



## MANAGEMENT OF THE NEONATE WITH PERINATAL HIV EXPOSURE UNIVERSITY OF MICHIGAN CLINICAL PRACTICE GUIDELINE

### I. OVERVIEW:

Human immunodeficiency virus (HIV) is a retrovirus that infects humans and may result in significant effects on immune function, potentially leading to the development of acquired immune deficiency syndrome (AIDS). The management of neonates with known or possible perinatal HIV exposure requires the immediate initiation of antiretroviral drugs for prophylaxis. The use of antiretroviral drugs reduces perinatal transmission by several mechanisms, including lowering maternal antepartum viral load and providing infant pre- and post-exposure prophylaxis. Therefore, combined antepartum, intrapartum, and neonatal antiretroviral prophylaxis is recommended to prevent perinatal transmission of HIV.

These guidelines are adapted from recommendations outlined by the [Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission](#), updated December 2021.

### II. PURPOSE:

The purpose of this document is to guide clinicians through the immediate postnatal management of neonates with known or possible perinatal HIV exposures.

### III. SCOPE:

This scope of this document encompasses the initial management (including diagnostic testing, antiretroviral prophylaxis, and necessary consultation and follow-up) for an infant born to a mother with either a known positive HIV status or unknown HIV status and cared for in the newborn nursery or the NICU.

### IV. DEFINITIONS:

**Perinatal HIV Exposure:** Exposure occurs when an infant is born, via any mode of delivery, to a mother who is positive for HIV. The infant is considered to have perinatal HIV exposure regardless of the mother's burden of disease (i.e., her HIV viral load), whether the mother received antepartum/intrapartum antiretroviral therapy, or the mode of delivery.

**Antepartum antiretroviral drugs:** Antiretroviral drugs given to the mother during pregnancy.

**Intrapartum antiretroviral drugs:** Antiretroviral drugs given to the mother at the time of delivery.

**Antiretroviral Prophylaxis:** The administration of one or more antiretroviral drugs to a newborn without documented HIV infection to reduce the risk of perinatal acquisition of HIV.

**Presumptive HIV Therapy:** The administration of a three-drug antiretroviral regimen to newborns who are at highest risk of perinatal acquisition of HIV. Presumptive HIV therapy is intended to be preliminary treatment for a newborn who is later documented to have HIV, but it also serves as prophylaxis against HIV acquisition for those newborns who are exposed to HIV in utero, during the birthing process, or during breastfeeding and who do not acquire HIV.

**Low risk infants:** Infants born to mothers with known HIV who received antiretroviral drugs during pregnancy with viral suppression (defined as a confirmed HIV RNA level <50 copies/ml) within four weeks prior to delivery with no concerns related to maternal antiretroviral medication adherence.

**High risk infants:** Infants born to mothers with known HIV who have not received any antepartum or intrapartum antiretroviral drugs, have received only intrapartum antiretroviral drugs, have received appropriate antepartum/intrapartum antiretroviral drugs but have had poor viral suppression (elevated HIV RNA level) within four weeks of delivery, or who had primary/acute HIV infection during pregnancy.

### V. GUIDELINE:

## Immediate Postnatal Management of the HIV-Exposed Neonate

### *Consults*

- Please consult Pediatric Infectious Diseases when an infant is born to a mother with known HIV infection, or when an infant is born to a mother with unknown HIV status who subsequently tests positive for HIV. This will allow the Pediatric Infectious Diseases service to establish care and answer questions for the family. Do not delay starting antiretroviral prophylaxis while waiting for the Pediatric Infectious Diseases consult to be completed.
- Social work should be consulted to evaluate infants with HIV infection and their families prior to discharge.

### *Prenatal Recommendations*

- In some cases, mothers with HIV infection may have had prenatal visits with Pediatric Infectious Diseases to discuss plans for infant treatment. These notes will be available in the mother's medical chart.
- Care coordination notes may also be found in mother's chart.
- Pediatric Infectious Diseases must still be consulted after birth even if a prenatal visit has been done.

