ANTIRETROVIRAL PROPHYLAXIS & CARE FOR INFANTS BORN TO A PERSON WITH HIV INFECTION

BILL HOLT PEDIATRIC HIV CLINIC GUIDANCE

Disclaimer

This clinical pathway is intended to provide general guidance and should not replace clinical judgment. It is meant to assist licensed practitioners and other health care providers in clinical decision-making by describing a range of generally acceptable approaches to the diagnosis and management of a particular condition. A particular patient's circumstances should always be taken into account when a practitioner is deciding on a course of management.This clinical pathway is current as of the date of publication and will be reviewed periodically to align with any updated best practices or evidence; however, new development may notbe represented in the published version. The treating practitioner assumes all risks associated with care decisions. Phoenix Children's accepts no liability for the content of this clinical pathway or the outcomes a patient might experience where a practitioner consulted the content of this clinical pathway.

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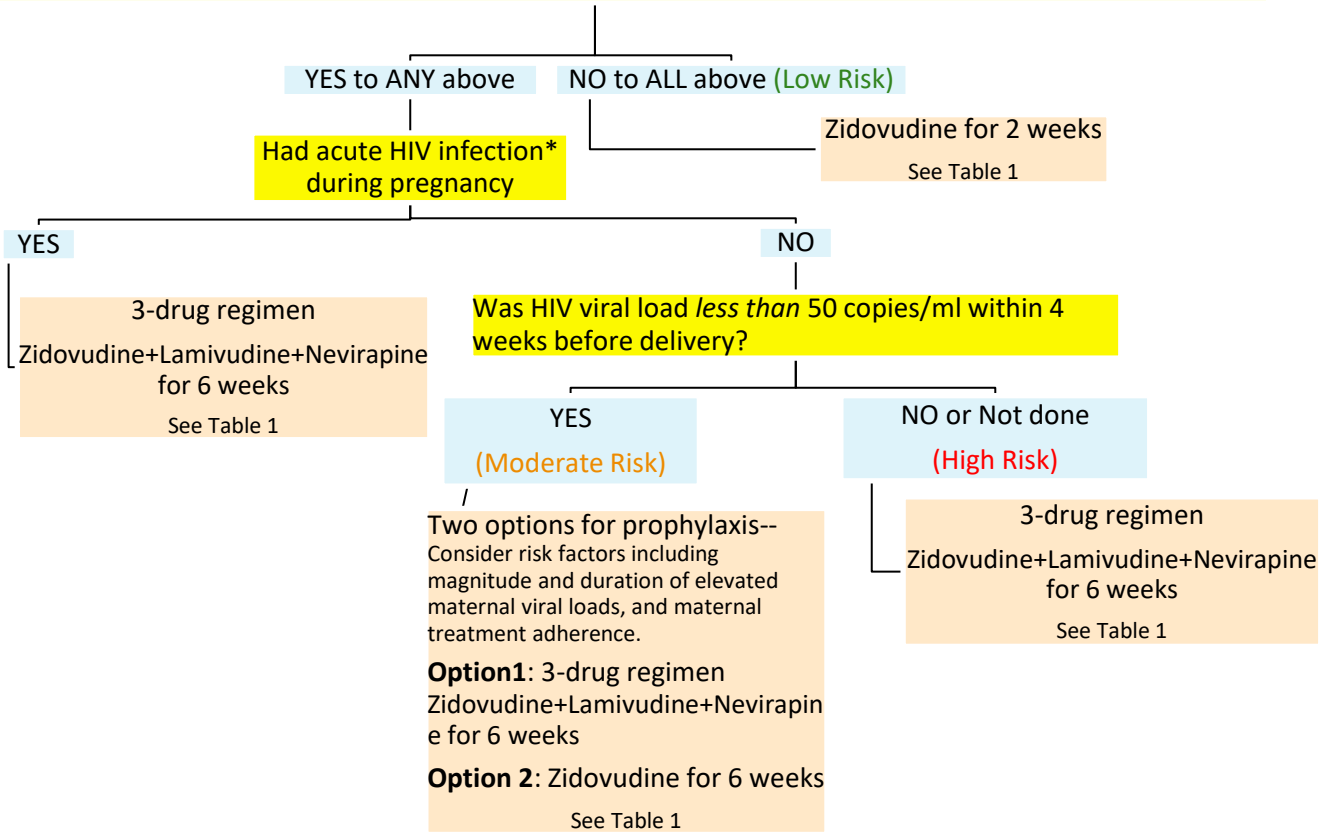
Pathway Flow Diagram

