

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

(Last updated **December 30, 2021**; last reviewed **December, 30 2021**)

Panel's Recommendations

- All newborns who were exposed perinatally to HIV should receive postpartum antiretroviral (ARV) drugs to reduce the risk of perinatal transmission of HIV **(AI)**.
- Newborn ARV regimens administered at doses that are appropriate for the infant's gestational age should be initiated as close to the time of birth as possible, preferably within 6 hours of delivery **(AII)**.
- A newborn's ARV regimen should be determined based on maternal and infant factors that influence the risk of perinatal transmission of HIV **(AII)**. The uses of ARV regimens in newborns include the following:
 - **ARV Prophylaxis:** The administration of one or more ARV 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 ARV 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.
 - **HIV Therapy:** The administration of a three-drug ARV regimen at treatment doses (called antiretroviral therapy [ART]) to newborns with documented HIV infection (see [Diagnosis of HIV Infection in Infants and Children](#)).
- A 4-week zidovudine (ZDV) ARV prophylaxis regimen can be used in newborns whose mothers received ART during pregnancy and had viral suppression **within 4 weeks prior to** delivery (defined as a confirmed HIV RNA level <50 copies/mL) and for whom maternal adherence is not of concern **(BII)**.
- Newborns at high risk of perinatal acquisition of HIV should begin presumptive HIV therapy (see Table 9 for recommended regimens). Newborns at high risk of HIV acquisition include those born to people with HIV who—
 - Have not received antepartum ARV drugs **(AI)**, *or*
 - Have received only intrapartum ARV drugs **(AI)**, *or*
 - Have received antepartum ARV drugs but who did not achieve viral suppression (defined as a confirmed HIV RNA level <50 copies/mL) **within 4 weeks of delivery** **(AII)**, *or*
 - Have primary or acute HIV infection during pregnancy **(AII)**.
- Presumptive HIV therapy should be administered to infants of mothers who have primary or acute HIV infection while breastfeeding **(AII)**.
- If a patient presents with unknown HIV status and has a positive expedited HIV test during labor or shortly after delivery, the infant should begin presumptive HIV therapy **(AII)**. If supplemental maternal testing is negative, the infant's ARV regimen should be discontinued **(AII)**.
- For newborns with HIV infection, ART should be initiated **(AI)**.
- The use of ARV drugs other than ZDV, lamivudine, and nevirapine cannot be recommended for any indication in premature newborns (<37 weeks gestational age) because of the lack of dosing and safety data **(BII)**.
- Providers with questions about ARV management of perinatal HIV exposure should consult the [National Perinatal HIV Hotline](#) (1-888-448-8765), which provides free clinical consultation on all aspects of perinatal HIV, including newborn care **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

General Considerations for Antiretroviral Management of Newborns Exposed to HIV or Born with HIV

All newborns with perinatal exposure to HIV should receive antiretroviral (ARV) drugs during the neonatal period to reduce the risk of perinatal HIV transmission, with selection of the appropriate ARV regimen guided by the level of transmission risk. HIV transmission can occur *in utero*, intrapartum, or during breastfeeding.

Maternal viral load is the most important risk factor for HIV transmission to a newborn. Newborns are at an increased risk for transmission when their mothers do not receive antiretroviral therapy (ART) during pregnancy, when mothers start antepartum treatment late in pregnancy, or when antepartum treatment does not result in viral suppression (defined as a confirmed HIV RNA level <50 copies/mL). Higher maternal viral load, especially in late pregnancy, correlates with higher risk of transmission. A spectrum of transmission risk depends on these and other maternal and infant factors, including mode of delivery, gestational age at delivery, and maternal health status.

Historically, the use of ARV drugs in the newborn period was referred to as ARV prophylaxis because it primarily focused on protection against newborn perinatal acquisition of HIV. More recently, clinicians have begun to identify newborns at highest risk for HIV acquisition and initiate three-drug ARV regimens as presumptive treatment of HIV. In this section, the following terms will be used:

- **ARV Prophylaxis:** The administration of ARV drugs to a newborn without documented HIV infection to reduce the risk of HIV acquisition. ARV prophylaxis includes administration of a single agent—usually zidovudine (ZDV)—as well as combinations of two or three ARV drugs.
- **Presumptive HIV Therapy:** The administration of a three-drug ARV regimen to newborns at highest risk of HIV acquisition. Presumptive HIV therapy is intended to be early treatment for a newborn who is later documented to have acquired HIV, but it also serves as ARV 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.
- **HIV Therapy:** The administration of a three-drug ARV regimen to newborns with documented HIV infection (see [Diagnosis of HIV Infection in Infants and Children](#)).

The terms ARV prophylaxis and presumptive HIV therapy describe the clinician's intent when prescribing ARV drugs, which may lead to an overlap between these two terms. For example, a presumptive HIV therapy regimen also provides ARV prophylaxis for a newborn. However, two-drug (or sometimes three-drug) ARV prophylaxis regimens, notably those that use prophylactic doses rather than therapeutic doses of nevirapine (NVP), are not considered presumptive HIV therapy.

The interval during which newborn ARV prophylaxis or presumptive HIV therapy can be initiated and still be beneficial is undefined; however, most studies support providing ARV drugs as early as possible after delivery.¹⁻⁶

Table 8 provides an overview of neonatal ARV management recommendations according to the risk of perinatal HIV transmission to the newborn, and Table 9 summarizes the recommendations for ARV drug dosing in newborns. Additional information about dose selection for newborns, including premature infants (<37 weeks' gestational age), can be found in the [Pediatric Antiretroviral Guidelines](#). Information about infants born to people with HIV-2 infection is available in [HIV-2 Infection and Pregnancy](#) and Table 8. In addition, the [National Perinatal HIV Hotline](#) (1-888-448-8765) is a federally funded service that provides free clinical consultation on difficult cases to providers who are caring for pregnant people with HIV and their newborns, and consultants can provide referrals to local or regional pediatric HIV specialists.

Table 8. Neonatal Antiretroviral Management According to Risk of HIV Infection in the Newborn

Drug selection and dosing considerations are related to the age and gestational age of the newborn. Consultation is available through the [National Perinatal HIV Hotline](#) (1-888-448-8765).