### *Antiretroviral Prophylaxis*

- Antiretroviral prophylaxis should be initiated **as soon as possible after birth** for all HIV-exposed neonates. Ideally, the first dose should be given within 6 hours of delivery and no later than 12 hours after delivery (see recommendations for regimens and dosing in Tables 1 and 2).
- **Infants at low risk of HIV transmission** should receive antiretroviral prophylaxis with a four-week course of zidovudine (see Table 2 for dosing recommendations).
- **Infants at high risk of HIV transmission** should receive **presumptive HIV therapy with a three-drug regimen:** zidovudine, lamivudine, and either nevirapine or raltegravir (see recommended regimens in Table 1 and dosing recommendations in Table 2).
  - For high-risk infants receiving presumptive therapy, zidovudine should be continued for six weeks. The duration of lamivudine and nevirapine or raltegravir depends on a variety of factors and will be determined during outpatient follow-up in the Pediatric Infectious Diseases Clinic.
- The recommendations for neonatal prophylaxis regimens described above still apply to infants born to mothers with HIV infection and known antiretroviral resistance.
- In cases where there is high risk of transmission, the physician managing the mother's HIV treatment should contact Pediatric Infectious Diseases, preferably prior to delivery, to discuss optimal antiretroviral prophylaxis for the newborn in greater detail.
  - The National Perinatal HIV Hotline (1-888-448-8765) provides free 24-hour clinical consultation on all aspects of perinatal HIV, including infant care, and may also be a helpful resource in this situation.

### *Infant Feeding*

- HIV-infected mothers should be counseled not to breastfeed their infants.
- Mothers with unknown HIV status that test positive on rapid HIV screening should not breastfeed until infection is ruled out with additional testing.
- Feeds with donor breast milk (if eligible) or formula should be initiated.

### *Laboratory Evaluation:*

- For low- and high-risk infants, baseline complete blood count and differential (CBCPD) should be obtained.
- For high-risk infants, HIV DNA/RNA PCR should also be obtained.

### *Discharge Preparation*

- Prescriptions for the infant's antiretroviral medications must be sent to the Taubman Outpatient Pharmacy and the medications must be in parents'/guardians' hands prior to infant's discharge from the hospital. Prescriptions should not be sent to other outpatient pharmacies (e.g., CVS, Walgreens), because liquid formulations of these medications are frequently not in stock.

- Medication administration should be reviewed with parents/guardians in detail prior to discharge to ensure that they are able to reliably give medication to the infant. Parents/guardians are highly encouraged to administer at least one dose under the supervision of the nurse prior to discharge.
- Please contact the Pediatric Infectious Diseases consult team prior to discharge to confirm that a follow-up appointment has been scheduled.

### **Special Considerations**

#### *Infants Born to Mothers with Unknown HIV Infection Status*

- For mothers with unknown HIV status, rapid HIV-1/2 antigen/antibody testing of the mother and/or infant is recommended as soon as possible.
  - Rapid testing should be performed on the mother on admission/prior to delivery.
  - If testing was not performed prior to delivery, it should be performed as soon as possible on the mother or infant. This order is found in MiChart under "Rapid HIV" and has a turn-around time of 60 minutes. For the infant, only 3-4 drops of blood are required and can likely be obtained via heel stick. The test is not validated on cord blood.
- In the setting of a positive maternal rapid HIV test, confirmatory testing with HIV RNA PCR should be performed on the mother as soon as possible in addition to HIV-1/2 antibody differentiation assay which is performed as a reflex test of rapid test, and the infant should immediately be started on three-drug presumptive HIV therapy. CBC with differential and HIV DNA/RNA PCR should be performed on the infant.
  - If the maternal HIV RNA PCR is negative, then the infant's antiretroviral prophylaxis should be discontinued.
  - If the maternal HIV RNA PCR is positive, three-drug presumptive HIV therapy should be continued for the infant and the management should follow that of high-risk exposure.
  - If the mother is unavailable or declines confirmatory testing, a positive HIV test result should be assumed. The infant should receive three-drug presumptive HIV therapy and the management should follow that of high-risk exposure.
- In the setting of a positive infant rapid HIV test, confirmatory testing with HIV DNA/RNA PCR should be performed on the infant as soon as possible and the infant should immediately be started on three-drug presumptive therapy.
  - If the infant HIV DNA/RNA PCR is negative, the positive rapid HIV test results suggests maternal HIV infection. However, the infant remains at risk, and the infant's three-drug presumptive therapy should be continued unless maternal infection can be excluded.
  - If the infant HIV DNA/RNA PCR is positive, this likely represents true HIV infection. HIV DNA/RNA PCR should be repeated to confirm the result. Three-drug presumptive therapy should be continued until confirmatory test results are available.
- Discharge of the infant should be delayed until maternal HIV status is clarified with rapid HIV testing and/or HIV RNA PCR. Results of HIV DNA/RNA PCR testing from infants may take up to a week or more to be available. As long as the infant is on an appropriate antiretroviral regimen based on maternal infection status, the infant's HIV DNA/RNA PCR result does not need to be available before discharge.
- When a mother declines HIV testing for herself or their infant, providers should have a risk/benefit discussion with the mother, document this in the newborn note, and ask the family to sign the refusal of maternal labs consent form as outlined in newborn refusal of care policy. If a mother is known to be at high risk for sexually transmitted diseases (STI) (e.g., IV drug use or past STIs), consultation with Pediatric Infectious Diseases is recommended to discuss potential empiric antiretroviral therapy.

