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

*(Last updated April 27, 2017; last reviewed April 27, 2017)*

<table>
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<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
<th>Estimated Frequency</th>
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<td><strong>Lactic Acidosis</strong></td>
<td>NRTIs, in particular, d4T and ddI (highest risk when co-administered)</td>
<td>Onset: 1–20 months after starting therapy (median onset 4 months in 1 case series)</td>
<td>Chronic, Asymptomatic Mild Hyperlactatemia (2.1–5.0 mmol/L)</td>
<td>Adults: Female gender, High BMI, Chronic HCV infection, African-American race, Prolonged NRTI use (particularly d4T and ddI), Co-administration of ddI with other agents (e.g., d4T, TDF, RBV, tetracycline), Co-administration of TDF with metformin, Overdose of propylene glycol, CD4 count &lt;350 cells/mm³, Acquired riboflavin or thiamine deficiency, Possibly pregnancy</td>
<td>Prevent: d4T and ddI should both be avoided individually, co-administration of d4T and ddI is contraindicated (no exception). Due to the presence of propylene glycol as a diluent, LPV/r oral solution should not be used in preterm neonates or any neonate before a postmenstrual age of 42 weeks and a postnatal age of ≥14 days has been attained. Lactate &gt;5.0 mmol/L (Confirmed with Second Test) or &gt;10.0 mmol/L (Any 1 Test): Monitor for clinical manifestations of lactic acidosis and promptly adjust therapy.</td>
<td>Lactate 2.1–5.0 mmol/L (Confirmed with Second Test): Replace ddI and d4T with other ARVs. As an alternative, temporarily discontinue all ARVs while conducting additional diagnostic workup. Lactate &gt;5.0 mmol/L (Confirmed with Second Test) or &gt;10.0 mmol/L (Any 1 Test): Discontinue all ARVs. Provide supportive therapy (IV fluids; some patients may require sedation and respiratory support to reduce oxygen demand and ensure adequate oxygenation of tissues). Anecdotal (Unproven) Supportive Therapies: Bicarbonate infusions, THAM, high-dose thiamine and riboflavin, oral antioxidants (e.g., L-carnitine, co-enzyme Q10, vitamin C) Following resolution of clinical and laboratory abnormalities, resume therapy, either with an NRTI-sparing regimen or a revised NRTI-containing regimen instituted with caution, using NRTIs less likely to inhibit mitochondria (ABC or TDF preferred; possibly FTC or 3TC), and monthly monitoring of lactate for at least 3 months.</td>
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<td><strong>Symptomatic Severe Hyperlactatemia (&gt;5.0 mmol/L)</strong></td>
<td>Adults: 0.2% to 5.7%</td>
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<td><strong>Symptomatic Lactic Acidosis/Hepatic Steatosis:</strong></td>
<td>Rare in all age groups (1.3–11 episodes per 1000 person-years; increased incidence with the use of d4T/ddI when co-administered), but associated with a high fatality rate (33% to 58%)</td>
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<td><strong>Preterm Infants or Any Neonates before Post-Menstrual Age of 42 Weeks and a Postnatal Age of ≥14 Days has Been Attained:</strong></td>
<td>Exposure to propylene glycol (e.g., present as a diluent in LPV/r oral solution) due to diminished ability to metabolize propylene glycol, thereby leading to accumulation and potential adverse events.</td>
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<td><strong>Consistent with Lactic Acidosis:</strong></td>
<td>Obtain blood lactate level. Additional diagnostic evaluations should include serum bicarbonate and anion gap and/or arterial blood gas, amylase and lipase, serum albumin, and hepatic transaminases.</td>
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<sup>a</sup> 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.

<sup>b</sup> Management can be initiated before 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; ddI = didanosine; FTC = emtricitabine; HCV = hepatitis C virus; IV = intravenous; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; RBV = ribavirin; TDF = tenofovir disoproxil fumarate; THAM = tris (hydroxymethyl) aminomethane

*Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*
References

General Reviews


Risk Factors


### Monitoring and Management


