

**Table 17g. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Lactic Acidosis**

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Lactic Acidosis	<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> <li>A few cases have been reported shortly after initiation in people with underlying liver disease.</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 multiorgan failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).</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> <li>Overdose in setting of renal insufficiency (e.g., 3TC)</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><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 work-up.</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>

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
				<p>Preterm Infants or Any Neonates Who Have Not Attained a Postmenstrual Age of 42 Weeks and a Postnatal Age of <math>\geq 14</math> Days</p> <ul style="list-style-type: none"> <li>Exposure to propylene glycol, which is used as a diluent in LPV/r oral solution, because these newborns have a diminished ability to metabolize propylene glycol may lead to accumulation, increasing the risk of adverse events.</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>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 (i.e., ABC, TAF, TDF, FTC, or 3TC). Lactate should be monitored monthly for <math>\geq 3</math> months.</p>

<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; 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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