#### *Two-Drug Prophylaxis*

- For some infants who do not meet all criteria for being at low risk of transmission but who have few high-risk features, it may be possible to use two-drug prophylaxis with zidovudine and nevirapine instead of three-drug presumptive therapy.

- Three-drug presumptive treatment remains the recommendation for all high-risk infants and two-drug prophylaxis should only be given in extenuating circumstances. The decision to pursue this approach should be made in discussion with and under the guidance of the Pediatric Infectious Diseases consult service.
- In this regimen, the infant will receive six weeks of zidovudine as well as three doses of nevirapine in the first week of life. (See Table 2 for nevirapine dosing for this scenario, which differs from dosing used for presumptive therapy.)

### **Subsequent Postnatal Management of the HIV-Exposed Neonate**

- Subsequent postnatal management will typically occur as an outpatient in the Pediatric Infectious Diseases Clinic. However, if an infant remains hospitalized for a prolonged length of stay, the Pediatric Infectious Diseases consult service will assist with ongoing management.
  - Virologic tests (listed in MiChart as “HIV-1 DNA and RNA Qualitative Detection by PCR, Plasma”) are optimal for diagnosis of HIV infection in infants <18 months of age and should be performed between 14–21 days of life, at 1–2 months of age, and at 4–6 months of age. In infants at high-risk who receive presumptive therapy, HIV DNA/RNA PCR should also be obtained 2-6 weeks after discontinuation of therapy.
  - HIV infection is **presumptively excluded** if two or more virologic tests are negative (one at age  $\geq 2$  weeks and one at age  $\geq 4$  weeks), if a virologic test at  $\geq 8$  weeks is negative, or if an HIV antibody test is negative at  $\geq 6$  months.
  - HIV infection is **definitively excluded** if two or more virologic tests are negative (one at  $\geq 1$  month of age and one at  $\geq 4$  months of age) or if two HIV antibody tests obtained from separate specimens are negative at  $\geq 6$  months. Note that antiretroviral therapy is discontinued after 4 or 6 weeks depending on whether the infant is high- or low-risk; HIV infection does not need to be definitively excluded prior to discontinuing antiretrovirals.
  - At a minimum, a CBC with differential should be repeated at 4 weeks of age for any infant on zidovudine or lamivudine. Further decisions about the timing of subsequent monitoring of hematologic parameters depend on baseline hematologic values, gestational age at birth, clinical condition of the infant, the zidovudine dose, concomitant medications, and maternal antepartum therapy.
  - If hematologic abnormalities are identified in infants receiving antiretroviral prophylaxis, decisions on whether to continue infant antiretroviral prophylaxis should be made on an individual basis in consultation with Pediatric Infectious Diseases.
  - To prevent *Pneumocystis jirovecii* pneumonia (PJP), all infants born to mothers with HIV infection should begin PJP prophylaxis at 4 to 6 weeks of age, after completing their antiretroviral prophylaxis regimen, unless HIV infection has been presumptively excluded with two or more negative virologic tests (one at age  $\geq 2$  weeks and one at age  $\geq 4$  weeks).

