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

**Key to Acronyms:**
- 3TC = lamivudine
- ABC = abacavir
- ARV = antiretroviral
- BMI = body mass index
- CD4 = CD4 T lymphocyte
- 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

#### Lactic Acidosis

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
<th>Estimated Frequency</th>
<th>Risk Factors</th>
<th>Prevention/Monitoring</th>
<th>Management</th>
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<tbody>
<tr>
<td>Lactic Acidosis</td>
<td>NRTIs: • ZDV; • Less likely with 3TC, FTC, ABC, TAF, and TDF</td>
<td>Lactic acidosis is associated with use of ddl and d4T. Cases are rare now that these NRTIs are no longer recommended.</td>
<td>Adults: • Female sex; • High BMI; • Chronic HCV infection; • African-American race; • Co-administration of TDF with metformin; • Overdose of propylene glycol; • CD4 cell count &lt;350 cells/mm³; • Acquired riboflavin or thiamine deficiency; • Possibly pregnancy.</td>
<td>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.</td>
<td>Monitoring Asymptomatic Patients: • Measurement of serum lactate is not recommended.</td>
<td>Lactate 2.1–5.0 mmol/L (Confirmed with a Second Test): • Consider discontinuing all ARV drugs temporarily while conducting additional diagnostic workup.</td>
</tr>
</tbody>
</table>

**Other Drugs:**
- • See Risk Factors and Prevention/ Monitoring columns for information regarding the toxicity of propylene glycol when LPV/r oral solution is used in neonates. | 3TC, FTC, ABC, TAF, and TDF are less likely to induce clinically significant mitochondrial dysfunction than ZDV. | Note: Patients may present with acute multi-organ failure (e.g., fulminant hepatic failure, pancreatic failure, respiratory failure). |

**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

**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 (e.g., present as a diluent in LPV/r oral solution). A diminished ability to metabolize propylene glycol may lead to accumulation and potential adverse events.

**Weeks and a Postnatal Age of ≥14 Days:**
- Measurement of serum 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.

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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.
References

General Reviews


Risk Factors


Monitoring and Management

