Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated April 16, 2019; last reviewed April 16, 2019) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Anemia[a]	ZDV	Onset: • Variable, weeks to months Presentation *Most Commonly:* • Asymptomatic • Mild fatigue • Pallor • Tachypnea *Rarely:* • Congestive heart failure	Newborns Exposed to HIV: • Severe anemia is uncommon but may be seen coincident with physiologic Hgb nadir. Children with HIV Who Are Taking ARV Drugs: • Anemia is two to three times more common with ZDV-containing regimens compared to all other regimens.	Newborns Exposed to HIV: • Premature birth • *In utero* exposure to ZDV-containing regimens • Advanced maternal HIV • Neonatal blood loss • Combination ARV prophylaxis or empiric HIV therapy, particularly with ZDV plus 3TC Children with HIV Who Are Taking ARV Drugs: • Underlying hemoglobinopathy (e.g., sickle cell disease, G6PD deficiency) • Myelosuppressive drugs (e.g., TMP-SMX, rifabutin) • Iron deficiency • Advanced or poorly controlled HIV disease • OIs of the bone marrow • Malnutrition	Newborns Exposed to HIV: • Obtain CBC at birth. • Consider repeating CBC at 4 weeks for neonates who are at higher risk (e.g., those born prematurely or who are known to have low birth Hgb) and for neonates who receive ZDV beyond 4 weeks. Children with HIV Who Are Taking ARV Drugs: • Avoid ZDV in children with severe anemia when alternative agents are available. • Obtain CBC as part of routine care (see Clinical and Laboratory Monitoring of Pediatric HIV Infection).	Newborns Exposed to HIV: • Anemia rarely requires intervention unless Hgb is <7.0 g/dL or is associated with symptoms. • ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). Children with HIV Who Are Taking ARV Drugs: • Discontinue non-ARV, marrow-toxic drugs, if feasible. • Treat coexisting iron deficiency, OIs, and malignancies. • For persistent, severe anemia that is thought to be associated with ARV drugs (typically macrocytic anemia), switch to a regimen that does not contain ZDV.
Macrocytosis	ZDV	Onset: • Within days to weeks of starting therapy Presentation: • Asymptomatic but MCV is often >100 fL • Sometimes associated with anemia	All Ages: • >90% to 95%	None	No monitoring required—macrocytosis can be detected if CBC is obtained as part of routine care (see Clinical and Laboratory Monitoring of Pediatric HIV Infection).	No management required.

Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects (Last updated April 16, 2019; last reviewed April 16, 2019) (page 2 of 2)

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Neutropenia[a]	ZDV	Onset: • Variable Presentation: • Asymptomatic	Newborns Exposed to HIV: • Rare Children with HIV Who Are Taking ARV Drugs: • 2% to 4% of children on ARV drugs • Highest rates occur in children on ZDV-containing regimens	Newborns Exposed to HIV: • *In utero* exposure to ARV drugs • Combination ARV prophylaxis, particularly with ZDV plus 3TC Children with HIV Who Are Taking ARV Drugs: • Advanced or poorly controlled HIV infection • Myelosuppressive drugs (e.g., TMP-SMX, ganciclovir, hydroxyurea, rifabutin)	Children with HIV Who Are Taking ARV Drugs: • Obtain CBC as part of routine care.	Newborns Exposed to HIV: • No established threshold for intervention; some experts would consider using an alternative NRTI for prophylaxis if ANC reaches <500 cells/mm^3. ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV). Children with HIV Who Are Taking ARV Drugs: • Discontinue non-ARV, marrow-toxic drugs, if feasible. • Treat coexisting OIs and malignancies. • For persistent, severe neutropenia that is thought to be associated with ARV drugs, change to a regimen that does not contain ZDV.

[a] HIV infection itself, OIs, and medications used to prevent OIs (e.g., TMP-SMX) may all contribute to anemia and neutropenia.

Key to Acronyms: 3TC = lamivudine; ANC = absolute neutrophil count; ARV = antiretroviral; CBC = complete blood count; dL = deciliter; fL = femtoliter; G6PD = glucose-6-phosphate dehydrogenase; Hgb = hemoglobin; MCV = mean cell volume; NRTI = nucleoside reverse transcriptase inhibitor; OI = opportunistic infection; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

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