This flow diagram should be followed during the assessment and management of a newborn born to a person with HIV:

Person with HIV:

1. Has not received HIV treatment during pregnancy, *or*
2. Has received only intrapartum HIV treatment, *or*
3. Has received HIV treatment but has HIV viral load ≥50 copies/ml at *any* point after 20 weeks' gestation through delivery, *or*
4. Had acute HIV infection* during pregnancy



THE MEDICATION(S) SHOULD BE STARTED AS SOON AS POSSIBLE, PREFERABLY WITHIN 6 HOURS AFTER BIRTH.
If one or two of the 3-drug regimen are not readily available, initiate the available drug(s) while working with your facility pharmacist to obtain the remainders of the regimen.

*Acute HIV infection (acute retroviral syndrome) presents with fever, enlarged lymph nodes, sore throat, rash, muscle ache, headache, or mucosal ulcers. Some may have no or mild symptoms. HIV viral load is typically very high >100,000 copies/mL.

Scope

To assist in the evaluation and management of an infant born to a person with HIV infection.

Inclusion Criteria:

1. An infant born to a person with confirmed HIV infection
2. An infant born to a person with suspected HIV infection according to the provider's discretion

Exclusion Criteria:

1. An infant born to a person without HIV infection

Pathway Goals

1. Provide up-to-date guidance to providers in the community on the management of perinatally HIV-exposed infants.
2. Advise providers in the community on initiation of perinatal HIV prophylaxis to infants in a timely and accurate manner.
3. Encourage providers in the community to properly discuss appropriate infant feeding, including the option of breastfeeding, with parents.
4. Outline HIV testing schedule for the infant based on specific scenarios.

Key Clinical Recommendations with Evidence Based Supporting Material

1. Perinatal HIV exposure risk assessment

Infants at high risk for HIV infection are those born to a parent who has not received HIV treatment during pregnancy, has received HIV treatment only during labor and delivery, or has received HIV treatment but has unsustained viral suppression (i.e., plasma HIV viral load ≥50 copies/ml) at any point after 20 weeks' gestation through delivery. Unsustained viral suppression (i.e., plasma HIV viral load ≥50 copies/ml) can be either documented or presumed (e.g., new diagnosis of HIV infection, acute HIV infection, or known lapse in treatment adherence). Infants born to a parent who had acute HIV infection during pregnancy are also at high risk for HIV infection. Acute HIV infection (acute retroviral syndrome) occurs among those who recently contracted the virus. They generally present with fever, enlarged lymph nodes, sore throat, rash, muscle ache, headache, and/or mucosal ulcers. Some may have no or mild symptoms. HIV viral load is typically very high >100,000 copies/mL during acute HIV infection.

Infants at low risk for HIV infection are those who do not meet the conditions above. Specifically, the parent has had good adherence to treatment and has had HIV viral loads <50 copies/ml after 20 weeks' gestation including the last 4 weeks prior to delivery. The risk of HIV transmission in this group is estimated to be less than 1%.

Infants at moderate risk for HIV infection are those born to a parent who had HIV viral loads ≥ 50 copies/ml after 20 weeks' gestation but had HIV viral loads <50 copies/mL within 4 weeks prior to delivery.

2. Antiretroviral prophylaxis (Table 1)

Antiretroviral prophylaxis for infants should be started as soon as possible, preferably within 6 hours after birth. If one or two of the 3-drug regimen are not readily available, providers should initiate the available drug(s) while working with the facility pharmacist to obtain the rest of the 3-drug regimen.

