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

Tables

April 29, 2009 Release

The in-text and appendix tables from the April 29, 2009, release of the Public Health Service Task Force ***Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States*** 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. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission

Study/Location/Mode Infant Feeding	Drugs	Antenatal and Intrapartum	Postpartum	Mother-to-Child Transmission Rate and Efficacy
PACTG 076, United States, France Formula feeding *[1]*	ZDV vs placebo	Long (from 14 weeks); intravenous IP	Long (6 weeks), infant only	• 8.3% in ZDV arm vs 25.5% in placebo arm at 18 months (68% efficacy)
CDC short-course ZDV trial, Thailand *[2]* Formula feeding	ZDV vs placebo	Short (from 36 weeks); oral IP	None	• 9.4% in ZDV arm vs 18.9% in placebo arm at 6 months (50% efficacy)
DITRAME (ANRS 049a) trial, Côte d'Ivoire, Burkina Faso *[3,4]* Breastfeeding	ZDV vs placebo	Short (from 36 weeks); oral IP	Short (1 week), mother only	• 18.0% in ZDV arm, 27.5% in placebo arm at 6 months (38% efficacy); 21.5% vs 30.6% at 15 months (30% efficacy) • 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 *[4,5]* Breastfeeding	ZDV vs placebo	Short (from 36 weeks); oral IP	None	• 16.5% in ZDV arm vs 26.1% in placebo arm at 3 months (37% efficacy) • 22.5% in ZDV arm vs 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy)
PETRA trial, South Africa, Tanzania and Uganda *[6]* Breastfeeding and formula feeding	Antenatal, 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	• 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 with placebo: 63%, 42%, and 0%, respectively) • 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 with placebo: 34%, 18%, and 0%, respectively)
HIVNET 012 trial, Uganda *[7]* Breastfeeding	SD NVP vs. ZDV	No AP ARV; oral IP: SD NVP vs oral ZDV	SD NVP within 72 hours of birth (infant only) vs ZDV (1 week), infant only	• 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 *[8]* Breastfeeding and formula feeding	SD NVP vs ZDV + 3TC	No AP ARV; oral IP: SD NVP vs ZDV + 3TC	SD NVP within 48 hours of birth (mother and infant) vs ZDV + 3TC (1 week), mother and infant	• 12.3% in SD NVP 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 *[9]* 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 6.5% in long-long arm vs 4.7% in long-short arm and 8.6% in the short-long arm at 6 months (no statistical difference); *in utero* transmission significantly higher with short vs long maternal therapy regimens (5.1% vs 1.6%)

Table 1. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission (cont)

