

**Table 15g. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lactic Acidosis**  
 (Last updated April 7, 2021; last reviewed April 7, 2021) (page 1 of 2)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
<b>Lactic Acidosis</b>	<p><b>NRTIs:</b></p> <ul style="list-style-type: none"> <li>• ZDV</li> <li>• Less likely with 3TC, FTC, ABC, TAF, and TDF</li> </ul> <p><b>Other Drugs:</b></p> <ul style="list-style-type: none"> <li>• See the Risk Factors and Prevention/Monitoring columns for information regarding the toxicity of propylene glycol when LPV/r oral solution is used in neonates.</li> </ul>	<p><b>Onset:</b></p> <ul style="list-style-type: none"> <li>• Generally after years of exposure</li> </ul> <p><b>Presentation:</b></p> <ul style="list-style-type: none"> <li>• Lactic acidosis may be clinically asymptomatic.</li> </ul> <p><i>Lactic Acidosis May Also Present with Insidious Onset of a Combination of Signs and Symptoms:</i></p> <ul style="list-style-type: none"> <li>• Generalized fatigue, weakness, and myalgias</li> <li>• Vague abdominal pain, weight loss, unexplained nausea, or vomiting</li> <li>• Dyspnea</li> <li>• Peripheral neuropathy</li> </ul> <p><b>Note:</b> Patients may present with acute multi-organ failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).</p>	<p>Lactic acidosis is associated with use of ddI and d4T. Cases are rare now that these NRTIs <b>are no longer recommended</b>.</p> <p>3TC, FTC, ABC, TAF, and TDF are less likely to induce clinically significant mitochondrial dysfunction than ZDV.</p>	<p><b>Adults:</b></p> <ul style="list-style-type: none"> <li>• Female sex</li> <li>• High BMI</li> <li>• Chronic HCV infection</li> <li>• African-American race</li> <li>• Coadministration of TDF with metformin</li> <li>• Overdose of propylene glycol</li> <li>• CD4 count &lt;350 cells/mm<sup>3</sup></li> <li>• Acquired riboflavin or thiamine deficiency</li> <li>• Possible pregnancy</li> </ul> <p><b>Preterm Infants or Any Neonates Who Have Not Attained a Post-Menstrual Age of 42 Weeks and a Postnatal Age of ≥14 Days:</b></p> <ul style="list-style-type: none"> <li>• Exposure to propylene glycol, which is used as a diluent in LPV/r oral solution--a. A diminished ability to metabolize propylene glycol may lead to accumulation, increasing the risk of adverse events.</li> </ul>	<p><b>Prevention:</b></p> <ul style="list-style-type: none"> <li>• Due to the presence of propylene glycol as a diluent, LPV/r oral solution <b>should not be used</b> in preterm neonates or any neonate who has not attained a postmenstrual age of 42 weeks and a postnatal age of ≥14 days.</li> <li>• Monitor for clinical manifestations of lactic acidosis and promptly adjust therapy.</li> </ul> <p><b>Monitoring</b></p> <p><i>Asymptomatic Patients:</i></p> <ul style="list-style-type: none"> <li>• Routine Measurement of serum lactate <b>is not recommended</b>.</li> </ul> <p><i>Patients with Clinical Signs or Symptoms Consistent with Lactic Acidosis:</i></p> <ul style="list-style-type: none"> <li>• Obtain blood lactate level.<sup>a</sup></li> <li>• Additional diagnostic evaluations should include serum bicarbonate, anion gap, and/or arterial blood gas; amylase and lipase; serum albumin; and hepatic transaminases.</li> </ul>	<p><b>For Patients with Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test):</b></p> <ul style="list-style-type: none"> <li>• Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup.</li> </ul> <p><b>For Patients with Lactate &gt;5.0 mmol/L (Confirmed With a Second Test)<sup>b</sup> or &gt;10.0 mmol/L (Any One Test):</b></p> <ul style="list-style-type: none"> <li>• Discontinue all ARV drugs.</li> <li>• 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).</li> </ul> <p><b>Anecdotal (Unproven) Supportive Therapies:</b></p> <ul style="list-style-type: none"> <li>• Administer bicarbonate infusions, THAM, high doses of thiamine and riboflavin, and oral antioxidants (e.g., L-carnitine, co-enzyme Q10, vitamin C).</li> </ul> <p>Following the resolution of clinical and laboratory abnormalities, resume therapy, either with an 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, TDF, FTC or 3TC). Lactate should be monitored monthly for ≥3 months.</p>

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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 receiving the results of the confirmatory test.

**Key:** 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

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