Level of Perinatal HIV Transmission Risk	Description	Neonatal ARV Management
Low Risk of Perinatal HIV Transmission	Mothers who received ART during pregnancy with viral suppression (defined as a confirmed HIV RNA level <50 copies/mL) within 4 weeks prior to delivery and no concerns related to adherence	ZDV for 4 weeks ^a
High Risk of Perinatal HIV Transmission ^{a,b}	<p>Mothers who did not receive antepartum ARV drugs</p> <p>Mothers who received only intrapartum ARV drugs</p> <p>Mothers who received antepartum ARV drugs but did not have viral suppression (defined as a confirmed HIV RNA level <50 copies/mL) within 4 weeks prior to delivery</p> <p>Mothers with acute or primary HIV infection during pregnancy or breastfeeding (in which case, the mother should immediately discontinue breastfeeding)^c</p>	Presumptive HIV therapy using either ZDV, 3TC, and NVP (treatment dose) <i>or</i> ZDV, 3TC, and RAL administered from birth up to 6 weeks ^d
Presumed Newborn HIV Exposure	<p>Mothers with unconfirmed HIV status who have at least one positive HIV test at delivery or postpartum</p> <p><i>or</i></p> <p>Mothers whose newborns have a positive HIV antibody test</p>	<p>ARV management as described above for newborns with a high risk of perinatal HIV transmission</p> <p>Infant ARV drugs should be discontinued immediately if supplemental testing confirms that the mother does not have HIV.</p>

Level of Perinatal HIV Transmission Risk	Description	Neonatal ARV Management
Newborn with HIV ^e	Positive newborn HIV virologic test/NAT	Three-drug ARV regimen using treatment doses. Refer to the What to Start in the Pediatric Antiretroviral Guidelines for specific treatment recommendations.

^a ZDV prophylaxis regimen is recommended for infants born to mothers with HIV-2 mono-infection, see [HIV-2 Infection and Pregnancy](#). If the mother has HIV-1 and HIV-2 infection, the infant ARV regimen should be based on the determination of low or high risk of HIV-1 transmission as described in the above table. Because HIV-2 is not susceptible to NVP, RAL should be considered for infants at high risk of perinatal HIV-2 transmission. See text for evidence that supports the use of presumptive HIV therapy and a two-drug ARV prophylaxis regimen.

^b See [Intrapartum Care for People with HIV](#) for guidance on indications for scheduled cesarean delivery and intrapartum intravenous ZDV to reduce the risk of perinatal HIV transmission for mothers with an elevated viral load at delivery.

^c Most Panel members would opt to administer presumptive HIV therapy to infants whose mothers had acute HIV during pregnancy because of the higher risk for *in utero* transmission. If acute HIV is diagnosed during breastfeeding, the mother should immediately discontinue breastfeeding.

^d The optimal duration of presumptive HIV therapy in newborns who are at a high risk for perinatal HIV transmission is unknown. If possible, newborns who are at a high risk for HIV acquisition should receive ZDV for 6 weeks. Additional medications—such as 3TC, RAL, or NVP—may need to be administered for 2 to 6 weeks; the recommended duration for these drugs varies depending on infant HIV NAT results, maternal viral load at the time of delivery, and additional risk factors for HIV transmission. Consultation with an expert in pediatric HIV is recommended when selecting a therapy duration because this decision should be based on case-specific risk factors and interim infant HIV NAT results. The two-drug regimen used in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development–HIV Prevention Trials Network (HPTN) 040/Pediatric AIDS Clinical Trials Group (PACTG) 1043 for infants who were at a high risk for HIV acquisition is described in the text (see the Two-Drug Antiretroviral Prophylaxis section).

^e Infant ART should be initiated without waiting for the results of confirmatory HIV NAT testing, given the low likelihood of a false-positive HIV NAT. However, the specimen for confirmatory HIV testing should be obtained prior to ART initiation.

Note: ARV drugs should be initiated as close to the time of birth as possible, preferably within 6 hours of delivery. See Table 9 for dosing specifics.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; NAT = nucleic acid test; NVP = nevirapine; Panel = Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission; RAL = raltegravir; ZDV = zidovudine

Table 9. Antiretroviral Drug Dosing Recommendations for Newborns^a

Newborns at Low Risk of Perinatal HIV Transmission	
Recommended Regimen	Recommended Duration
ZDV	ZDV administered for 4 weeks at the doses listed below.
Newborns at High Risk of Perinatal HIV Transmission	
Recommended Regimen	Recommended Duration
Three-drug HIV therapy: ZDV plus 3TC plus (NVP <i>or</i> RAL)	ZDV administered for 6 weeks, with no increase to the 12-mg/kg dose unless the infant has confirmed HIV infection (see ZDV dosing recommendations below). Dosing for 3TC, NVP, and RAL is described below.
Newborns with HIV Infection	
Recommended Regimen	Lifelong Duration Recommended ^b
Refer to Pediatric Antiretroviral Guidelines for specific treatment recommendations.	Lifelong therapy in accordance with current treatment guidelines. The ARV regimen should be individualized based on the infant's age and clinical determinants. Refer to the Pediatric Antiretroviral Guidelines for specific treatment recommendations.

Drug	Drug Doses by Gestational Age at Birth								
<p>ZDV</p> <p>Note: For newborns who are unable to tolerate oral agents, the IV dose is 75% of the oral dose while maintaining the same dosing interval.</p>	<p>≥35 Weeks' Gestation at Birth</p> <p><i>Birth to Age 4 Weeks:</i></p> <ul style="list-style-type: none"> ZDV 4 mg/kg per dose orally twice daily <p><i>Age >4 Weeks:</i></p> <ul style="list-style-type: none"> ZDV 12 mg/kg per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection. <p>Simplified Weight-Band Dosing for Newborns Aged ≥35 Weeks' Gestation from Birth to 4 Weeks</p> <table border="1"> <thead> <tr> <th>Weight Band</th> <th>Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</th> </tr> </thead> <tbody> <tr> <td>2 to <3 kg</td> <td>1 mL</td> </tr> <tr> <td>3 to <4 kg</td> <td>1.5 mL</td> </tr> <tr> <td>4 to <5 kg</td> <td>2 mL</td> </tr> </tbody> </table>	Weight Band	Volume of ZDV 10 mg/mL Oral Syrup Twice Daily	2 to <3 kg	1 mL	3 to <4 kg	1.5 mL	4 to <5 kg	2 mL
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	<p>≥30 to <35 Weeks' Gestation at Birth</p> <p><i>Birth to Age 2 Weeks</i></p> <ul style="list-style-type: none"> ZDV 2 mg/kg per dose orally twice daily <p><i>Age 2 Weeks to 6 to 8 Weeks</i></p> <ul style="list-style-type: none"> ZDV 3 mg/kg per dose orally twice daily <p><i>Age >6 to 8 Weeks</i></p> <ul style="list-style-type: none"> ZDV 12 mg/kg per dose orally twice daily; make this dose increase only for infants with confirmed HIV infection. 								