Study/Location/Mode Infant Feeding	Drugs	Antenatal and Intrapartum	Postpartum	Mother-to-Child Transmission Rate and Efficacy
PACTG 316 trial, Bahamas, Belgium, Brazil, France, Germany, Italy, Spain, Sweden, Switzerland, United Kingdom, United States *[10]* Formula feeding	SD NVP vs placebo among women already receiving ZDV alone (23%) or ZDV + other ARV drugs (77% combination therapy)	Non-study ARV regimen; oral IP: placebo vs SD NVP + intravenous ZDV	Placebo vs SD NVP within 72 hours of birth + non-study 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 SD NVP arm vs 1.6% in placebo arm (53% of MTCT was *in utero*)
Perinatal HIV Prevention Trial (PHPT-2), Thailand *[11]* Formula feeding	ZDV alone vs ZDV + maternal and infant SD NVP vs ZDV + maternal SD NVP	ZDV from 28 weeks; oral IP: ZDV alone or ZDV + SD NVP	ZDV for 1 week with or without SD NVP, 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 SD NVP, MTCT rate did not differ significantly between the infant receiving or not receiving SD NVP (2.0% vs 2.8%)
DITRAME Plus (ANRS 1201.0) trial, Abidjan, Côte d'Ivoire *[12]* Breastfeeding and formula feeding	Open label, ZDV + SD NVP	ZDV from 36 weeks; oral IP: ZDV plus SD NVP	SD NVP + ZDV for 1 week, infant only	• 6.5% (95% CI 3.9–9.1%) at 6 weeks; historical control group receiving short ZDV only had MTCT 12.8% (98% breastfed in historical control group)
DITRAME Plus (ANRS 1201.1) trial, Abidjan, Côte d'Ivoire *[12]* Breastfeeding and formula feeding	Open label, ZDV + 3TC + SD NVP	ZDV + 3TC from 32 weeks (stopped at 3 days PP); oral IP: ZDV + 3TC + SD NVP	SD NVP + ZDV for 1 week, infant only	• 4.7% (95% CI 2.4–7.0%) at 6 weeks; historical control group receiving short ZDV only had MTCT 12.8% (98% breastfed in historical control group)
NVAZ trial, Malawi *[13]* Breastfeeding	Neonatal SD NVP vs SD NVP + ZDV	No AP or IP ARV (latecomers)	SD NVP with or without ZDV for 1 week, infant only	• 15.3% in SD NVP + ZDV arm and 20.9% in SD NVP only arm at 6 to 8 weeks; MTCT rate at 6 to 8 weeks among infants who were HIV-uninfected at birth 7.7% and 12.1%, respectively (36% efficacy)
Postnatal NVP + ZDV trial, Malawi *[14]* Breastfeeding	Neonatal SD NVP vs SD NVP + ZDV	No AP ARV; oral IP: SD NVP	SD NVP with or without ZDV for 1 week, infant only	• 16.3% in NVP + ZDV arm and 14.1% in SD NVP-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 6.5% and 16.9%, respectively
Post-exposure Infant Prophylaxis, South Africa *[15]* Breastfeeding and formula feeding	Neonatal SD NVP vs ZDV for 6 weeks	No AP or IP ARV	SD NVP vs ZDV for 6 weeks	• Formula-fed infants only, 14.3% in SD NVP arm and 14.1% in ZDV arm at 6 weeks (not significant, p=0.30); breastfed infants only, 12.2% in SD NVP arm and 19.6% in ZDV arm (p=0.03).

Table 1. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child HIV Transmission (cont)

Study/Location/Mode Infant Feeding	Drugs	Antenatal and Intrapartum	Postpartum	Mother-to-Child Transmission Rate and Efficacy
MASHI, Botswana *[16,17]* Breastfeeding and formula feeding	Initial: short-course ZDV with/without maternal and infant SD NVP and with/without breastfeeding Revised: short-course ZDV + infant SD NVP with/without maternal SD NVP and with/without breastfeeding; women with CD4 <200 receive HAART	1st randomization ZDV from 34 weeks ; oral IP: ZDV + either SD NVP vs. placebo	2nd randomization Breastfeeding + ZDV (infant) 6 months + SD NVP, infant only vs. Formula feeding + ZDV (infant) 4 weeks + SD NVP, infant only	• Initial design: In formula-feeding arm, MTCT at 1 month, 2.4% in maternal & infant SD NVP arm and 8.3% in placebo arm (p=0.05); in breastfeeding + infant ZDV arm, MTCT at 1 month 8.4% in SD NVP arm and 4.1% in placebo arm (difference not statistically significant) • Revised design: MTCT at 1 month 4.3% in maternal + infant SD NVP arm and 3.7% in maternal placebo + infant SD NVP arm (no significant difference; no interaction with mode of infant feeding) • MTCT at 7 months 9.1% in breastfeeding + ZDV arm and 5.6% in formula feeding arm; mortality at 7 months, 4.9% breastfeeding + ZDV vs 9.3% formula feeding; HIV-free survival at 18 months 15.6% breastfeeding + ZDV vs 14.2% formula feeding
SWEN, Uganda, Ethiopia, India *[18]* Breastfeeding	SD NVP vs NVP for 6 weeks	No AP ARV; oral IP: SD NVP	SD NVP vs NVP for 6 weeks	• MTCT at 6 weeks 5.3% in SD NVP arm vs 2.5% in extended NVP arm (risk ratio 0.54, p=0.009) • MTCT at 6 months 9.0% in SD NVP 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 *[19]* Breastfeeding	SD NVP + ZDV for 1 week (control) vs two extended regimens (NVP or NVP/ZDV) for 14 weeks	No AP ARV; oral IP: SD NVP (if mother presents in time)	SD NVP + ZDV for 1 week (control) vs control + NVP for 14 weeks vs control + NVP/ZDV for 14 weeks	• MTCT at 6 weeks 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 10.0% 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, but more hematologic toxicity with NVP/ZDV.
Kisumu Breastfeeding Study (KiBS), Kenya *[20]* Breastfeeding	Maternal HAART (observational)	AZT/3TC/NVP (NFV if CD4 250) from 34 weeks through labor	Maternal AZT/3TC/NVP (NFV if CD4 250) during breastfeeding up to 6 months postpartum	• MTCT at 6 months 5.0% (postnatal MTCT between 7 days to 6 months 2.6%)
MITRA-PLUS, Tanzania *[21]*	Maternal HAART (observational)	AZT/3TC/NVP from 34 weeks through labor	Maternal AZT/3TC/NVP during breastfeeding up to 6 months postpartum	• MTCT at 6 months 5.0% (postnatal MTCT between 6 weeks to 6 months 0.9%) • MTCT at 6 months in MITRA study of infant (3TC) prophylaxis for 6 months 4.9% (postnatal MTCT between age 6 weeks to 6 months 1.1%)