Infants in the low risk group are recommended to receive zidovudine monotherapy for 2 weeks. See dosing in Table 1.

Infants in the high risk group are recommended to receive the 3-drug regimen which includes zidovudine, lamivudine and nevirapine. See dosing in Table 1. Although the optimal duration of the 3-drug regimen is unknown, most experts recommend a duration of 6 weeks. The regimen may be adjusted subsequently based on the infant's HIV test results as well as the overall risk of HIV transmission on a case-by-case basis. Consultation with an infectious diseases or HIV specialist is recommended.

Infants in the moderate risk group are recommended to receive either one of the two prophylactic regimens.

Option 1: 3-drug regimen which includes zidovudine, lamivudine and nevirapine

Option 2: Zidovudine monotherapy for 6 weeks

Factors such as the magnitude and duration of elevated HIV viral loads and treatment adherence of the parent as well as parental input should be included in decision-making when selecting the prophylactic option. Consultation with an infectious diseases or HIV specialist is recommended.

3. HIV testing (Table 2)

HIV-exposed infants should receive virologic diagnostic testing using either HIV RNA or DNA PCR. Both RNA PCR and DNA PCR are generally equally recommended. HIV antibody and HV antigen/antibody tests should not be used in this setting.

The PCR test should be performed at birth, 2-3 weeks, 1-2 months, and 4-6 months of age. Testing at birth may not be necessary for the low-risk infants. See Table 2.

For infants receiving the 3-drug regimen, an additional HIV PCR testing is recommended at 2-3 months of age when the infant has completed the prophylactic regimen for at least 2 weeks. See Table 2. Infants on the 3-drug regimen should be monitored for anemia and neutropenia at 2-3 weeks and 1-2 months of age while on the prophylactic regimen.

For the low-risk infants who are being breastfed, HIV PCR test should be performed at birth, 2-3 weeks, 1-2 months, and 4-6 months of age. An additional testing is recommended if the gap between the tests at 1-2 months and 4-6 months is more than 3 months. If breastfeeding continues beyond 6 months of age, PCRs should be performed every 2-3 months during breastfeeding. In addition, PCRs should be performed at 4-6 weeks and 4-6 months after cessation of breastfeeding, irrespective of when breastfeeding ends. See Table 2.

4. Infant feeding

Avoidance of breastfeeding is the only infant feeding option with zero risk of HIV transmission. However, parents with HIV infection may express a desire to breastfeed. The risk of HIV transmission via breastfeeding from a parent who is receiving antiretroviral treatment and has sustained viral suppression is estimated to be less than 1%. Thus, providers should be prepared to offer a family-centered, nonjudgmental and safe approach to parents who desire breastfeeding. See Infant Feeding diagram.

Breastfeeding should be supported for parents who strongly desire to breastfeed after proper counseling if all the following criteria are met:

a. HIV treatment was initiated early in or before pregnancy.
b. There is evidence of sustained viral suppression in the parent (i.e., HIV viral loads <50 copies/mL).
c. The parent demonstrates a commitment to taking their own medication and to giving infant antiretroviral prophylaxis.

d. The parent has continuous access to treatment.

Providers should recommend the following strategies to reduce the risk of HIV transmission via breastfeeding:

a. Exclusive breastfeeding (no formula or other foods) during the first 6 months.
b. The parent continues to take HIV treatment to maintain undetectable HIV viral loads throughout the duration of breastfeeding.
c. Regular assessment of parent's HIV viral loads every 1-2 months.
d. Infant antiretroviral prophylaxis in consultation with an infectious diseases/HIV specialist.
e. Gradual weaning of breastfeeding should occur over a 2-4 week period.

Breastfeeding is not recommended for parents who are not on antiretroviral treatment, who do not take the medication consistently, who do not have sustained undetectable HIV viral loads <50 copies/mL, or who are newly diagnosed with HIV during pregnancy or postpartum.

