Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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### Table 15g. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lactic Acidosis

**(Last updated April 16, 2019; last reviewed April 16, 2019)**

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<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>
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<td>Lactic Acidosis</td>
<td>NRTIs: ZDV; 3TC, FTC, ABC, TAF, and TDF</td>
<td>Onset: Generally, after years of exposure</td>
<td>Lactic acidosis is associated with use of ddI and d4T. Cases are rare now that these NRTIs are no longer recommended.</td>
<td>Adults: Female sex; High BMI; Chronic HCV infection; African-American race; Co-administration of TDF with metformin; Overdose of propylene glycol; CD4 cell count &lt;350 cells/mm³; Acquired riboflavin or thiamine deficiency.</td>
<td>Due to the presence of propylene glycol as a diluent, LPV/r oral solution should not be used in preterm neonates or any neonate who has not attained a postmenstrual age of 42 weeks and a postnatal age of ≥14 days.</td>
<td>Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test): Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup. Lactate &gt;5.0 mmol/L (Confirmed With a Second Test) or &gt;10.0 mmol/L (Any One Test): Discontinue all ARV drugs. Provide supportive therapy (e.g., IV fluids; some patients may require sedation and respiratory support to reduce oxygen demand and ensure adequate oxygenation of tissues). Anecdotal (Unproven) Supportive Therapies: Administer bicarbonate infusions, THAM, high doses of thiamine and riboflavin, oral antioxidants (e.g., L-carnitine, coenzyme Q10, vitamin C). Following the resolution of clinical and laboratory abnormalities, resume therapy, either with a NRTI-sparing regimen or a revised NRTI-containing regimen. Institute a revised NRTI-containing regimen with caution, using NRTIs that are less likely to induce mitochondrial dysfunction (ABC, TAF, or TDF preferred; possibly FTC or 3TC). Lactate should be monitored monthly for ≥3 months.</td>
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<td>Other Drugs:</td>
<td>See Risk Factors and Prevention/ Monitoring columns for information regarding the toxicity of propylene glycol when LPV/r oral solution is used in neonates.</td>
<td>Presentation: Lactic acidosis may be clinically asymptomatic. Insidious Onset of a Combination of Signs and Symptoms: Generalized fatigue, weakness, and myalgias; Vague abdominal pain, weight loss, unexplained nausea, or vomiting; Dyspnea; Peripheral neuropathy.</td>
<td>Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).</td>
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<td>Preterm Infants or Any Neonates Who Have Not Attained a Post-Menstrual Age of 42 Weeks and a Postnatal Age of ≥14 Days: Exposure to propylene glycol (e.g., present as a diluent in LPV/r oral solution). A diminished ability to metabolize propylene glycol may lead to accumulation and potential adverse events.</td>
<td>Prevention: Measurement of serum lactate is not recommended. Patients with Clinical Signs or Symptoms Consistent with Lactic Acidosis: Obtain blood lactate level. Additional diagnostic evaluations should include serum bicarbonate, anion gap, and/or arterial blood gas; amylase and lipase; serum albumin; and hepatic transaminases.</td>
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<td>Asymptomatic Patients:</td>
<td>Monitoring:</td>
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</table>

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BMI = body mass index; CD4 = CD4 T lymphocyte; d4T = stavudine; ddI; didanosine; FTC = emtricitabine; HCV = hepatitis C virus; IV = intravenous; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; THAM = tris (hydroxymethyl) aminomethane; ZDV = zidovudine

*Blood for lactate determination should be collected, without prolonged tourniquet application or fist clenching, into a pre-chilled, gray-top, fluoride-oxalate-containing tube and transported on ice to the laboratory to be processed within 4 hours of collection.*

*Management can be initiated before receiving the results of the confirmatory test.*

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References

General Reviews


Risk Factors


Monitoring and Management


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