3TC: lamivudine; AP: antepartum; ARV: antiretroviral; HAART: highly active antiretroviral therapy; IP: intrapartum; MTCT: mother-to-child transmission; NFV: nelfinavir; NVP: nevirapine; PP: postpartum; SD: single-dose; ZDV: zidovudine

Table 1 References

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Table 2. Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy

(see *Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy* for more detail on drugs)

Antiretroviral drug	FDA pregnancy category †	Placental passage (newborn: mother drug ratio)	Long-term animal carcinogenicity studies	Animal teratogen studies
Nucleoside and nucleotide analogue reverse transcriptase inhibitors				
Abacavir (Ziagen, ABC)	C	Yes (rats)	Positive (malignant and non-malignant tumors of liver, thyroid in female rats, and preputial and clitoral gland of mice and rats)	Positive (rodent anasarca and skeletal malformations at 1,000 mg/kg (35x human exposure based on AUC during organogenesis; not seen at 8.5x human exposure in rabbits)
Didanosine (Videx, ddI)	B	Yes (human) [0.5]	Negative (no tumors, lifetime rodent study at 0.7–3x maximum human exposure)	Negative (at 12x and 14.2x the human exposure in rabbits and rats, respectively)
Emtricitabine (Emtriva, FTC)	B	Yes (mice and rabbits) [0.4–0.5]	Negative (no tumors, lifetime rodent study at 26–31x human exposure at the recommended dose)	Negative (at 60x, 60x, 120x the human exposure in rats, mice, and rabbits, respectively)
Lamivudine (Epivir, 3TC)	C	Yes (human) [~1.0]	Negative (no tumors, lifetime rodent study at 10–58x human exposure at the recommended dose)	Negative (at 35x of the plasma levels of humans in both the rat and rabbit; however, embryolethality seen in rabbits with 1x human exposure)
Stavudine (Zerit, d4T)	C	Yes (rhesus monkey) [0.76]	Positive (mice and rats, at very high dose exposure, liver and bladder tumors [rats only] at 250x and 732x the human exposure in mice and rats, respectively)	Negative (at 399x (rats) and 183x (rabbits) human exposure based on Cmax, although sternal bone ossification is decreased and rat neonatal mortality increased at 399x human exposure in rats)
Tenofovir DF (Viread)	B	Yes (human) [0.95–0.99]	Positive (hepatic adenomas [female mice only] at 16x human exposure)	Negative (14x and 19x the human dose based on body surface area in rats and rabbits, respectively)
Zidovudine† (Retrovir, AZT, ZDV)	C	Yes (human) [0.85]	Positive (nonmetastisizing vaginal epithelial tumors at 3x to 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 rat and rabbits, respectively, with no developmental abnormalities)
Non-nucleoside reverse transcriptase inhibitors				
Efavirenz (Sustiva)	D	Yes (cynomologus monkey, rat, rabbit) [~1.0]	Positive (hepatocellular adenomas and carcinomas and pulmonary alveolar/bronchiolar adenomas in female but not male 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 cynomolgous monkey at drug concentrations comparable to humans; no reproductive toxicities in pregnant rabbits at 0.5–1x human exposure)

Table 2. Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy (cont) (see *Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy* for more detail on drugs)

