Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 15g. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lactic Acidosis
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<th>Adverse Effects</th>
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| Lactic Acidosis | NRTIs: ZDV  
| Other Drugs: | Less likely with 3TC, FTC, ABC, TAF, and TDF  
| 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 | Adults: Female sex  
| • High BMI  
| • Chronic HCV infection  
| • Cockramination of TDF with metformin  
| • Overdose of propylene glycol  
| • CD4 count <350 cells/mm³  
| • 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.³  
| • 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)³ 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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Table 15g. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lactic Acidosis (Last updated April 14, 2020; last reviewed April 14, 2020) (page 2 of 2)

*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

References

General Reviews


Risk Factors


**Monitoring and Management**