	<p><30 Weeks' Gestation at Birth</p> <p><i>Birth to Age 4 Weeks</i></p> <ul style="list-style-type: none"> • ZDV 2 mg/kg per dose orally twice daily <p><i>Age 4 to 8 to 10 Weeks</i></p> <ul style="list-style-type: none"> • ZDV 3 mg/kg per dose orally twice daily <p><i>Age >8 to 10 Weeks</i></p> <ul style="list-style-type: none"> • ZDV 12 mg/kg per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection
<p>ABC^c</p> <p>Note: ABC is not approved by the FDA for use in neonates and infants aged <1 month. However, dosing recommendations have been modeled using PK simulation.</p>	<p>≥37 Weeks' Gestation at Birth</p> <p><i>Birth to 1 Month:</i></p> <ul style="list-style-type: none"> • ABC 2 mg/kg per dose orally twice daily <p><i>Age 1 Month to <3 Months:</i></p> <ul style="list-style-type: none"> • ABC 4 mg/kg per dose orally twice daily
3TC	<p>≥32 Weeks' Gestation at Birth</p> <p><i>Birth to Age 4 Weeks</i></p> <ul style="list-style-type: none"> • 3TC 2 mg/kg per dose orally twice daily <p><i>Age >4 Weeks</i></p> <ul style="list-style-type: none"> • 3TC 4 mg/kg per dose orally twice daily
NVP ^d	<p>≥37 Weeks' Gestation at Birth</p> <p><i>Birth to Age 4 Weeks</i></p> <ul style="list-style-type: none"> • NVP 6 mg/kg per dose orally twice daily <p><i>Age >4 Weeks</i></p> <ul style="list-style-type: none"> • NVP 200 mg/m² BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection. <p>≥34 to <37 Weeks' Gestation at Birth</p> <p><i>Birth to Age 1 Week</i></p> <ul style="list-style-type: none"> • NVP 4 mg/kg per dose orally twice daily <p><i>Age 1 to 4 Weeks</i></p> <ul style="list-style-type: none"> • NVP 6 mg/kg per dose orally twice daily <p><i>Age >4 Weeks</i></p> <ul style="list-style-type: none"> • NVP 200 mg/m² BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection. <p>≥32 to <34 Weeks' Gestation at Birth</p> <p><i>Birth to Age 2 Weeks</i></p> <ul style="list-style-type: none"> • NVP 2 mg/kg per dose orally twice daily <p><i>Age 2 to 4 Weeks</i></p> <ul style="list-style-type: none"> • NVP 4 mg/kg per dose orally twice daily <p><i>Age 4 to 6 Weeks</i></p> <ul style="list-style-type: none"> • NVP 6 mg/kg per dose orally twice daily <p><i>Age >4 Weeks</i></p>

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RAL Note: If the mother has taken RAL 2 to 24 hours prior to delivery, the neonate's first dose of RAL should be delayed until 24 to 48 hours after birth; additional ARV drugs should be started as soon as possible. ⁷	<p>≥37 Weeks' Gestation at Birth and Weighing ≥2 kg^e</p> <p><i>Birth to Age 6 Weeks</i></p> <table border="1"> <thead> <tr> <th>Body Weight</th> <th>Volume (Dose) of RAL 10 mg/mL Suspension</th> </tr> </thead> <tbody> <tr> <td colspan="2">Birth to 1 Week: Once-Daily Dosing</td> </tr> <tr> <td></td> <td>Approximately 1.5 mg/kg per dose</td> </tr> <tr> <td>2 to <3 kg</td> <td>0.4 mL (4 mg) once daily</td> </tr> <tr> <td>3 to <4 kg</td> <td>0.5 mL (5 mg) once daily</td> </tr> <tr> <td>4 to <5 kg</td> <td>0.7 mL (7 mg) once daily</td> </tr> <tr> <td colspan="2">1 to 4 Weeks: Twice-Daily Dosing</td> </tr> <tr> <td></td> <td>Approximately 3 mg/kg per dose</td> </tr> <tr> <td>2 to <3 kg</td> <td>0.8 mL (8 mg) twice daily</td> </tr> <tr> <td>3 to <4 kg</td> <td>1 mL (10 mg) twice daily</td> </tr> <tr> <td>4 to <5 kg</td> <td>1.5 mL (15 mg) twice daily</td> </tr> <tr> <td colspan="2">4 to 6 Weeks: Twice-Daily Dosing</td> </tr> <tr> <td></td> <td>Approximately 6 mg/kg per dose</td> </tr> <tr> <td>3 to <4 kg</td> <td>2.5 mL (25 mg) twice daily</td> </tr> <tr> <td>4 to <6 kg</td> <td>3 mL (30 mg) twice daily</td> </tr> <tr> <td>6 to <8 kg</td> <td>4 mL (40 mg) twice daily</td> </tr> </tbody> </table>	Body Weight	Volume (Dose) of RAL 10 mg/mL Suspension	Birth to 1 Week: Once-Daily Dosing			Approximately 1.5 mg/kg per dose	2 to <3 kg	0.4 mL (4 mg) once daily	3 to <4 kg	0.5 mL (5 mg) once daily	4 to <5 kg	0.7 mL (7 mg) once daily	1 to 4 Weeks: Twice-Daily Dosing			Approximately 3 mg/kg per dose	2 to <3 kg	0.8 mL (8 mg) twice daily	3 to <4 kg	1 mL (10 mg) twice daily	4 to <5 kg	1.5 mL (15 mg) twice daily	4 to 6 Weeks: Twice-Daily Dosing			Approximately 6 mg/kg per dose	3 to <4 kg	2.5 mL (25 mg) twice daily	4 to <6 kg	3 mL (30 mg) twice daily	6 to <8 kg	4 mL (40 mg) twice daily
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^a The optimal duration of presumptive HIV therapy in newborns who are at a high risk for perinatal HIV transmission is unknown. If possible, newborns who are at a high risk for HIV acquisition should receive ZDV for 6 weeks. Additional medications—such as 3TC, RAL, or NVP—may need to be administered for 2 to 6 weeks; the recommended duration for these drugs varies based on infant HIV nucleic acid test (NAT) results, maternal viral load at the time of delivery, and additional risk factors for HIV transmission. Consultation with an expert in pediatric HIV is recommended when selecting a therapy duration because this decision should be based on case-specific risk factors and interim infant HIV NAT results. The two-drug regimen used in NICHD-HPTN 040/PACTG 1043 for infants who were at a high risk for HIV acquisition is described in the text (see the Two-Drug Antiretroviral Prophylaxis section).