There may be other specific or unique scenarios not included in this guidance. Please consult an infectious diseases/HIV specialist for any questions or concerns.

Medication Recommendations

Table 1: Antiretroviral Drug Dosing for Infants for Perinatal HIV Prophylaxis

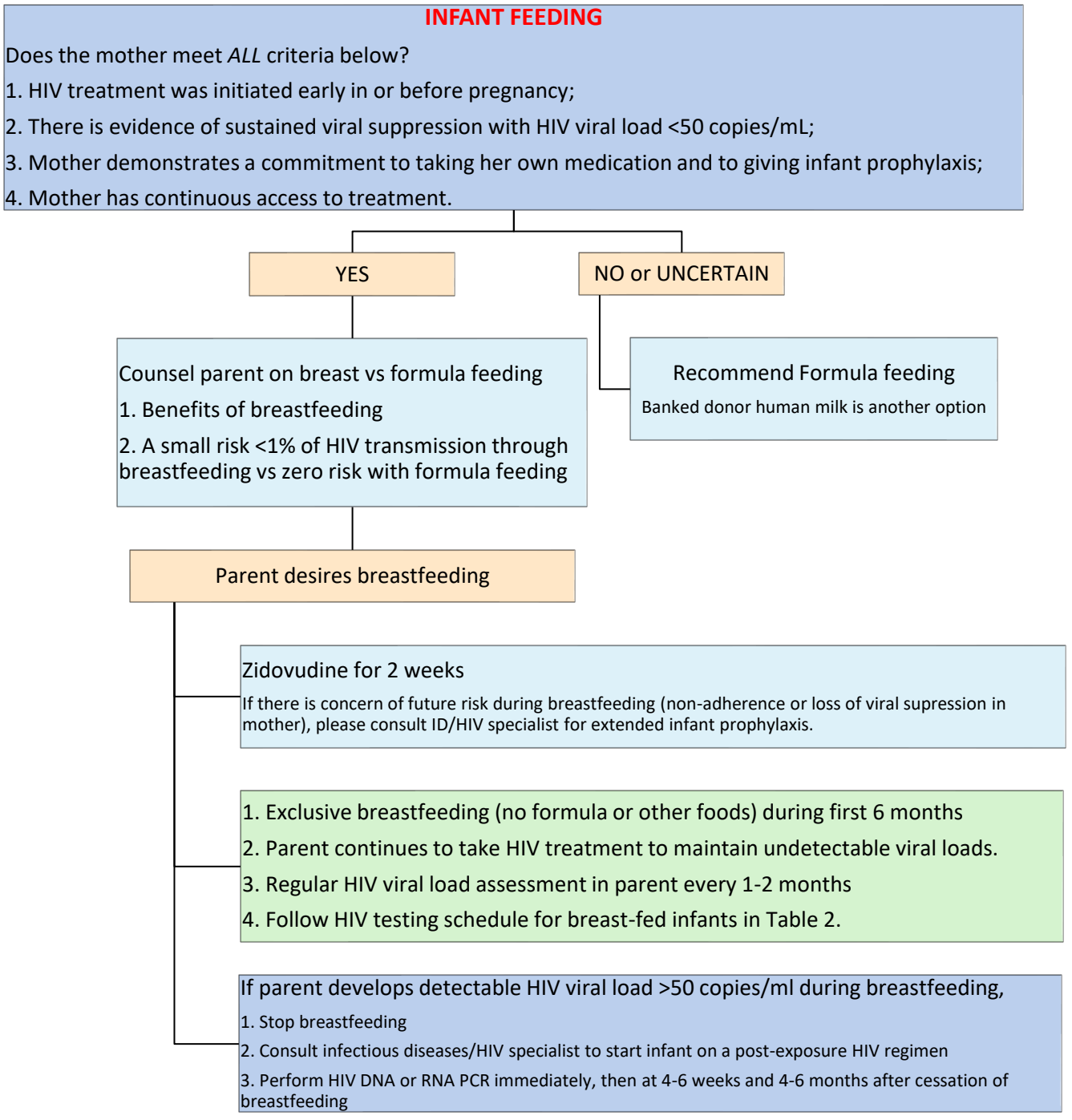
Drug	Drug Doses by Gestational Age at Birth
Zidovudine If oral or enteral route is not feasible, IV zidovudine can be given at 75% of oral doses.	**≥35 Weeks Gestation at Birth** *Birth to Age ≤6 Weeks* • 4 mg/kg per dose orally twice daily
	≥30 to <35 Weeks' Gestation at Birth *Birth to Age 2 Weeks* • 2 mg/kg per dose orally twice daily *Age 2 Weeks to ≤6 Weeks* • 3 mg/kg per dose orally twice daily
	<30 Weeks' Gestation at Birth *Birth to Age 4 Weeks* • 2 mg/kg per dose orally twice daily *Age 4 Weeks to ≤6 Weeks* • 3 mg/kg per dose orally twice daily
Lamivudine No IV formulation	**≥32 Weeks' Gestation at Birth** *Birth to Age <4 Weeks* • 2 mg/kg per dose orally twice daily Age **≥***4 Weeks to ≤6 Weeks* • 4 mg/kg per dose orally twice daily
	Consult Infectious Diseases or HIV specialist at Phoenix Children's Hospital for infants <32 weeks' gestation
Nevirapine No IV formulation	**≥37 Weeks' Gestation at Birth** *Birth to Age ≤6 Weeks* • 6 mg/kg per dose orally twice daily