Antiretroviral drug	FDA pregnancy category †	Placental passage (newborn: mother drug ratio)	Long-term animal carcinogenicity studies	Animal teratogen studies
Non-nucleoside reverse transcriptase inhibitors (cont)				
Etravirine (Intelence)	B	Unknown	Carcinogenicity studies in rodents are ongoing. Not mutagenic or clastogenic in *in vitro* and *in vivo* assays	Negative (rats and rabbits at exposures comparable to humans)
Nevirapine (Viramune)	B	Yes (human) [~1.0]	Positive (hepatocellular adenomas and carcinomas in mice and rats at systemic exposures lower than human)	Negative (rats and rabbits at 1–1.5x human exposure. However, decreased fetal body weight in rats at 1.5x human exposure)
Protease inhibitors				
Atazanavir (Reyataz)	B	Minimal/variable (human)	Positive (benign hepatocellular adenomas in female mice at 7.2x the human exposure)	Negative (2x and 1x the human exposure in rats and rabbits, respectively)
Darunavir (Prezista)	B	Unknown	Positive (hepatic adenomas, carcinomas [male mice], thyroid neoplasms [rat 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 (Lexiva)	C	Unknown	Positive (hepatic adenomas and carcinomas [mice and rats]; thyroid adenomas, interstitial cell hyperplasia and uterine endometrial adenocarcinoma [rat only]; relative human exposures varied from 0.1–0.7x [mouse] to 0.3–1.4x [rat] depending on the human dosing regimen)	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 (Crixivan)	C	Minimal (human)	Positive (thyroid adenomas in male rats at 1.3x human exposure)	Negative (however extra ribs in rats at exposures below or slightly above those in humans)
Lopinavir/ Ritonavir (Kaletra)	C	Yes (human) [0.20 +/- 0.13]	Positive (hepatic adenomas & carcinomas at 1.6–2.2x and 0.5x human exposure in mice and rats, respectively)	Positive (no effects in rabbits and dogs [~1x human exposure]; decreased fetal viability, body weight, delayed skeletal ossification and increase in skeletal variations in rats at maternally toxic doses [lopinavir 0.7x / ritonavir 1.8x human exposure])
Nelfinavir (Viracept)	B	Minimal/variable (human)	Positive (thyroid follicular adenomas and carcinomas in rats at 1–3x human exposure in rats)	Negative (in rats with comparable exposure to humans and rabbits at significantly lower exposure than humans)

Table 2. Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy (cont) (see *Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy* for more detail on drugs)

Antiretroviral drug	FDA pregnancy category †	Placental passage (newborn: mother drug ratio)	Long-term animal carcinogenicity studies	Animal teratogen studies
Protease inhibitors (cont)				
Ritonavir (Norvir)	B	Minimal (human)	Positive (liver adenomas and carcinomas in male mice at 0.3x human exposure)	Positive (early resorptions, decreased fetal body weight and ossification delays and developmental variations in the rat at maternally toxic dose [~0.3x human exposure]; cryptorchidism in rats [0.22x human exposure])
Saquinavir (Fortovase)	B	Minimal (human)	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 the rat and the rabbit, respectively)
Tipranavir (Aptivus)	C	Unknown	In progress	Negative (decreased ossification and pup weights in rats associated with fetal toxicity at dose exposure 0.8x human exposure)
Entry inhibitors				
Enfuvirtide (Fuzeon)	B	None based on very limited human data	Not conducted	Negative
Maraviroc (Selzentry)	B	Unknown	Negative (transgenic mice; rats at 11x human exposure)	Negative (no evidence for harm to fetus at 20x and 5x human exposure in rats and rabbits, respectively)
Integrase inhibitors				
Raltegravir (Isentress)	C	Yes (rats [1.5–2.5], rabbits [0.02])#	In progress	Negative (however supernumerary ribs at 3x human exposure in rats)

AUC: Area under the curve; Cmax: Maximum concentration

* No longer available in the United States.

Values obtained from fetal (not newborn) blood samples. See text in Raltegravir (Isentress™): Placental and breast milk passage section

† 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.

Table 3. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy

*(see also "**Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy**" supplement for additional toxicity data and "**Guidelines for the Use of Antiretroviral Agents in HIV-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 (ZDV 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; 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; a much smaller percentage are fatal and are usually associated with rechallenge. Rate in pregnancy 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.
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.

