Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/ Clinical Manifestations</th>
<th>Estimated Frequency</th>
<th>Risk Factors</th>
<th>Prevention/ Monitoring</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia*</td>
<td>ZDV</td>
<td>Onset: • Variable, weeks to months</td>
<td>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.</td>
<td>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</td>
<td>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).</td>
<td>Newborns Exposed to HIV: • Anemia rarely requires intervention unless Hgb is &lt;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.</td>
</tr>
<tr>
<td>Macrocytosis</td>
<td>ZDV</td>
<td>Onset: • Within days to weeks of starting therapy</td>
<td>All Ages: • &gt;90% to 95%</td>
<td>None</td>
<td>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).</td>
<td>No management required.</td>
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### Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects

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<tr>
<td>Neutropeniaa</td>
<td>ZDV</td>
<td>Onset:</td>
<td>Newborns Exposed to HIV:</td>
<td>Newborns Exposed to HIV:</td>
<td>Children with HIV Who Are Taking ARV Drugs:</td>
<td>Newborns Exposed to HIV:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Variable</td>
<td>• Rare</td>
<td>• In utero exposure to ARV drugs</td>
<td>• Obtain CBC as part of routine care.</td>
<td>• No established threshold for intervention; some experts would consider using an alternative NRTI for prophylaxis if ANC reaches &lt;500 cells/mm³. ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV).</td>
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<td></td>
<td></td>
<td>Presentation:</td>
<td>Children with HIV Who Are Taking ARV Drugs:</td>
<td>Combination ARV prophylaxis, particularly with ZDV plus 3TC</td>
<td>Children with HIV Who Are Taking ARV Drugs:</td>
<td>Children with HIV Who Are Taking ARV Drugs:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Asymptomatic</td>
<td>• 2% to 4% of children on ARV drugs</td>
<td>• Advanced or poorly controlled HIV infection</td>
<td>• Discontinue non-ARV, marrow-toxic drugs, if feasible.</td>
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<td></td>
<td></td>
<td>• Highest rates occur in children on ZDV-containing regimens</td>
<td>• Myelosuppressive drugs (e.g., TMP-SMX, ganciclovir, hydroxyurea, rifabutin)</td>
<td>• Treat coexisting OIs and malignancies.</td>
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</tr>
<tr>
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<td></td>
<td>Newborns Exposed to HIV:</td>
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<td>For persistent, severe neutropenia that is thought to be associated with ARV drugs, change to a regimen that does not contain ZDV.</td>
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**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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**References**


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*Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* K-20

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