^b For ARV management after the first 6 weeks of life, see the [Pediatric Antiretroviral Guidelines](#).

^c ABC is approved by the FDA for use in children aged ≥3 months when administered as part of an ARV regimen. ABC also has been reported to be safe in infants and children ≥1 month of age. More recently, an ABC dosing recommendation using PK simulation models has been endorsed by the WHO using weight-band dosing for full-term infants from birth to 1 month of age.

See [Abacavir in Appendix A: Pediatric Antiretroviral Drug Information](#) for additional information about the use of ABC between birth and 1 month of age. At this time, the Panel does not recommend ABC as part of a presumptive HIV therapy regimen. However, in situations where ZDV is not available or the infant has ZDV-associated toxicity, ABC could be considered an alternative to ZDV. This substitution should be considered in circumstances where increased risk of ZDV toxicity may exist, such as in infants with anemia or neutropenia. Because of ABC-associated hypersensitivity, negative testing for HLA-B5701 allele should be confirmed prior to administration of ABC.

^d The NVP doses for infants ≥ 34 to < 37 weeks gestation at birth and infants ≥ 37 weeks gestation at birth are not yet approved by the FDA. The FDA also has not approved a dose of NVP for infants aged < 1 month. The doses for infants ≥ 32 to < 34 weeks gestation at birth are based on modeling and might underestimate potential toxicity in infants of 32 to < 34 weeks gestational age because the doses used to develop the model were lower than the doses now recommended. See the Two-Drug Antiretroviral Prophylaxis section in the text for prophylactic NVP dosing if using the NICHD-HPTN 040/PACTG 1043 prophylaxis regimen. See [Nevirapine in Appendix A: Pediatric Antiretroviral Drug Information](#) for additional information about dosing.

^e RAL dosing is increased at 1 week and 4 weeks of age because metabolism by UGT1A1 is low at birth and increases rapidly during the next 4 to 6 weeks of life. No dosing information is available for preterm infants or infants weighing < 2 kg at birth. In infants with HIV infection, twice-daily RAL can be replaced with once-daily DTG at ≥ 4 weeks of age (see [Dolutegravir](#) and [What to Start](#) in the [Pediatric Antiretroviral Guidelines](#)).

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BSA = body surface area; DTG = dolutegravir; FDA = U.S. Food and Drug Administration; IV = intravenous; NICHD-HPTN 040/PACTG 1043 = *Eunice Kennedy Shriver* National Institute of Child Health and Human Development–HIV Prevention Trials Network 040/Pediatric AIDS Clinical Trials Group 1043; NVP = nevirapine; the Panel = the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission; PK = pharmacokinetic; RAL = raltegravir; UGT = uridine diphosphate glucotransferase; WHO = World Health Organization; ZDV = zidovudine

Recommendations for Antiretroviral Drugs in Specific Clinical Situations

In this section and Table 8, the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission (the Panel) presents available data and recommendations for management of newborns with documented HIV and newborns born to mothers who—

- Received antepartum ARV drugs and achieved effective viral suppression (defined as a confirmed HIV RNA level <50 copies/mL) within 4 weeks prior to delivery
- Are at high risk for transmitting HIV to their newborns, including mothers who—
 - Did not receive antepartum ARV drugs, *or*
 - Received only intrapartum ARV drugs, *or*
 - Received antepartum ARV drugs but do not have effective viral suppression (defined as a confirmed HIV RNA level <50 copies/mL) within 4 weeks prior to delivery
- Had acute or primary HIV infection during pregnancy or breastfeeding
- Have unknown HIV status
- Have known ARV drug-resistant virus

Newborns Born to Mothers Who Achieved Viral Suppression on Antepartum Antiretroviral Drugs

The risk of HIV acquisition in newborns born to people who received ART during pregnancy and labor and who had undetectable viral load near or at the time of delivery is <1%. In the Pediatric AIDS Clinical Trials Group (PACTG) 076 study, ZDV alone reduced the incidence of perinatal HIV transmission by 66%, and ZDV is recommended as prophylaxis for neonates whose mothers received ART that resulted in consistent viral suppression during pregnancy.⁸ The optimal minimum duration of neonatal ZDV prophylaxis has not been established in clinical trials. A 6-week ZDV regimen was studied in newborns in PACTG 076. However, the evidence that supports a reduced duration of ZDV prophylaxis in infants born to women who were suppressed virologically during pregnancy and at the time of delivery is mounting.⁹⁻¹¹ In the United Kingdom and many other European countries, a 2-week neonatal ZDV prophylaxis regimen is recommended for infants born to women who have a very low risk of HIV transmission. These women have been on ART for longer than 10 weeks and have had at least two documented maternal HIV viral loads <50 copies/mL at least 4 weeks apart and have viral loads <50 copies/mL at or after 36 weeks' gestation. A 4-week course of ZDV is recommended¹² if any of these criteria are not fulfilled but the maternal viral load is <50 copies/mL at or after 36 weeks' gestation. Compared with the 6-week ZDV regimen, 2 to 4 weeks on this regimen has been reported to allow earlier recovery from anemia in otherwise healthy newborns.^{13,14} The Swiss Federal Office of Public Health does not recommend infant ARV prophylaxis for infants of women with regular follow-up, ART use during pregnancy, and where maternal viral load is <50 copies/mL, ideally sustained throughout pregnancy, but at least at the last two consecutive measurements before delivery where viral load testing is performed at least 4 weeks apart and the last viral load is measured after week 36 of pregnancy.¹⁵

Currently, the Panel recommends a 4-week neonatal ZDV prophylaxis regimen for newborns if the mother achieved viral suppression (defined as a confirmed HIV RNA level <50 copies/mL) on ART during pregnancy within 4 weeks of delivery and maternal adherence is not of concern. Some Panel

members are supportive of the shorter 2-week ZDV regimen, as recommended by the British HIV Association and implemented in the United Kingdom and other European countries, in cases where there is very low risk of HIV transmission as defined above. Dosing recommendations for ZDV are available for premature newborns, and an intravenous preparation of ZDV is available. Table 9 shows recommended neonatal ZDV dosing based on gestational age and birthweight.