Table 3. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (cont)

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

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Alternate agents (cont)			
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. Phase I study in late pregnancy in progress.	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 that 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/mm3 when first initiating therapy *[16,17]*; unclear if pregnancy increases risk.	Nevirapine should be initiated in pregnant women with CD4 counts >250 cells/mm3 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.

Table 3. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (cont)

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

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Use in special circumstances			
Efavirenz†	Small study in 13 women in Rwanda of 600 mg once daily; third trimester peak levels 61% higher than in non-pregnant 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 5 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 risks and avoidance of pregnancy. Because of the known failure rates of contraception, alternate regimens should be strongly considered in women of child-bearing 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		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 underway, 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 underway, 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 3. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (cont)

*(see also "**Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy**" supplement for additional toxicity data and "**Guidelines for the Use of Antiretroviral Agents in HIV-infected Adults and Adolescents**" for detailed guidelines regarding treatment options)*

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 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 similar study of pregnant women in their second and third trimester dosed at 1,250mg given twice daily, women in the third trimester had lower concentration of nelfinavir than women in their 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 HAART only for perinatal prophylaxis. In clinical trials of initial therapy in non-pregnant 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 3. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (cont)

*(see also "**Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy**" supplement for additional toxicity data and "**Guidelines for the Use of Antiretroviral Agents in HIV-infected Adults and Adolescents**" for detailed guidelines regarding treatment options)*

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Recommendations for Use in Pregnancy
Alternate agents (cont)			
Ritonavir	Phase I/II study in pregnancy showed lower levels during pregnancy compared to postpartum *[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-hard gel capsule [HGC] (Invirase®) (combined with low-dose ritonavir boosting)	Limited pharmacokinetic data on saquinavir-hard gel capsule (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 non-pregnant 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 3. Antiretroviral Drug Use in Pregnant HIV-Infected Women: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy (cont)

*(see also "**Safety and Toxicity of Individual Antiretroviral Drugs in Pregnancy**" supplement for additional toxicity data and "**Guidelines for the Use of Antiretroviral Agents in HIV-infected Adults and Adolescents**" for detailed guidelines regarding treatment options)*

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.

HGC = hard gel capsule; NRTI = nucleoside reverse transcriptase inhibitor; NtRTI = nucleotide reverse transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; SGC = soft gel capsule.

* 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.

† 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 HAART regimens. Triple NRTI regimens should be used only when an NNRTI- or PI-based HAART regimen cannot be used (e.g., due to significant drug interactions).

Table 3 References

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Table 4. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal HIV-1 Transmission in the United States

Clinical Situation	Recommendation
HIV-infected woman of childbearing potential but not pregnant, and who has indications for initiating antiretroviral therapy	• Initiate HAART as per adult treatment guidelines. • Avoid drugs with teratogenic potential (e.g., EFV) in women of childbearing age unless adequate contraception ensured. Exclude pregnancy before starting treatment with EFV.
HIV-infected woman who is receiving HAART and becomes pregnant	**Woman:** • Continue current HAART regimen if successfully suppressing viremia, except avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI). • HIV antiretroviral drug resistance testing is recommended if the woman has detectable viremia on therapy. • In general, if woman requires treatment, antiretroviral drugs should not be stopped during the 1st trimester. • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion[1] during labor while other antiretroviral agents are continued orally) and postpartum. • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant:** • ZDV for 6 weeks started within 6 to 12 hours after birth.[2]
HIV-infected pregnant woman who is antiretroviral naïve <u>and</u> has indications for antiretroviral therapy	**Woman:** • HIV antiretroviral drug resistance testing is recommended prior to the initiation of therapy, and if suboptimal viral suppression after initiation of HAART. • Initiate HAART regimen. - Avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI). - Use of ZDV as a component of the antiretroviral regimen is recommended when feasible. - NVP can be used as a component of HAART for women with CD4 count ≤250 cells/mm^3, but should only be used as a component of therapy in women with CD4 counts >250 cells/mm^3 if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • For women who require immediate initiation of therapy for their own health, treatment should be initiated as soon as possible, including in the first trimester. • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion[1] during labor while other antiretroviral agents are continued orally) and postpartum. • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant:** • ZDV for 6 weeks started within 6 to 12 hours after birth.[2]

Table 4. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal HIV-1 Transmission in the United States (cont)

