### Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects

(First published October 2003; last updated April 14, 2020; last reviewed April 14, 2020) (page 1 of 2)

<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:</td>
<td>Newborns Exposed to HIV:</td>
<td>Newborns Exposed to HIV:</td>
<td>Newborns Exposed to HIV:</td>
<td>Newborns Exposed to HIV:</td>
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<tr>
<td></td>
<td></td>
<td>Variable; weeks to months after starting therapy</td>
<td>• Severe anemia is uncommon, but may be seen coincident with physiologic Hgb nadir.</td>
<td>• Premature birth is the most common risk factor</td>
<td>• Obtain CBC at birth.</td>
<td>• Anemia rarely requires intervention unless it is symptomatic or Hgb &lt;7.0 g/dL.</td>
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<tr>
<td></td>
<td></td>
<td>Presentation</td>
<td>Children with HIV Who Are Taking ARV Drugs:</td>
<td>In utero exposure to ZDV-containing regimens</td>
<td>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.</td>
<td>• ZDV administration can be limited to 4 weeks in low-risk neonates (see Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More Common:</td>
<td>Anemia is two to three times more common with ZDV-containing regimens than with all other regimens.</td>
<td>Advanced maternal HIV</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>Neonatal blood loss</td>
<td>Neonatal blood loss</td>
<td>• Underlying hemoglobinopathy (e.g., sickle cell disease, G6PD deficiency)</td>
<td>• Avoid using ZDV in children with severe anemia when alternative agents are available.</td>
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<tr>
<td></td>
<td></td>
<td>• Mild fatigue</td>
<td>Combination ARV prophylaxis or presumptive HIV therapy, particularly ZDV plus 3TC</td>
<td>Myelosuppressive drugs (e.g., TMP-SMX, rifabutin)</td>
<td>Children with HIV Who Are Taking ARV Drugs:</td>
<td>Obtain CBC as part of routine care (see Clinical and Laboratory Monitoring of Pediatric HIV Infection).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pallor</td>
<td>Iron deficiency</td>
<td>Iron deficiency</td>
<td>• Advanced or poorly controlled HIV disease</td>
<td>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></td>
<td></td>
<td>• Tachypnea</td>
<td>Advanced or poorly controlled HIV disease</td>
<td>OIs of the bone marrow</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>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare:</td>
<td>Malnutrition</td>
<td>Malnutrition</td>
<td>New 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 monitoring required.</td>
</tr>
<tr>
<td>Macrocytosis</td>
<td>ZDV</td>
<td>Onset:</td>
<td>&gt;90% to 95% for all ages</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>New 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>
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**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 using 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).

**Risk Factors:**
- Premature birth
- In utero exposure to ZDV-containing regimens
- Advanced maternal HIV
- Neonatal blood loss
- Combination ARV prophylaxis or presumptive HIV therapy, particularly ZDV plus 3TC
- 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

**Prevention/ Monitoring:**
- 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 using 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).
Table 15d. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Hematologic Effects *(Last updated April 14, 2020; last reviewed April 14, 2020)* (page 2 of 2)

<table>
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<tr>
<td>Neutropenia*</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>• In utero exposure to ARV drugs</td>
<td>• Combination ARV prophylaxis, particularly ZDV plus 3TC</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 HIV Infection).</td>
</tr>
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<td>Presentation:</td>
<td>Children with HIV Who Are Taking ARV Drugs:</td>
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<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>
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<td></td>
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<td>• Highest rates occur in children on ZDV-containing regimens</td>
<td>• Myelosuppressive drugs (e.g., TMP-SMX, ganciclovir, hydroxyurea, rifabutin)</td>
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</tr>
</tbody>
</table>

* HIV infection itself, OIs, and medications that are used to prevent OIs (e.g., TMP-SMX) may all contribute to anemia and neutropenia.

Key: 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

References