**VI: TABLES**

**Table 1: Antiretroviral Regimens for the Prevention of Perinatal Transmission of HIV**

Gestational Age	<32 weeks		≥32 to <34 weeks		≥34 to <37 weeks		≥37 weeks	
Birthweight	Any weight	<1.5 kg	≥1.5 kg	<1.5 kg	≥1.5 kg	<2 kg	≥2 kg	
<b>Low Risk</b>	Zidovudine Monotherapy							
<b>High Risk Presumptive Regimen<sup>a</sup></b>	Zidovudine Monotherapy	Zidovudine + Lamivudine	Zidovudine + Lamivudine + Nevirapine	Zidovudine + Lamivudine	Zidovudine + Lamivudine + Nevirapine	Zidovudine + Lamivudine + Nevirapine	Zidovudine + Lamivudine + Raltegravir	
<b>High Risk 2-Drug Alternative Regimen</b>	Zidovudine + Nevirapine (prophylactic dosing)							

<sup>a</sup> Consider discussing choice of regimen with the National Perinatal HIV hotline, particularly for infants who are unable to receive raltegravir.

**Table 2: Antiretroviral Dosing for the Prevention of Perinatal Transmission of HIV<sup>a,b</sup>**

Drug	Gestational Age	Postnatal Age	Weight	Dose	Frequency
<b>Lamivudine</b>	≥32 weeks	Birth-4 weeks	[Redacted]	2 mg/kg/dose	Q12h
		4-6 weeks		4 mg/kg/dose	Q12h
<b>Nevirapine<sup>c</sup> (prophylactic therapy)</b>	ALL	ALL	1.5-2 kg	8 mg dose	1 <sup>st</sup> dose: within 48h birth 2 <sup>nd</sup> dose: 48h after 1 <sup>st</sup> dose 3 <sup>rd</sup> dose: 96h after 2 <sup>nd</sup> dose
			>2 kg	12 mg dose	
<b>Nevirapine<sup>c</sup> (presumptive therapy)</b>	≥32 to <34 weeks	Birth-2 weeks	[Redacted]	2 mg/kg/dose	Q12h
		2-4 weeks		4 mg/kg/dose	Q12h
		4-6 weeks		6 mg/kg/dose	Q12h
	≥34 to <37 weeks	Birth-1 week		4 mg/kg/dose	Q12h
		1-6 weeks		6 mg/kg/dose	Q12h
	≥37 weeks	Birth-6 weeks		6 mg/kg/dose	Q12h
<b>Raltegravir<sup>d,e</sup></b>	≥37 weeks	Birth-1 week	1.5 mg/kg/dose	Q24h	
		1-4 weeks	3 mg/kg/dose	Q12h	
		4-6 weeks	6 mg/kg/dose	Q12h	
<b>Zidovudine</b>	<30 weeks	Birth-4 weeks	[Redacted]	2 mg/kg/dose	Q12h
		4-6 weeks		3 mg/kg/dose	Q12h
	≥30 to <35 weeks	Birth-2 weeks		2 mg/kg/dose	Q12h
		2-6 weeks		3 mg/kg/dose	Q12h
	≥35 weeks	Birth-6 weeks		4 mg/kg/dose	Q12h

<sup>a</sup> A four-week course of zidovudine is recommended for low-risk infants and a six-week course of zidovudine is recommended for high-risk infant. For high-risk infants on three-drug presumptive therapy, the duration of lamivudine and nevirapine or raltegravir may be up to six weeks and will be determined during outpatient follow-up in the Pediatric Infectious Diseases Clinic

<sup>b</sup> Doses provided are for oral/enteral formulations. If intravenous formulation is required, please discuss dosing adjustments with pharmacist

<sup>c</sup> Not recommended for infants <1.5kg.

<sup>d</sup> Not recommended for infants <2kg.

<sup>e</sup> If the mother has taken raltegravir or raltegravir-containing medication within 2 to 24 hours prior to delivery, the neonate's first dose of **raltegravir only** should be delayed until 24 to 48 hours after birth

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- Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States. Accessed January 23, 2022; pp 1-570.
- Available at [https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Perinatal\\_GL.pdf](https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Perinatal_GL.pdf)

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*The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider's professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.*

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