zidovudine given as continuous infusion[1] during labor while other antiretroviral agents are continued orally). • Evaluate need for continuing the combination regimen postpartum; discontinue the combination regimen unless the woman has indications for continued therapy. If regimen includes drug with long half-life like NNRTI, consider stopping NRTIs at least 7 days after stopping NNRTI. (Only limited data exist on this; see **Stopping Antiretroviral Therapy** and **Prevention of Antiretroviral Drug Resistance**.) • Schedule cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant**: • Start zidovudine as soon as possible after birth and administer for 6 weeks.[2]
HIV-infected pregnant woman who is antiretroviral experienced but not currently receiving antiretroviral drugs	**Woman:** • Obtain full antiretroviral treatment history, including prior resistance testing, and evaluate need for antiretroviral treatment for maternal health. • Perform HIV antiretroviral drug resistance testing prior to initiating repeat antiretroviral prophylaxis or therapy and repeat after initiating combination antiretroviral regimen if suboptimal viral suppression. • Initiate a combination antiretroviral regimen (e.g., at least 3 drugs), with regimen chosen based on resistance testing and prior therapy history. - Avoid use of efavirenz or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for the mother (e.g., combination stavudine/didanosine). - Use zidovudine as a component of the antiretroviral regimen when feasible. - If woman has CD4 count >250 cells/mm^3, use nevirapine as a component of therapy only if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • Continue the combination regimen during intrapartum period (zidovudine given as continuous infusion[1] during labor while other antiretroviral agents are continued orally). • Evaluate need for continuing the combination regimen postpartum; discontinue the combination regimen unless the woman has indications for continued therapy. If regimen includes drug with long half-life like NNRTI, consider stopping NRTIs at least 7 days after stopping NNRTI. (Limited data exist on this; see **Stopping Antiretroviral Therapy** and **Prevention of Antiretroviral Drug Resistance**.)

Table 6. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal Transmission of HIV-1 in the United States

Clinical Scenario	Recommendations
	• Schedule cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant**: • Start zidovudine as soon as possible after birth and administer for 6 weeks.[2]
HIV-infected woman who has received no antiretroviral therapy prior to labor	Zidovudine **Woman:** Give zidovudine as continuous infusion[1] during labor. **Infant:** Start zidovudine as soon as possible after birth and administer for 6 weeks.[2] ***OR*** Combination Zidovudine + Single-dose Nevirapine **Woman:** Give zidovudine as continuous infusion[1] during labor, plus single-dose nevirapine [3] at onset of labor. Consider adding lamivudine during labor and maternal zidovudine/lamivudine for at least 7 days postpartum, which may reduce development of nevirapine resistance. **Infant:** Give single-dose nevirapine[3] plus zidovudine for 6 weeks. ***OR*** **Woman:** Give zidovudine as continuous infusion[1] during labor. **Infant:** Although some clinicians may choose to use zidovudine in combination with additional drugs in the infant, appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consider consultation with a pediatric HIV specialist. • Evaluate need for initiation of maternal therapy postpartum.
Infant born to HIV-infected woman who has received no antiretroviral therapy prior to or during labor	• Start zidovudine as soon as possible after birth and administer for 6 weeks.[2] ***OR*** • Although some clinicians may choose to use zidovudine in combination with additional drugs, appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consider consultation with a pediatric HIV specialist. • Evaluate need for initiation of maternal therapy postpartum.

[1] Zidovudine continuous infusion: 2 mg/kg zidovudine intravenously over 1 hour, followed by continuous infusion of 1 mg/kg/hour until delivery.

[2] Zidovudine dosing for infants <35 weeks gestation at birth is 1.5 mg/kg/dose intravenously or 2.0 mg/kg/dose orally, every 12 hours, advancing to every 8 hours at 2 weeks of age if ≥30 weeks gestation at birth or at 4 weeks of age if <30 weeks gestation at birth.

[3] Single-dose nevirapine: Mother: 200 mg given once orally at onset of labor; Infant: 2 mg/kg body weight given once orally at 2–3 days of age if mother received intrapartum single-dose nevirapine or given at birth if mother did not receive intrapartum single-dose nevirapine.