Newborns Born to Mothers Who Received No Antepartum Antiretroviral Drugs, Who Received Intrapartum Antiretroviral Drugs Only, Who Received Antiretroviral Drugs and Were Not Virally Suppressed Near Delivery, or Who Acquired HIV During Pregnancy or Breastfeeding

The Panel recommends that all newborns born to mothers who do not have viral suppression (defined as a confirmed HIV RNA level <50 copies/mL) within 4 weeks prior to delivery, who received only intrapartum ARV drugs, or who received no ARV drugs during pregnancy are at high risk for HIV acquisition and **should receive presumptive HIV therapy**.^{5,16-21} Primary or acute HIV infection during pregnancy also is associated with an increased risk of perinatal transmission of HIV. Infants born to people who acquired HIV during pregnancy **should receive presumptive HIV therapy** (see [Acute HIV Infection](#)). The experience with these two strategies is described below.

Presumptive HIV Therapy

Early effective treatment of HIV infection in infants restricts the viral reservoir size, reduces HIV genetic variability, and modifies the immune response.²²⁻³⁰ Because of these potential benefits of early ART, the Panel recommends a three-drug ARV presumptive HIV therapy regimen consisting of ZDV, lamivudine (3TC), and either NVP (at treatment dose) or raltegravir (RAL) for newborns at high risk of perinatal acquisition of HIV.

Although no clinical trials have compared the safety and efficacy of presumptive ART with single-drug or two-drug regimens, emerging data suggest that early presumptive HIV therapy has not been associated with serious adverse events. In the International Maternal, Pediatric, Adolescent AIDS Clinical Trials (IMPAACT) P1115, 438 neonates who were at least 34 weeks gestational age at birth and enrolled within 48 hours of birth received a presumptive HIV therapy regimen containing two nucleoside reverse transcriptase inhibitors (NRTIs) (97% received ZDV and 3TC) and NVP dosed at 6 mg/kg twice daily for term neonates (≥ 37 weeks gestational age) or 4 mg/kg twice daily for 1 week and 6 mg/kg twice daily therapy for preterm neonates (34 to <37 weeks gestational age). Among the study participants, 7% reported Division of AIDS (DAIDS) Grade 3 or 4 adverse events at least possibly related to ART. These Grade 3 or 4 events included 6% with neutropenia and 1% with anemia.²¹ The Early Infant Treatment Study in Botswana initiated ART consisting of NVP 6 mg/kg twice daily, ZDV, and 3TC at <7 days gestational age in 40 infants who were ≥ 35 weeks gestational age and ≥ 2 kg at birth with HIV infection. Eighteen percent of these infants had Grade 3 or 4 hematologic toxicity, mostly neutropenia.³¹ Similar findings have been reported from other smaller studies of presumed HIV therapy or early treatment of confirmed HIV infection.³¹⁻³³ In a prospective cohort in Thailand, infants who received a presumptive HIV therapy regimen that contained ZDV, 3TC, and NVP were more likely to have Grade 2 or higher anemia at 1 and 2 months of life compared with infants who received ZDV alone (48.5% vs. 32.3%; $P = 0.02$). However, no difference was found in the incidence of severe anemia (Grade 3) between the two groups.³⁴ Additionally, in a Canadian study, nonspecific signs and symptoms (e.g., vomiting, diarrhea, rash, jitteriness, irritability) that were potentially attributable to medication-related adverse effects were

reported among the newborns who received presumptive HIV therapy but not among those who received ZDV only (10.2% vs. 0%; $P < 0.001$). Infants were more likely to discontinue presumptive HIV therapy prematurely than a regimen of ZDV alone (9.5% vs. 2.1%; $P = 0.01$).³³

The Centers for Disease Control and Prevention recommends a three-drug ARV regimen for HIV-postexposure prophylaxis following occupational and nonoccupational HIV exposure. HIV acquisition risk in these circumstances is often lower than for newborns who are at high risk for HIV acquisition.^{35,36} The pharmacokinetic (PK) and safety data of presumptive HIV therapy have provided reassuring evidence for its use in the neonatal period. Although the use of NVP to prevent perinatal HIV transmission has been found to be safe in neonates and newborns of low birthweight, these prophylaxis-dose regimens target trough drug levels that are at least 10-fold lower than targeted therapeutic levels. However, recent studies of therapeutic doses of NVP and RAL have established safe doses that achieve targeted PK parameters.³⁷⁻⁴²

At this time, if a presumptive HIV therapy regimen is required, the Panel recommends using a combination of ZDV, 3TC, and NVP (treatment dose) or ZDV, 3TC, and RAL (see Table 8 and Table 9). The optimal duration of presumptive HIV therapy in newborns at high risk of perinatal HIV transmission is unknown. Some Panel members opt to discontinue additional medications if infant birth nucleic acid test (NAT) results are negative, whereas others would continue presumptive HIV therapy for 2 to 6 weeks depending on the risk of HIV transmission. In all cases, ZDV should be continued for 6 weeks. If HIV infection is confirmed and the infant is receiving NVP, NVP should be replaced with an integrase strand transfer inhibitor or a boosted protease inhibitor. Information about selecting an agent and recommended dosing can be found in [What to Start in the Pediatric Antiretroviral Guidelines](#).