	≥34 to <37 Weeks' Gestation at Birth *Birth to Age <1 Week* • 4 mg/kg per dose orally twice daily *Age ≥1 Week to ≤6 Weeks* • 6 mg/kg per dose orally twice daily
	≥32 to <34 Weeks' Gestation at Birth *Birth to Age <2 Weeks* • 2 mg/kg per dose orally twice daily *Age ≥2 Weeks to <4 Weeks* • 4 mg/kg per dose orally twice daily *Age ≥4 Weeks to ≤6 Weeks* • 6 mg/kg per dose orally twice daily
	Consult Infectious Diseases or HIV specialist at Phoenix Children's Hospital for infants <32 weeks' gestation
Although Raltegravir is another option if nevirapine cannot be used, it may be difficult to obtain through pharmacies and is more difficult to prepare by parent. Raltegravir may be considered if birthing parent had drug resistance to nevirapine or non-nucleoside reverse transcriptase inhibitors (NNRTI) or has HIV-2 infection (rare in the US).	

HIV Testing Recommendations

Table 2: HIV Testing for Infants

CHRONOLOGICAL AGE	TEST	NOTE
HIGH- and MODERATE RISK INFANT		
Birth	HIV RNA PCR or HIV DNA PCR	HIV RNA PCR or HIV DNA PCR is generally equally recommended. Some experts consider both tests for high-risk infants.
2-3 weeks	HIV RNA PCR or HIV DNA PCR CBC with differential	
1-2 months	HIV RNA PCR or HIV DNA PCR CBC with differential	
2-3 months	HIV RNA PCR or HIV DNA PCR	
4-6 months	HIV RNA PCR or HIV DNA PCR	
LOW-RISK INFANT		
2-3 weeks	HIV RNA PCR or HIV DNA PCR	HIV testing at birth is optional. HIV RNA PCR or HIV DNA PCR is generally equally recommended.
1-2 months	HIV RNA PCR or HIV DNA PCR	
4-6 months	HIV RNA PCR or HIV DNA PCR	
BREAST-FED INFANT		
Birth	HIV RNA PCR or HIV DNA PCR	HIV RNA PCR or HIV DNA PCR is generally equally recommended. Some experts consider both tests for high-risk infants.
Subsequent testing is based on risk above	HIV RNA PCR or HIV DNA PCR	
• An additional testing is needed if the gap between the tests at 1-2 months and 4-6 months is >3 months. • If breastfeeding continues beyond 6 months of age, PCRs should be performed every 2-3 months during breastfeeding. • In addition to the testing time points above, PCRs also should be performed at 4-6 weeks and 4-6 months after cessation of breastfeeding, irrespective of when breastfeeding ends.		


