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 May 22, 2018; last reviewed May 22, 2018)  
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<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>
<tbody>
<tr>
<td>Dyslipidemia</td>
<td>PIs:</td>
<td>• All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV with or without RTV.</td>
<td> </td>
<td>Advanced-stage HIV disease</td>
<td>Prevention:</td>
<td>Assessment of additional CVD risk factors should be done in all patients. Patients living with HIV are considered to be at moderate risk of CVD.(^b)</td>
</tr>
<tr>
<td></td>
<td>NRTIs:</td>
<td>• Especially d4T  </td>
<td> </td>
<td>High-fat, high-cholesterol diet</td>
<td> </td>
<td>Counsel on lifestyle modification and dietary interventions (e.g., a diet low in saturated fat, cholesterol, and refined sugars, particularly in cases of ↑TG, elimination of trans fat in the diet, increase in physical activity, smoking cessation) for an adequate trial period (3–6 months). Consider consultation with dietician.</td>
</tr>
<tr>
<td></td>
<td>NNRTIs:</td>
<td>• Lower incidence reported with TDF than TAF</td>
<td> </td>
<td>Lack of exercise</td>
<td> </td>
<td>ART regimen changes can be considered. Discontinue d4T or substitute a PI-sparing regimen or PI-based regimen with a more favorable lipid profile.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lower incidence reported with NVP, RVP, and ETR than EFV</td>
<td> </td>
<td>Obesity</td>
<td> </td>
<td>Consider lipid-lowering therapy in consultation with a lipid specialist if ≥6-month trial of lifestyle modification fails.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• As early as 2 weeks to months after beginning therapy</td>
<td> </td>
<td>Hypertension</td>
<td> </td>
<td>Some experts suggest treating 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.(^b)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↑LDL-C, TC, and TG</td>
<td> </td>
<td>Smoking</td>
<td> </td>
<td>The minimal goal of therapy should be to achieve and maintain a LDL-C value below 130 mg/dL, while minimizing side effects and maintaining viral control.</td>
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<tr>
<td></td>
<td></td>
<td>• ↑LDL-C, TC, and HDL-C</td>
<td> </td>
<td>Family history of dyslipidemia or premature CVD</td>
<td> </td>
<td> </td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↑LDL-C, TC, and TG</td>
<td> </td>
<td>Metabolic syndrome</td>
<td> </td>
<td> </td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td> </td>
<td>Fat maldistribution</td>
<td> </td>
<td> </td>
</tr>
</tbody>
</table>

\(^b\) CVD: cardiovascular disease; ART: antiretroviral therapy; FLP: fasting lipid panel; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglycerides; LFTs: liver function tests; CK: creatine kinase; BMI: body mass index; EFV: efavirenz; PI: protease inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; d4T: stavudine; TDF: tenofovir disoproxil fumarate; TAF: tenofovir alafenamide; DRV/r: darunavir/ritonavir; ATV: atazanavir; RTV: ritonavir.
### Table 15b. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia

(Last updated May 22, 2018; last reviewed May 22, 2018)  
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<td>Dyslipidemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Statins such as pravastatin, atorvastatin, or rosuvastatin&lt;sup&gt;a&lt;/sup&gt; can be considered.&lt;sup&gt;4&lt;/sup&gt; Pravastatin has lower lipid-lowering potency compared to other statins. Statin-induced lipid lowering effect appears more pronounced than ARV substitution. Statin-related toxicities include liver enzyme elevation and myopathy, and risk may be increased by drug interactions with ART, particularly PIs.&lt;sup&gt;c&lt;/sup&gt; Statins may also increase the risk of insulin resistance and type 2 diabetes mellitus, but data are conflicting. Risks must be weighed against potential benefits. Cholesterol absorption inhibitors (e.g., ezetimibe) can be considered as alternatives. Drug therapy for severe hypertriglyceridemia (TG ≥500 mg/dL) can be considered. Fibrates (gemfibrozil and fenofibrate) and N-3 PUFAs derived from fish oils may be used. The long-term risks of lipid abnormalities in children receiving ART are unclear. However, persistent dyslipidemia in children may lead to premature CVD.</td>
<td></td>
</tr>
</tbody>
</table>

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<sup>a</sup> Given the burden of collecting fasting blood samples, some practitioners routinely measure cholesterol and triglycerides from nonfasting blood samples and follow up abnormal values with a test done in the fasted state.

<sup>b</sup> Refer to NHLBI guidelines at [https://www.nhlbi.nih.gov/sites/default/files/media/docs/peds_guidelines_full.pdf](https://www.nhlbi.nih.gov/sites/default/files/media/docs/peds_guidelines_full.pdf).

<sup>c</sup> 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.

<sup>d</sup> Statins (HMG-CoA reductase inhibitors) are contraindicated in pregnancy (due to being potentially teratogenic) and should not be used in patients who may become pregnant. Multiple drug interactions exist between ARV drugs and statins (except for 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 INI Drug Interactions Tables in the Adult and Adolescent Guidelines.

<sup>e</sup> d4T is no longer recommended for use in an ARV regimen

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