New dosing recommendations for abacavir (ABC) in neonates based on IMPAACT P1106 trial and two observational European and African cohorts are now available from the World Health Organization (WHO). ABC is not approved by the U.S. Food and Drug Administration (FDA) for use in neonates and infants aged <3 months. However, a 2 mg/kg per dose twice-daily dose has been modeled using PK simulation and is endorsed by WHO using weight-band dosing for full-term infants from birth through 1 month of age. Limited observational data suggested safety of ABC when initiated in neonates <1 month of age (see [Abacavir](#) in the [Pediatric Antiretroviral Guidelines](#)). At this time, the Panel does not recommend ABC as part of a presumptive HIV therapy regimen. However, in situations where ZDV is not available or the infant has ZDV-associated toxicity, ABC could be considered an alternative to ZDV. This substitution should be considered in circumstances where increased risk of ZDV toxicity may exist, such as in infants with anemia or neutropenia. It also is suggested that negative testing for HLA-B5701 allele be confirmed prior to administration of ABC. Consulting an expert in pediatric HIV is recommended when selecting a therapy duration based on case-specific risk factors and interim HIV NAT results.⁴³⁻⁴⁵

Two-Drug Antiretroviral Prophylaxis

To date, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development–HIV Prevention Trials Network 040/Pediatric AIDS Clinical Trials Group 1043 (NICHD-HPTN 040/PACTG 1043) trial is the only randomized clinical trial of multi-ARV prophylaxis in newborns at high risk of HIV acquisition.⁵ In this study, 1,746 formula-fed infants born to women with HIV who did not receive any ARV drugs during pregnancy were randomized to receive one of three newborn prophylaxis regimens: the standard 6-week ZDV regimen; 6 weeks of ZDV plus three doses of NVP given during the first week of life (first dose given at birth or within 48 hours of birth,

second dose 48 hours after the first dose, and third dose 96 hours after the second dose); and 6 weeks of ZDV plus 2 weeks of 3TC plus nelfinavir (NFV).

Forty-one percent of the mothers received ZDV during labor. The risk of intrapartum transmission was significantly lower in the two-drug and three-drug arms (2.2% and 2.5%, respectively, vs. 4.9% for 6 weeks of ZDV alone; $P = 0.046$ for each experimental arm vs. ZDV alone).⁵ The NICHD-HPTN 040/PACTG 1043 regimen was associated with NRTI resistance in 3 of 53 participants (5.7%) with *in utero* infection who were treated with ZDV alone and in 6 of 33 participants (18.2%) who were treated with ZDV plus NVP ($P > 0.05$). In addition, the third drug in the three-arm regimen was NFV, which has highly variable PKs in this age group and did not reach the NFV target plasma concentration in 46% of study participants.⁴⁶

Although transmission rates with the two regimens were similar, neutropenia was significantly more common with the three-drug regimen than with the two-drug or ZDV-alone regimens (27.5% vs. 14.9% vs. 16.4%; $P < 0.001$ for both comparisons). For newborns who are at a high risk for HIV acquisition, the two-drug regimen used in NICHD-HPTN 040/PACTG 1043 is an option for preventing HIV transmission in infants aged ≥ 32 weeks' gestation with a birthweight of ≥ 1.5 kg. This two-drug regimen consists of 6 weeks of ZDV plus three doses of the prophylactic dose of NVP, with the NVP doses given within 48 hours of birth, 48 hours after the first dose, and 96 hours after the second dose. The prophylactic doses are NVP 12 mg per dose orally for infants weighing > 2 kg and NVP 8 mg per dose orally for infants weighing 1.5 kg to 2 kg. **These are the actual doses, not the milligram per kilogram doses.** ZDV dosing is shown in Table 9.

Choosing Between Presumptive HIV Therapy and Two-Drug Antiretroviral Prophylaxis

Because a spectrum of transmission risk depends on maternal viral load and other maternal and infant factors **and** no randomized trials have compared the safety and efficacy of presumptive HIV therapy and two-drug ARV prophylaxis, experts have differing opinions about when to initiate presumptive HIV therapy and when to initiate two-drug prophylaxis. For instance, among people who received ARV drugs during pregnancy but who have a detectable viral load **within 4 weeks prior to** delivery, the level of maternal viremia that would prompt the use of a two-drug ARV prophylaxis regimen or presumptive HIV therapy is not definitively known.

In two large observational studies of women on combination antenatal ARV drugs, perinatal transmission rates were 0.05% and 0.3% when the mother had a viral load < 50 copies/mL at delivery. Rates of transmission in these studies increased to 1.1% and 1.5 percent when viral load was 50 to 399 copies/mL and 2.8% and 4.1% when viral load was > 400 copies/mL.^{47,48} Although most Panel members would recommend initiating presumptive HIV therapy with any detectable level of viremia **within 4 weeks prior to delivery**, others may opt for a two-drug prophylaxis regimen if maternal viral load was less than 200 to 400 copies/mL. Emerging data about the lack of serious safety issues associated with presumptive HIV therapy in newborns is reassuring, even though mild-to-moderate adverse events may occur more frequently.

In summary, in scenarios where the infant is at high risk for HIV transmission, most Panel members recommend presumptive HIV therapy. In some situations, a two-drug ARV prophylaxis regimen may be considered (see Two-Drug Antiretroviral Prophylaxis in this section). Choosing between these regimens will depend on the clinician's assessment of the likelihood of HIV transmission, and a decision should be made after weighing the risks and benefits of the proposed regimen and discussing these transmission prevention strategies with the parents.

Consulting an expert in pediatric HIV or the [National Perinatal HIV Hotline](#) (1-888-448-8765) is recommended when selecting a regimen based on case-specific risk factors.

Newborns Born to Mothers with Unknown HIV Status Who Present in Labor

Expedited HIV testing is recommended during labor for people with unknown HIV status; if testing is not performed during labor, it should be performed as soon as possible after birth for the mothers and/or their newborns (see [Maternal HIV Testing and Identification of Perinatal HIV Exposure](#)). Expedited test results should be available within 60 minutes. If maternal or infant expedited testing is positive, the newborn **should begin presumptive HIV therapy immediately** without waiting for the results of supplemental tests. Expedited HIV testing should be available on a 24-hour basis at all facilities with a maternity service and/or neonatal intensive care unit or special care or newborn nursery.

A positive initial test result in mothers or newborns should be presumed to indicate maternal HIV until supplemental testing clarifies maternal and newborn status. If appropriate test results for a mother (or newborn) are negative, newborn ARV drugs can be discontinued. Clinicians should be aware of their state laws because not all states allow HIV testing in infants without parental consent.

