CLINICIAN CONSULTATION CENTER
National rapid response for HIV management and bloodborne pathogen exposures.

CCC ARV Dosing Recommendations for HIV-exposed infants Updated 7.15.16

USERS NOTE: Please note this document does not provide guidance on overall decision-making regarding what medication(s) to use for HIV-exposed infants. This document is meant to facilitate ARV dosing for HIV-exposed infants, AFTER conversation with a CCC consultant in reference to a particular case. Please do NOT keep this document for reference for other patients, as information may be out of date. 24/7 expert telephone consultation is available via the National Perinatal HIV Hotline: 888-448-8765 (nccc.ucsf.edu).

The optimal approach to preventing perinatal transmission of HIV includes treatment with antiretroviral (ARV) medications throughout pregnancy and labor to maintain an undetectable maternal HIV viral load, followed by administering zidovudine prophylaxis to the infant. When HIV-positive mothers have not received antepartum ARVs or when maternal HIV viral load is not suppressed late in pregnancy, however, neonates are at higher risk for *in utero* or intrapartum transmission. The DHHS perinatal guidelines[1] define infants at higher risk as "those born to HIV-infected women who have received only intrapartum [ARVs] or have not received antepartum or intrapartum [ARVs] or have received antepartum [ARVs] but have had suboptimal viral suppression (> 1000 copies/mL) near delivery". Additionally, many experts would classify an infant born to a mother who had a viral load > 1,000 copies/mL at some point in the 3rd trimester (not just near delivery) as higher risk, and others are additionally concerned about any detectable HIV viremia, even if ≤ 1000 copies/mL.

Two strategies are currently being used to reduce perinatal transmission for higher risk infants. 1) The DHHS perinatal guidelines recommend combination prophylaxis with zidovudine plus 3 doses of nevirapine. This regimen was shown to reduce intrapartum transmission to infants born to mothers who had not received any antepartum ARVs. 2) Some experts treat higher risk HIV-exposed infants with a multi-drug regimen that aims to provide therapeutic drug levels (i.e. "treatment dose") of zidovudine, lamivudine and nevirapine. While there are no data to support this specific strategy, the goal of this approach is to provide full treatment to infants who are born with HIV infection established *in utero* or **further reduce** the risk of intrapartum transmission to those not yet infected. The DHHS perinatal guidelines recommend that a decision to administer three-drug ARVs be made **only in consultation with a specialist**. Currently, treatment doses of nevirapine remain investigational and only available for infants > 34 weeks gestational age who weigh ≥ 1.5kg.

Clinicians should refer to the DHHS perinatal guidelines (https://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0) for guidance. Our Perinatal HIV Hotline (888-448-8765) is pleased to provide decision support for clinicians making these challenging management decisions. Consultation involves a careful consideration of risks and benefits of each approach as well as regimen and dosing recommendations. Ultimately, an informed discussion between the treating clinician(s) and the infant's parent/guardian(s) will be essential in selecting a strategy.

The antiretroviral medication dosing in this document is from DHHS Pediatric HIV Guidelines (https://aidsinfo.nih.gov/guidelines/html/2/pediatric-arv-guidelines/0), unless otherwise noted; refer to these Guidelines for the most current information. The dosing for nevirapine for premature/low birth weight infants and for presumptive

[1] Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. 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. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf.

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treatment is based on CCC expert opinion, *not* the FDA or DHHS Perinatal HIV Guidelines panel. This dosing should be offered to families/parents/guardians ONLY in conjunction with comprehensive counseling about known risks and potential benefits.

Zidovudine (ZDV, AZT, Retrovir®) is given to ALL HIV-exposed infants: begin as soon as possible after birth • **Continued for 4 or 6 weeks as prophylaxis for low risk infants, see Perinatal guidelines for details[2]** • **Continued for 6 weeks as component of prophylaxis for higher risk infants** • **Closely monitor weight gain over the first 4-6 weeks of life in order to appropriately adjust dosing as indicated**	
Infants < 30 weeks gestational age:	
Tolerating oral feeds	☐ postnatal age ≤ 28 days: zidovudine syrup 2 mg/kg/dose =____mg PO q12 hours **OR** ☐ postnatal age > 28 days: zidovudine syrup 3 mg/kg/dose =____mg PO q12 hours
NPO	☐ postnatal age ≤ 28 days: zidovudine 1.5 mg/kg/dose =___mg IV q12 hours **OR** ☐ postnatal age > 28 days: zidovudine 2.3 mg/kg/dose =___mg IV q12 hours
Infants ≥ 30 to < 35 weeks gestational age:	
Tolerating oral feeds	☐ postnatal age ≤ 14 days: zidovudine syrup 2 mg/kg/dose =___mg PO q12 hours **OR** ☐ postnatal age > 14 days: zidovudine syrup 3 mg/kg/dose =____mg PO q12 hours
NPO	☐ postnatal age ≤ 14 days: zidovudine 1.5 mg/kg/dose =___mg IV q12 hours **OR** ☐ postnatal age > 14 days: zidovudine 2.3 mg/kg/dose =___mg IV q12 hours
Infants ≥ 35 weeks gestational age:	
Tolerating oral feeds	☐ zidovudine syrup 4 mg/kg/dose =_____mg PO q12 hours
NPO	☐ zidovudine 3 mg/kg/dose =_____mg IV q12 hours

[2] https://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/187/infant-antiretroviral-prophylaxis

