Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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# Table 15b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia

*Last updated April 27, 2017; last reviewed April 27, 2017*  
*page 1 of 2*

<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>
</tr>
</thead>
</table>
| Dyslipidemia    | PIs:            | Onset:                        | 10% to 20% in young children receiving LPV/RTV. 40% to 75% of older children and adolescents with prolonged ART history will have lipid abnormalities. Higher abnormal fasting serum lipids in EVG/CObI/FTC/TAF vs. EVG/CObI/FTC/TDF regimen in studies of treatment-naive adults. | Advanced-stage HIV disease  
High-fat, high-cholesterol diet  
Lack of exercise  
Obesity  
Hypertension  
Smoking  
Family history of dyslipidemia or premature CVD  
Metabolic syndrome  
Fat maldistribution | Prevention:  
• Low-fat diet  
• Exercise  
• Smoking-prevention counseling  
• Avoid d4T  
| Monitoring:  
Adolescents and Adults:  
• Monitor 12-hour FLP, which includes TC, HDL-C, non-HDL-C, LDL-C, and TG, every 6–12 months. Obtain FLPs twice (>2 weeks but ≤3 months apart, average results) before initiating or changing lipid-lowering therapy.  
Children (Aged ≥2 Years) without Lipid Abnormalities or Additional Risk Factors:  
• Obtain non-fasting screening lipid profiles at entry into care and then, if levels are normal, every 6–12 months. If TG or LDL-C is elevated, obtain fasting blood tests.  
Children with Lipid Abnormalities and/or Additional Risk Factors:  
• Obtain 12-hour FLP before initiating or changing therapy and every 6 months thereafter (more often if indicated).  
ART regimen changes can be considered. Discontinue d4T or substitute a PI-sparing regimen or PI-based regimen with a more favorable lipid profile.  
Consider lipid-lowering therapy in consultation with a lipid specialist if ≥6-month trial of lifestyle modification fails.  
Some experts suggest treatment in children receiving ARV drugs according to NHLBI cardiovascular risk reduction guidelines for children aged ≥10 years: LDL-C ≥190 mg/dL, regardless of additional risk factors; LDL-C ≥160 mg/dL or LDL-C ≥130 mg/dL based on presence of additional risk factors and risk conditions.  
The minimal goal of therapy should be to achieve and maintain a LDL-C value below 130 mg/dL, while maintaining viral control. |

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### Table 1b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia

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<tbody>
<tr>
<td>Dyslipidemia, continued</td>
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<td>Children Receiving Lipid-Lowering Therapy with Statins or Fibrates:</td>
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<td>• Obtain 12-hour FLP, LFTs, and CK at 4 and 8 weeks, and 3 months after starting lipid therapy.</td>
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<td>• If minimal alterations in AST, ALT, and CK, monitor every 3–4 months in the first year and every 6 months thereafter (or as clinically indicated).</td>
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<td>• Repeat FLPs 4 weeks after increasing doses of antihyperlipidemic agents.</td>
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<td>Statins such as pravastatin, atorvastatin, or rosuvastatin can be considered. Statin-induced lipid lowering effect appears more pronounced than ARV substitution.</td>
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<td>Statin-related toxicities include liver enzyme elevation and myopathy, and risk may be increased by drug interactions with ART, particularly PIs. Statins may also increase the risk of insulin resistance and diabetes mellitus. Risks must be weighed against potential benefits.</td>
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<td>Cholesterol absorption inhibitors (e.g., ezetimibe) can be considered as alternative.</td>
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<td>Drug therapy for severe hypertriglyceridemia (TG ≥ 500 mg/dL) can be considered.</td>
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<td>Fibrates (gemfibrozil and fenofibrate) and N-3 PUFAs derived from fish oils may be used.</td>
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<td>The long-term risks of lipid abnormalities in children receiving ART are unclear. However, persistent dyslipidemia in children may lead to premature CVD.</td>
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</tbody>
</table>

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*Given the burden of collecting fasting blood samples, some practitioners routinely measure cholesterol and triglycerides from non-fasting blood samples and follow up abnormal values with a test done in the fasted state.


*The risks of new treatment-related toxicities and virologic failure that could occur with changes in therapy must be weighed against the potential risk of drug interactions and toxicities associated with the use of lipid-lowering agents.

*Statins (HMG-CoA reductase inhibitors) are contraindicated in pregnancy (potentially teratogenic) and should not be used in patients who may become pregnant. Multiple drug interactions exist between ARV drugs and statins (exception pravastatin, which is not dependent on CYP3A4 for metabolism). Pravastatin, atorvastatin, rosuvastatin (Crestor®), fluvastatin, and ezetimibe (Zetia®) are approved for use in children aged ≥10 years. For additional information, see the PI, NNRTI, NRTI, and INSTI Drug Interactions Tables in the [Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents](https://aidsinfo.nih.gov/guidelines).

**Key to Acronyms:** ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; CK = creatine kinase; CVD = cardiovascular disease; CYP3A4 = cytochrome P450 3A4; d4T = stavudine; DRV = darunavir; DRV/r = ritonavir-boosted darunavir; EFV = efavirenz; ETR = etravirine; FLP = fasting lipid profile; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; LFT = liver function test; LPV = lopinavir; NHLBI = National Heart, Lung, and Blood Institute; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PUFA = polyunsaturated fatty acid; RPV = rilpivirine; RTV = ritonavir; TC = total cholesterol; TG = triglyceride
References


*Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*