A nursing mother who is suspected of having HIV based on an initial positive antibody or antibody/antigen test result should discontinue breastfeeding immediately until HIV is confirmed or ruled out. Pumping and temporarily discarding or freezing breast milk can be recommended. If HIV is ruled out, breastfeeding can resume. If HIV is confirmed, breastfeeding should be discontinued permanently.⁴⁹

Newborns Born to Mothers with Antiretroviral Drug-Resistant Virus

The optimal ARV regimen for newborns born to mothers with ARV drug-resistant virus is unknown. Although some studies have suggested that ARV drug-resistant virus may have decreased replicative capacity (reduced viral fitness) and transmissibility,⁵⁰ perinatal transmission of multidrug-resistant virus does occur.⁵¹⁻⁵⁶ Whether resistant virus in the mother increases the antepartum/intrapartum risk of HIV acquisition by the infant also is unknown. A recently reported secondary analysis of data from the NICHD-HPTN 040/PACTG 1043 study demonstrated that the risk of perinatal transmission was not related to the presence of drug resistance mutations in mothers who had not received ARV drugs before the start of the study (adjusted odds ratio 0.8; 95% confidence interval, 0.4–1.5).⁵⁶ Maraviroc (MVC) was approved recently for infants ≥ 2 kg and may provide an additional treatment option for newborns of mothers carrying multidrug-resistant HIV-1 that remains CCR5-trophic.⁵⁷ However, the lack of data about MVC as prophylaxis or treatment in infants and the risk of drug interactions will limit its role for routine use in neonates. The ARV regimen for newborns born to mothers with known or suspected drug resistance should be determined in consultation with a pediatric HIV specialist before delivery or through consultation via the [National Perinatal HIV Hotline](#) (1-888-448-8765). Additionally, no evidence exists that shows that neonatal prophylaxis regimens customized based on presence of maternal drug resistance are more effective than standard neonatal prophylaxis regimens.

Newborns with HIV Infection

Until recently, neonatal ARV regimens were designed for prophylaxis against perinatal HIV transmission and were intended to be as simple as possible for practical use. There was little reason

to develop ARV regimens for the treatment of neonates because the long turnaround times to receive HIV NAT results meant that neonatal infections, in general, were not diagnosed during the first weeks of life. HIV NAT results are now available within a few days, and HIV in newborns is being diagnosed as early as the first days of life in many centers. A positive HIV NAT must be repeated to confirm HIV. However, ART initiation should not be delayed while waiting for the results of the confirmatory HIV NAT, given the low likelihood of a false-positive HIV NAT. **A confirmatory specimen should be obtained prior to ART initiation.** To date, evidence that early treatment (before age 2 weeks) will lead conclusively to prolonged remission or better outcomes in newborns with HIV is lacking.

Information regarding the safety of early treatment of HIV in newborns has been reported from two studies. In the IMPAACT P1115 study, 54 infants with HIV began presumptive HIV therapy between 0.4 and 40 hours of life. Grade 3 or 4 related events—most of which were hematologic—occurred in 22 of 54 infants (41%) through 52 weeks of the study.⁵⁸ Forty infants with HIV in Botswana began treatment with NVP plus ZDV plus 3TC at a median age of 2 days (range 1–5 days) and transitioned to lopinavir/ritonavir (LPV/r) plus ZDV plus 3TC at approximately 2 weeks of age. These infants had minimal toxicity during the first 12 weeks of treatment. Only one instance of Grade 3 neutropenia was reported, and no instances of Grade 3 or 4 anemia were reported.³¹

Earlier diagnosis of HIV in newborns and the increasing use of presumptive HIV therapy in newborns at high risk for HIV acquisition have necessitated the investigation of dosing and the safety of ARV drugs in term and preterm newborns. Although data are still incomplete, especially for preterm newborns, PK and safety profiles of ARV drugs are increasingly available. As already noted, the recommended neonatal ARV doses for prophylaxis and for treatment are the same, with the important exception of [NVP](#) (see the [Pediatric Antiretroviral Guidelines](#)).

Sufficient data exist to provide dosing recommendations for the treatment of HIV in neonates using the following medications (see the [Pediatric Antiretroviral Guidelines](#)):

- From birth in term and preterm newborns: [ZDV](#), [3TC](#), [NVP](#)
- From birth in term newborns: [emtricitabine](#), [RAL](#), [MVC](#), [ABC](#)
- From age 2 weeks in term newborns: [LPV/r](#)
- From age 4 weeks in term newborns: [DTG](#)

Dosing recommendations for **premature** newborns are available for ZDV, 3TC, and NVP only. Neonatal dosing advice—including dosing advice for premature newborns—is summarized in Table 9. For more detailed information about neonatal dosing recommendations and considerations when using these drugs, please see the [Pediatric Antiretroviral Guidelines](#). **Consultation with an expert in pediatric HIV is recommended to assist with management of infants born at <32 weeks gestation.**

Newborns of Mothers Who Receive an HIV Diagnosis While Breastfeeding

People with suspected HIV (e.g., a positive initial screening test) should discontinue breastfeeding immediately until HIV is ruled out. Pumping and temporarily discarding or freezing breast milk can be recommended to mothers who are suspected of having HIV but whose HIV serostatus is not yet confirmed and who want to continue to breastfeed. If HIV is ruled out, breastfeeding can resume. Breastfeeding **is not recommended** for people with confirmed HIV in the United States, including

those receiving ART (see [Counseling and Managing Individuals with HIV in the United States Who Desire to Breastfeed](#)).⁵⁹

The risk of HIV acquisition associated with breastfeeding depends on multiple newborn and maternal factors, including maternal viral load and CD4 T lymphocyte (CD4) cell count.⁶⁰ Newborns of people who develop acute HIV while breastfeeding are at greater risk of acquiring HIV than those whose mothers have chronic HIV infection⁶¹ because acute HIV infection is accompanied by a rapid increase in viral load and a corresponding decrease in CD4 count.⁶²

Other than discontinuing breastfeeding, optimal strategies for managing a newborn who was breastfed by a mother with HIV (often because the mother just learned of her own HIV diagnosis) have yet to be defined. Some Panel members would consider the use of postexposure prophylaxis in newborns for 4 to 6 weeks after cessation of breastfeeding. Postexposure prophylaxis, however, is less likely to be effective in this circumstance than with other nonoccupational exposures because the exposure to breast milk is likely to have occurred over a prolonged period rather than during a single exposure to the virus.⁶³

Several studies of newborns who were breastfed by women with chronic HIV infection in low-resource settings have shown that a newborn's daily regimen of NVP, 3TC, LPV/r, or NVP plus ZDV can reduce the risk of postnatal infection during breastfeeding.⁶⁴⁻⁶⁸ [See Counseling and Managing Individuals with HIV in the United States Who Desire to Breastfeed for additional information.](#) No trials have evaluated the use of multidrug regimens to prevent transmission after cessation of breastfeeding in mothers with acute HIV infection.