Table 7. Intrapartum Maternal and Neonatal Zidovudine (ZDV) Dosing for Prevention of Mother-to-Child Transmission of HIV

Maternal Intrapartum		
Drug	**Dosing**	**Duration**
ZDV	2 mg per kg body weight intravenously over 1 hour, followed by continuous infusion of 1 mg per kg body weight per hour	Onset of labor until delivery of infant
Neonatal		
Drug	**Dosing**	**Duration**
ZDV	≥35 weeks gestation: 2 mg per kg body weight per dose given orally [1, 2] (or 1.5 mg per kg body weight per dose given intravenously) started within 6–12 hours of delivery, then every 6 hours	Birth to 6 weeks
ZDV	<35 to >30 weeks gestation: 2 mg per kg body weight per dose given orally (or 1.5 mg per kg body weight per dose given intravenously) started within 6–12 hours of delivery, then every 12 hours, advanced to every 8 hours at 2 weeks of age	Birth to 6 weeks
ZDV	≤30 weeks gestation: 2 mg per kg body weight per dose given orally (or 1.5 mg/kg/dose given intravenously) started within 6–12 hours of delivery, then every 12 hours, advanced to every 8 hours at 4 weeks of age	Birth to 6 weeks

[1] Zidovudine dosing of 4 mg per kg body weight per dose given every 12 hours has been used for infant prophylaxis in some international perinatal studies. Although there are no definitive data to show equivalent pharmacokinetic parameters or efficacy in preventing transmission, a regimen of zidovudine 4 mg per kg body weight per dose given orally twice daily instead of 2 mg per kg body weight per dose given orally 4 times daily may be considered when there are concerns about adherence to drug administration to the infant.

[2] A simplified zidovudine dosing regimen has been developed for use in low resource settings. This regimen consists of 10 mg orally twice daily for infants weighing less than 2.5 kg at birth and 15 mg twice daily for infants weighing more than 2.5 kg at birth. See discussion in **Neonatal Postnatal Care: Infant Antiretroviral Prophylaxis**. This regimen could be considered for infants in higher resource settings born after 35 weeks gestation if simplicity in zidovudine dosing and administration is of prime importance.

Table 8. Intrapartum Maternal and Neonatal Dosing for Additional Antiretroviral Drugs to be Considered Only in Selected Circumstances

(See Special Considerations Regarding the Use of Antiretroviral Drugs by HIV-Infected Pregnant Women and their Infants and Antiretroviral Drug Resistance and Resistance Testing in Pregnancy for further discussion.)

Maternal Intrapartum/Postpartum		
Drug	**Dosing**	**Duration**
NVP (as single dose intrapartum)[1]	200 mg given orally as single dose	Single dose at onset of labor
ZDV + 3TC (given with single dose NVP as "tail" to reduce NVP resistance)	ZDV: intravenously intrapartum as per Table 7, then after delivery 300 mg orally twice daily 3TC: 150 mg orally twice daily starting at onset of labor	Through 1 week postpartum
Neonatal		
Drug	**Dosing**	**Duration**
NVP (as single dose)[2]	2 mg per kg body weight given orally as single dose	Single dose between birth and 72 hours of age. If maternal dose is given ≤ 2 hours before delivery or not received, infant dose should be administered as soon as possible following birth.[3]
ZDV + 3TC (given with single dose NVP as "tail" to reduce NVP resistance)	ZDV: neonatal dosing as per Table 5 3TC: 2 mg per kg body weight given orally twice daily	ZDV: Birth to 6 weeks 3TC: Birth to 1 week

Key to Abbreviations: NVP = nevirapine, ZDV = zidovudine, 3TC = lamivudine

[1] Given *in addition* to intravenous intrapartum ZDV; if intrapartum single-dose NVP is given to mother, administration of intrapartum oral 3TC followed by administration of ZDV and 3TC for at least 7 days postpartum to reduce development of NVP-resistant virus is recommended.

[2] Given *in addition* to 6 weeks of infant ZDV; addition of at least 7 days of 3TC may be considered to reduce development of NVP-resistant virus.