INFANT FEEDING
Does the mother meet *ALL* criteria below?
1. HIV treatment was initiated early in or before pregnancy;
2. There is evidence of sustained viral suppression with HIV viral load <50 copies/mL;
3. Mother demonstrates a commitment to taking her own medication and to giving infant prophylaxis;
4. Mother has continuous access to treatment.
YES
NO or UNCERTAIN
Counsel parent on breast vs formula feeding
1. Benefits of breastfeeding
2. A small risk <1% of HIV transmission through breastfeeding vs zero risk with formula feeding
Recommend Formula feeding
Banked donor human milk is another option
Parent desires breastfeeding
Zidovudine for 2 weeks
If there is concern of future risk during breastfeeding (non-adherence or loss of viral supression in mother), please consult ID/HIV specialist for extended infant prophylaxis.
1. Exclusive breastfeeding (no formula or other foods) during first 6 months
2. Parent continues to take HIV treatment to maintain undetectable viral loads.
3. Regular HIV viral load assessment in parent every 1-2 months
4. Follow HIV testing schedule for breast-fed infants in Table 2.
If parent develops detectable HIV viral load >50 copies/ml during breastfeeding,
1. Stop breastfeeding
2. Consult infectious diseases/HIV specialist to start infant on a post-exposure HIV regimen
3. Perform HIV DNA or RNA PCR immediately, then at 4-6 weeks and 4-6 months after cessation of breastfeeding

Patient and Family Education/Discharge Planning

1. Providers should call the Bill Holt HIV Clinic at Phoenix Children's (Tel 602-933-0955, M-F 9:00 AM-4:30 PM) to schedule a 2-week follow-up visit BEFORE discharge.
2. Parent/Guardian must have the infant's medication bottle(s) with enough supply BEFORE discharge. Providers may request assistance from their facility pharmacist on this matter.
3. A primary pediatrician has been selected for the infant for well childcare and vaccination BEFORE discharge; Bill Holt Clinic is a specialty clinic and does not provide well childcare or vaccination.
4. Our team at Bill Holt HIV Clinic is available for consultation with medical providers and families.

BILL HOLT HIV CLINIC INFORMATION:

Location: Phoenix Children's Ambulatory Building, Second Floor
1919 E Thomas Road
Phoenix, AZ 85016
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Our website

Our team: Chokechai Rongkavilit, MD (also known as Dr. Chai)
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After hours & weekends: (602) 290-3212

Specialty Pharmacies that carry HIV drugs:

Walgreens Specialty Pharmacy
2302 N. Central Ave, Phoenix AZ 85004, Tel (602) 313-2042

CVS Specialty Pharmacy
1002 E. McDowell Rd, Phoenix AZ 85006, Tel (602) 258-7051

Mail-Meds: Tel (602) 609-2912

References

1. Bekker A, Mirochnick M, Clarke DF, et al. Lamivudine dosing for preterm infants exposed to HIV: a population pharmacokinetic modelling and simulation study. *J Antimicrob Chemother* 2024;76:2570-4. https://doi.org/10.1093/jac/dkae259.
2. Bekker A, Hanan N, Violari A, et al. Population pharmacokinetics of nevirapine in preterm infants and prediction of doses needed for treatment. *International Workshop on HIV Pediatrics*, 2019.
3. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States, 2024. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new . Accessed date: December 21, 2024.
4. Abuogi L, Noble L, Smith C. Infant feeding for persons living with and at risk for HIV in the United States: Clinical report. *Pediatrics* 2024;153: e2024066843. https://doi.org/10.1542/peds.2024-066843

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Approved by Pharmacy & Therapeutics Committee: January 2025

Approved by Clinical Effectiveness Committee: February, 2025