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 multiorgan failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure).	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 • Possible pregnancy **Preterm Infants or Any Neonates Who Have Not Attained a Postmenstrual 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, because these newborns have a diminished ability to metabolize propylene	**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* • Routine 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;	**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 work-up. **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, and oral antioxidants (e.g., L-carnitine, co-enzyme Q10, vitamin C).

Adverse Effects	Associated ARVs	Onset/ Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
				glycol may lead to accumulation, increasing the risk of adverse events.	serum albumin; and hepatic transaminases.	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.

[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; 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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