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HIGHER RISK Prophylaxis Protocol • **3TC added if concern for transmitted resistant virus**	
1. Zidovudine (ZDV)	Dosing per page 2, for 6 weeks
2. Nevirapine (NVP, Viramune®) suspension (Note: there is no IV formulation of NVP)[3]	GA < 27 weeks OR birth weight < 0.75 kg[4]:
	☐ 2 mg/kg/dose =___mg PO x 2 doses Dose #1: x1 immediately after delivery Dose #2: x1 seven days after Dose #1 *Discuss with parents risks/benefits/alternatives of off-guidelines prophylactic dosing.*
	GA 27 – 31.6 weeks AND birth weight 0.75 - 1.5 kg[4]:
	☐ 4 mg/kg/dose =___mg PO x 2 doses Dose #1: x1 immediately after delivery Dose #2: x1 seven days after Dose #1 *Discuss with parents risks/benefits/alternatives regarding use of un-approved dosing.*
	GA ≥ 32 weeks OR birth weight ≥1.5 kg:
	☐ birth weight 1.5 - 2 kg: 8 mg PO per dose x 3 doses [this is approximately 4 mg/kg/dose] ☐ birth weight > 2 kg: 12 mg PO per dose x 3 doses [approximately 4 mg/kg/dose] Dose #1: x1 immediately after delivery Dose #2: x1 48 hours after Dose #1 Dose #3: x1 96 hours after Dose #2
3. Lamivudine (3TC,	GA ≥ 32 weeks AND birth weight ≥ 1.5 kg[5]:

[3] PO dosing of NVP: PO NVP can be given to extremely low birth weight infants, even if otherwise NPO (e.g., gut immaturity, ischemia, concern for NEC). The concentration is 12 mg/ml, so the volume is very small. There is NO IV formulation of NVP. Some neonatologists may hesitate to give any oral medication to NPO preemies, but it can be safely given as early as 24 weeks gestation (even if concern for NEC) given the small volume. Strongly consider calling CCC consultant and/or offer to have neonatologist discuss case directly with CCC. Small infants rarely vomit large volumes, but if it appears that the majority of the dose was vomited within 30 minutes of administration, it should be repeated.

[4] Dosing for NVP for infants ≥ 32 weeks is from HPTN 040. NVP dosing here is extended to infants < 1.5kg (who were excluded from 040) but spaced to doses on day 0 and 7 in lieu of 3 doses over the first week based on principle of prolonged half-life (CCC/internal and Mugabo SAMJ 2011). **There are no data about that schedule in particular.** Some institutions may have the ability to check NVP levels; while this may be useful to assess for toxicity, given limited data, is it not possible to provide dosing guidelines based on NVP drug levels.

[5] Dosing and duration(?) of 3TC for ≥ 32 weeks or birth weight ≥1.5 kg is from HPTN 040 (Nielsen-Saines NEJM 2012 and Mirochnik PIDJ 2011). Some also use a fixed dose of 6mg for all infants over 3 kg, because this is the dose used in the protocol from HPTN 040. Per their protocol, the dose is based on data from pharmacokinetic studies of 3TC in the newborn period and with the recognition that it would mean 2mg/kg/dose for the common 3kg infant. Two mg/kg of 3TC was the dose used in perinatal prophylaxis studies including the PETRA study and was the dose used in PACTG 353. In the SAINT trial, a standard 3TC dose of 6 mg BID was safely administered to infants greater than 2000 grams and 2 mg/kg/dose BID for infants less than 2000 grams.

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Epivir®) solution *(Optional: can be added in cases of suspected resistance)*	☐ 2 mg/kg/dose =___mg PO q12 hours x 2 weeks

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Presumptive Treatment Protocol • Start all three medications ASAP • **Only for infants > 34 weeks gestational age AND birth weight ≥ 1.5 kg**	
1. Zidovudine (ZDV)	Dosing per page 2
2. Nevirapine (NVP, Viramune®) suspension • **For infants ≤ 34 weeks or birth weight < 1.5 kg, <u>there is no NVP treatment dosing</u>. Must use prophylactic dosing for these infants (see page 3).**	GA 34 $^{1}/_{7}$ – 36 $^{6}/_{7}$ weeks: ☐ 4 mg/kg/dose=_____mg PO q12 hours[6] on days 0-6 of life, then 6 mg/kg/dose=_____mg PO q12 hours[6] on day 7 of life and after GA ≥ 37 weeks: ☐ 6 mg/kg/dose=_____mg PO q12 hours[6]
3. Lamivudine (3TC, Epivir®) solution	Birth weight ≥ 1.5 kg5: ☐ 2 mg/kg/dose =__mg PO q12 hours

- HIV nucleic acid (HIV RNA or DNA) should be sent ASAP, within first 48 hours of life.
- Send CBC/electrolytes with lactate/LFTs if infant has any symptoms/signs of toxicity.
- See separate CCC document outlining testing recommendations for HIV-exposed infants for information on laboratory monitoring.

[6] There is no FDA or DHHS-endorsed treatment dose for NVP for infants < 14 days old. The provider in Mississippi utilized 2 mg/kg/dose BID of NVP. The Int'l Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) developed a NVP treatment dose based on PK modeling for its trials; the 6 mg/kg provisional dose is also reported in the current DHHS Perinatal HIV guidelines. ***Providers should discuss risks/benefits/alternatives of using investigational treatment dosing with parents/guardians.***