Table 15g. 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	**NRTIs:** • ZDV • Less likely with 3TC, FTC, ABC, TAF, and TDF **Other Drugs:** • 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.	**Onset:** • Generally after years of exposure **Presentation:** • Lactic acidosis may be clinically asymptomatic. *Lactic Acidosis May Also Present with 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 **Note:** Patients may present with acute multi-organ failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).	Lactic acidosis is associated with use of ddI and d4T. Cases are rare now that these NRTIs **are no longer recommended**. 3TC, FTC, ABC, TAF, and TDF are less likely to induce clinically significant mitochondrial dysfunction than ZDV.	**Adults:** • Female sex • High BMI • Chronic HCV infection • African-American race • Coadministration of TDF with metformin • Overdose of propylene glycol • CD4 count <350 cells/ mm^3 • Acquired riboflavin or thiamine deficiency • Possibly pregnancy **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, which is used as a diluent in LPV/r oral solution. A diminished ability to metabolize propylene glycol may lead to accumulation, increasing the risk of adverse events.	**Prevention:** • 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. • Monitor for clinical manifestations of lactic acidosis and promptly adjust therapy. **Monitoring** *Asymptomatic Patients:* • Measurement of serum lactate **is not recommended**. *Patients with Clinical Signs or Symptoms Consistent with Lactic Acidosis:* • Obtain blood lactate level.[a] • Additional diagnostic evaluations should include serum bicarbonate, anion gap, and/or arterial blood gas; amylase and lipase; serum albumin; and hepatic transaminases.	**For Patients with Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test):** • Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup. **For Patients with Lactate >5.0 mmol/L (Confirmed With a Second Test)[b] or >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 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.

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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: 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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