Given the higher risk of postnatal transmission from a person with acute HIV infection who is breastfeeding, an alternative approach favored by some Panel members is to offer presumptive HIV therapy until the infant's HIV status can be determined. If the infant's initial HIV NAT is negative, the optimal duration of presumptive HIV therapy is unknown. A 28-day course may be reasonable based on current recommendations for nonoccupational HIV exposure.⁶³ When making decisions about ARV management, clinicians should consult a pediatric HIV specialist and counsel the parents on the potential risks and benefits of a particular treatment strategy. The [National Perinatal HIV Hotline](#) (1-888-448-8765) can provide referrals to local or regional pediatric HIV specialists.

Newborns exposed to HIV during breastfeeding should be tested for HIV infection prior to initiating presumptive HIV therapy, as well as 4 to 6 weeks and 4 to 6 months after diagnosis of maternal HIV infection and cessation of breastfeeding. An additional virologic test should be performed 2 to 4 weeks after discontinuing presumptive HIV therapy (see [Diagnosis of HIV Infection in Infants and Children](#)). If an HIV-exposed newborn is already receiving an ARV prophylaxis regimen other than presumptive HIV therapy and is found to have HIV, prophylaxis should be discontinued and treatment for HIV should be initiated. Resistance testing should be performed, and the ART should be modified if needed (see the [Pediatric Antiretroviral Guidelines](#)).

Short-Term Antiretroviral Drug Safety

Newborn prophylaxis with ZDV has been associated with only minimal toxicity, primarily transient hematologic toxicity (mainly anemia), which generally resolves by age 12 weeks (see [Initial Postnatal Management of the Neonate Exposed to HIV](#)). Data on toxicities in newborns who were exposed to multiple ARV drugs are limited.

Other than ZDV, 3TC is the NRTI with the most clinical experience for neonatal prophylaxis. In early studies, neonatal exposure to combination ZDV/3TC therapy was limited, in general, to 1 week^{19,69,70} or 2 weeks.⁵ Six weeks of ZDV/3TC exposure in newborns also has been reported. These studies suggest that hematologic toxicity may be greater with ZDV/3TC than with ZDV alone, although the newborns in these studies also had *in utero* exposure to maternal HIV therapy that may have contributed to the toxicity.

In a French study, more cases of severe anemia and neutropenia were observed in newborns who were exposed to 6 weeks of ZDV/3TC prophylaxis plus maternal antepartum ZDV/3TC than in a historical cohort of newborns who were exposed only to maternal and newborn ZDV. Anemia was reported in 15% of newborns, and neutropenia was reported in 18% of newborns who were exposed to ZDV/3TC, with 2% of newborns requiring blood transfusion and 4% requiring treatment discontinuation for toxicity.⁷¹ Similarly, in a Brazilian study of maternal antepartum ZDV/3TC and 6-week newborn ZDV/3TC prophylaxis, neonatal hematologic toxicity was common, with anemia seen in 69% and neutropenia seen in 13% of newborns.⁷²

Recent data from the IMPAACT P1106 trial and two observational European and African cohorts provided reassuring data on the safety of ABC in infants when initiated at <3 months of age, including infants with weight <3 kg.⁷³⁻⁷⁵ See the [Abacavir](#) section of the [Pediatric Antiretroviral Guidelines](#) for additional information. At this time, the Panel suggests using ABC as an alternative to ZDV in certain situations and after negative HLA-B5701 allele testing.

Experience with other NRTI drugs for neonatal prophylaxis is more limited.^{76,77} Hematologic and mitochondrial toxicity may be more common with exposure to multiple NRTI drugs than with exposure to a single NRTI.^{71,78-81}

In rare cases, chronic multiple-dose NVP prophylaxis in pregnant women has been associated with severe and potentially life-threatening rash and hepatic toxicity.⁸² These toxicities have not been observed in newborns receiving prophylactic dosing with single-dose NVP or the two-drug ZDV regimen plus three doses of NVP in the first week of life used in NICHD-HPTN 040/PACTG 1043 or in breastfeeding newborns receiving NVP prophylaxis daily for 6 weeks to 18 months to prevent transmission of HIV via breast milk.^{5,64-66,68,83}

The FDA approved infant dosing of RAL for term neonates aged ≥ 37 weeks' gestation at birth and weighing ≥ 2 kg. Dosing information for RAL is not available for preterm or low-birthweight infants. PK modeling studies in infants with birthweight <2.5 kg with gestational age at birth ranging from 32.7 to 40 weeks suggests that prematurity reduces RAL clearance, and a modified dosing regimen may be needed to avoid elevated plasma RAL concentrations.⁸⁴ Infant RAL dosing needs to be increased at 1 week and 4 weeks of age. RAL is metabolized by uridine diphosphate glucuronosyltransferase (UGT) 1A1, the same enzyme responsible for the elimination of bilirubin. UGT enzyme activity is low at birth, and RAL elimination is prolonged in neonates. In addition, bilirubin and RAL may compete for albumin binding sites, and extremely elevated neonatal plasma RAL concentrations could pose a risk of kernicterus.⁴⁰ IMPAACT P1110 is a Phase 1, multicenter trial that enrolled full-term neonates who were exposed to HIV and who were at risk for acquiring perinatal HIV-1 infection, with or without *in utero* RAL exposure. Daily RAL was safe and well tolerated during the first 6 weeks of life. Infants were treated for ≤ 6 weeks from birth and followed for 24 weeks. Only one episode of Grade 4 neutropenia, possibly related to RAL, was reported. Among infants with RAL exposure (infants whose mothers received RAL within 2 to 24 hours before

delivery), the first dose of RAL should be delayed for 24 to 48 hours after birth.⁸⁵ See the [Raltegravir](#) section of the [Pediatric Antiretroviral Guidelines](#) for additional information.

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