Clinical Situation	Recommendation
HIV-infected pregnant woman who is antiretroviral naïve and does <u>not</u> require treatment for her own health	**Woman:** • HIV antiretroviral drug resistance testing is recommended prior to the initiation of therapy, and if suboptimal viral suppression after initiation of HAART. • HAART is recommended for prophylaxis of perinatal transmission in women who do not require treatment for their own health. - Consider delaying HAART initiation until after first trimester is completed. - Avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI). - Use of ZDV as a component of the antiretroviral regimen is recommended when feasible. - NVP should only be used as a component of therapy in women with CD4 counts >250 cells/mm^3 if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • Use of ZDV prophylaxis alone is controversial, but may be considered for those women with plasma HIV RNA levels <1,000 copies/mL on no therapy. • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion[1] during labor while other antiretroviral agents are continued orally). • Evaluate need for continued therapy postpartum; discontinue HAART unless has indications for continued therapy. If regimen includes drug with long half-life like NNRTI, consider stopping NRTIs 7 days after stopping NNRTI. (Limited data exist on this.) • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant**: • ZDV for 6 weeks started within 6 to 12 hours after birth.[2]
HIV-infected pregnant woman who is antiretroviral experienced but not currently receiving antiretroviral drugs	**Woman:** • Obtain full antiretroviral treatment history and evaluate need for antiretroviral treatment for own health. • Perform HIV antiretroviral drug resistance testing prior to initiating repeat antiretroviral prophylaxis or therapy, and if suboptimal viral suppression after initiation of HAART. • Initiate HAART, with regimen chosen based on resistance testing and prior therapy history. - Avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI). - Use of ZDV as a component of the ARV regimen is recommended when feasible. - NVP should only be used as a component of therapy in women with CD4 counts >250 cells/mm^3 if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion[1] during labor while other antiretroviral agents are continued orally). • Evaluate need for continued therapy postpartum; discontinue HAART unless has indications for continued therapy. If regimen includes drug with long half-life like NNRTI, consider stopping NRTIs 7 days after stopping NNRTI. (Limited data exist on this.) • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery. **Infant**: • ZDV for 6 weeks started within 6 to 12 hours after birth.[2]

Table 4. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-Infected Women and Prevention of Perinatal HIV-1 Transmission in the United States (cont)

Clinical Situation	Recommendation
HIV-infected woman who has received no antiretroviral therapy prior to labor	ZDV **Woman*:*** ZDV given as continuous infusion[1] during labor. **Infant:** ZDV for 6 weeks started within 6 to 12 hours after birth.[2] ***OR*** Combination ZDV + Single-Dose NVP: **Woman:** ZDV given as continuous infusion[1] during labor, plus single-dose NVP[3] at onset of labor. Consideration should be given to adding 3TC during labor and maternal ZDV/3TC for 7 days postpartum, which may reduce development of NVP resistance. **Infant:** Single-dose NVP[3] plus ZDV for 6 weeks. ***OR*** **Woman*:*** ZDV given as continuous infusion[1] during labor. **Infant:** Some clinicians may choose to use ZDV in combination with additional drugs in the infant, but appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consultation with a pediatric HIV specialist is recommended. • 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	• ZDV given for 6 weeks to the infant, started as soon as possible after birth.[2] ***OR*** • Some clinicians may choose to use ZDV in combination with additional drugs, but appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consultation with a pediatric HIV specialist is recommended. • Evaluate need for initiation of maternal therapy postpartum.

3TC: Lamivudine; EFV: Efavirenz; HAART: Highly active antiretroviral therapy, a minimum of three antiretroviral agents; NVP: Nevirapine; ZDV: Zidovudine

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

[2] ZDV 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 NVP: 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 NVP, or given at birth if mother did not receive intrapartum single-dose NVP.