[3] Some experts recommend a second NVP dose at 48–72 hours of life to babies born in this circumstance.

Table 9. Clinical Scenarios and Recommendations Regarding Mode of Delivery to Reduce Perinatal Transmission of HIV

Clinical Scenario	Recommendations
HIV-infected woman presenting in late pregnancy (after about 36 weeks gestation), known to be HIV-infected but not receiving antiretroviral therapy, and who has HIV RNA level and CD4 count pending but unlikely to be available before delivery.	• The woman should be started on antiretroviral therapy as per **Table 6**. • The woman should be counseled that scheduled cesarean delivery is likely to reduce the risk of transmission to her infant. She should also be informed of the increased risks to her of cesarean delivery, including increased rates of postoperative infection, anesthesia risks, and other surgical risks. • If cesarean delivery is chosen, the procedure should be scheduled at 38 weeks gestation based on the best available clinical information. • When scheduled cesarean delivery is performed, the woman should receive continuous intravenous zidovudine infusion beginning 3 hours before surgery. • Use of prophylactic antibiotics at the time of cesarean delivery is generally recommended. • Options for continuing or initiating combination antiretroviral therapy after delivery should be discussed with the woman as soon as her viral load and CD4 count results are available. • The infant should receive 6 weeks of zidovudine after birth (see **Table 6**).
HIV-infected woman who initiated prenatal care early in the third trimester, is receiving a combination antiretroviral regimen, and has an initial virologic response but has HIV RNA levels that remain substantially greater than 1,000 copies/mL at 36 weeks gestation.	• The current combination antiretroviral regimen should be continued because the HIV RNA level is dropping appropriately. • The woman should be counseled that although she is responding to the antiretroviral therapy, it is unlikely that her HIV RNA level will fall below 1,000 copies/mL before delivery. Therefore, scheduled cesarean delivery may provide additional benefit in preventing intrapartum transmission of HIV. She should also be informed of the increased risks to her of cesarean delivery, including risks related to anesthesia and surgery and increased rates of postoperative infection. • If the woman chooses scheduled cesarean delivery, the procedure should be performed at 38 weeks gestation as determined by last menstrual period and ultrasonography. Intravenous zidovudine should be started at least 3 hours before surgery. • Other antiretroviral medications should be continued on schedule as much as possible before and after surgery. • Use of prophylactic antibiotics at the time of cesarean delivery is generally recommended. • The importance of adhering to therapy after delivery for the woman's health should be emphasized. • The infant should receive 6 weeks of zidovudine after birth (see **Table 6**).
HIV-infected woman on a combination antiretroviral regimen with an undetectable HIV RNA level at 36 weeks gestation.	• The woman should be counseled that her risk of perinatal transmission of HIV with a persistently undetectable HIV RNA level is low, probably 1% or less, even with vaginal delivery. There is currently no evidence that performing a scheduled cesarean delivery will lower her risk further. • Cesarean delivery has an increased risk of complications for the woman compared to vaginal delivery, and these risks must be balanced against the uncertain benefit of cesarean delivery in this case. • The infant should receive 6 weeks of zidovudine after birth (see **Table 6**).

Table 9. Clinical Scenarios and Recommendations Regarding Mode of Delivery to Reduce Perinatal Transmission of HIV

Clinical Scenario	Recommendations
HIV-infected woman who has elected scheduled cesarean delivery but presents after rupture of membranes at >37 weeks gestation.	• Intravenous zidovudine should be started immediately. • Decision regarding mode of delivery should be individualized and based on clinical factors such as duration of rupture, anticipated progress of labor, plasma RNA level, and current antiretroviral therapy. • If the decision is made to proceed with vaginal delivery, some clinicians may consider administration of oxytocin, if clinically appropriate, in order to expedite delivery. Scalp electrodes and other invasive monitoring and operative delivery should be avoided if possible. • If the decision is made to proceed with cesarean delivery, administration of the loading dose of intravenous zidovudine should be completed prior to cesarean delivery. • The infant should receive 6 weeks of zidovudine after birth (see **Table 6**).