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

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<table>
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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>
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<td>Lactic Acidosis</td>
<td>NRTIs; • ZDV; • Less likely with 3TC, FTC, ABC, TAF, and TDF</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 • Coadministration of TDF with metformin • Overdose of propylene glycol • CD4 cell count &lt;350 cells/mm² • Acquired riboflavin or thiamine deficiency • Possibly pregnancy</td>
<td>Lactate ≥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, co-enzyme 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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Other Drugs:

• See Risk Factors and Prevention/Monitoring columns for information regarding the toxicity of propylene glycol when LPV/r oral solution is used in neonates.

Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).

**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

**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.

**Asymptomatic Patients:**

• 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.

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*a* 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.

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

**Key to Acronyms:**

3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BMI = body mass index; CD4 = CD4 T lymphocyte; d4T = stavudine; ddl; 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

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*Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* K-28

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References

General Reviews


Risk Factors


Monitoring and Management