Table 5. Intrapartum Maternal and Neonatal Zidovudine Dosing for Prevention of Mother to Child HIV Transmission

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 (term [≥35 weeks] infant)	2 mg per kg body weight per dose given orally (or 1.5 mg per kg body weight per dose given intravenously) started as close to birth as possible (by 6-12 hours of delivery), then every 6 hours*	Birth to 6 weeks
ZDV (<35 weeks but >30 weeks)	2 mg per kg body weight per dose given orally (or 1.5 mg per kg body weight per dose given intravenously) every 12 hours, advanced to every 8 hours at 2 weeks of age	Birth to 6 weeks
ZDV (<30 weeks)	2 mg per kg body weight per dose given orally (or 1.5 mg/kg/dose given intravenously) every 12 hours, advanced to every 8 hours at 4 weeks of age	Birth to 6 weeks

ZDV = zidovudine

* ZDV 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. While there are no definitive data to show equivalent pharmacokinetic parameters or efficacy in preventing transmission, a regimen of ZDV 4 mg per kg body weight per dose given orally twice daily instead of 2 mg per kg body weight per dose given orally four times daily may be considered when there are concerns about adherence to drug administration to the infant.

Table 6. Intrapartum Maternal and Neonatal Dosing for Additional Antiretroviral Drugs to be Considered Only in Selected Circumstances (see pages 42, 51-55 for further discussion)

Maternal Intrapartum/Postpartum		
Drug	**Dosing**	**Duration**
NVP (as single dose intrapartum)*	200 mg given orally as single dose	Given once at onset of labor
ZDV + 3TC (given with single dose NVP as "tail" to reduce NVP resistance)	ZDV: intravenous infusion intrapartum as per table 5, then after delivery 300 mg orally twice daily 3TC: 150 mg orally twice daily starting at labor onset	Through 1 week postpartum
Neonatal		
Drug	**Dosing**	**Duration**
NVP (as single dose)**	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 $\leq$ 2 hours before delivery, infant dose should be administered as soon as possible following birth.
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

NVP = nevirapine, ZDV = zidovudine, 3TC = lamivudine

* 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 7 days postpartum to reduce development of NVP resistant virus is recommended.

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

Table 7. Clinical Scenarios and Recommendations Regarding Mode of Delivery to Reduce Perinatal HIV Transmission

Clinical Situation	Recommendation
HIV-infected women presenting in late pregnancy (after about 36 weeks gestation), known to be HIV-infected but not receiving antiretroviral therapy, and who have 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 4**. • The woman should be counseled that scheduled cesarean section is likely to reduce the risk of transmission to her infant. She should also be informed of the increased risks to her from cesarean section, including increased rates of postoperative infection, anesthesia risks, and other surgical risks. • If cesarean section is chosen, the procedure should be scheduled at 38 weeks gestation based on the best available clinical information. • When scheduled cesarean section is performed, the woman should receive continuous intravenous ZDV infusion beginning 3 hours before surgery and her infant should receive 6 weeks of ZDV therapy after birth (see **Table 4**). • 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.
HIV-infected women who initiated prenatal care early in the third trimester, are receiving HAART, and have an initial virologic response, but have HIV RNA levels that remain substantially more than 1,000 copies/mL at 36 weeks gestation.	• The current combination antiretroviral regimen should be continued as 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 section may provide additional benefit in preventing intrapartum transmission of HIV. She should also be informed of the increased risks to her of cesarean section, including increased rates of postoperative infection, anesthesia risks, and surgical risks. • If she chooses scheduled cesarean section, it should be performed at 38 weeks gestation according to the best available dating parameters, and intravenous ZDV should be begun at least 3 hours before surgery and her infant should receive 6 weeks of ZDV therapy after birth (see **Table 4**). • 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 be treated with 6 weeks of ZDV therapy after birth (see **Table 4**).
HIV-infected women on HAART 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 2% or less, even with vaginal delivery. There is currently no information to evaluate whether performing a scheduled cesarean section will lower her risk further. • Cesarean section 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 section in this case.
HIV-infected women who have elected scheduled cesarean section but present in early labor or shortly after rupture of membranes.	• Intravenous ZDV should be started immediately since the woman is in labor or has ruptured membranes. • If labor is progressing rapidly, the woman may deliver vaginally. • If cervical dilatation is minimal and a long period of labor is anticipated, some clinicians may choose to administer the loading dose of intravenous ZDV and proceed with cesarean section to minimize the duration of membrane rupture and avoid vaginal delivery. Others might begin pitocin augmentation to enhance contractions and potentially expedite delivery. • If the woman is allowed to labor, scalp electrodes and other invasive monitoring and operative delivery should be avoided if possible. • The infant should be treated with 6 weeks of ZDV therapy after birth (see **Table 4**).