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  
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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>
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<tbody>
<tr>
<td>Dyslipidemia</td>
<td>PIs:</td>
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<td></td>
<td>• All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV with or without RTV.</td>
<td>Onset: • As early as 2 weeks to months after beginning therapy</td>
<td>Reported frequency varies with specific ARV regimen, duration of ART, and the specific laboratory parameters used to diagnose lipid abnormalities. 10% to 20% in young children receiving LPV/r. 40% to 75% of older children and adolescents with prolonged ART history will have lipid abnormalities. Higher abnormal fasting serum lipids have also been noted in ART-naive adults who received EVG/COBI/FTC/TAF than in those who received EVG/COBI/FTC/TDF. Increase in serum lipids from baseline has also been noted in adolescents receiving EVG/COBI/FTC/TAF.</td>
<td>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</td>
<td>Prevention: • Low-fat diet • Exercise • Smoking-prevention counseling When possible, use ARVs associated with a lower prevalence of dyslipidemia. These include INSTIs and newer PIs (e.g., ATV, DRV). Monitoring: Adolescents and Adults: • Obtain FLP (TC, HDL-C, non-HDL-C, LDL-C, and TG) twice (&gt;2 weeks but ≤3 months apart, average these results) every 6 months–12 months. Children (Aged ≥2 Years) without Lipid Abnormalities or Additional Risk Factors: • Obtain nonfasting screening lipid profiles at entry into care and then every 6 months–12 months, depending on the results. If TG or LDL-C is elevated or if a patient has additional risk factors, obtain FLP. 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). Children Receiving Lipid-Lowering Therapy with Statins or Fibrates: • Obtain 12-hour FLP, LFT, and CK at 4 and 8 weeks, and 3 months after starting lipid therapy.</td>
<td>Assess all patients for additional CVD risk factors. Patients living with HIV are considered to be at moderate risk of CVD. ART regimen changes should be considered, especially when the patient is receiving older PIs (e.g., LPV/r) and/or ritonavir boosting. Substituting a PI-sparing regimen, a PI-based regimen with a more favorable lipid profile, or COBI boosting causes a decline in LDL-C or TG values. However, the lipid-lowering effect for LDL-C is less pronounced than treatment results with statin therapy. Refer patients to a lipid specialist early if LDL-C ≥250 mg/dL or TG ≥500 mg/dL. If LDL-C is ≥130 mg/dL but &lt;250 mg, or TG is ≥150 mg/dL but &lt;500 mg/dL, a staged treatment approach is recommended by the NHLBI guidelines. • Implement diet, nutrition, and lifestyle management for 6 months to 9 months. Consult with a dietician if one is available. If a 6-month to 9-month trial of lifestyle modification fails and the patient is aged ≥10 years, consider implementing lipid-lowering therapy after consulting a lipid specialist.</td>
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<td>NRTIs:</td>
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<td></td>
<td>• Lower incidence with TDF than with TAF</td>
<td>Presentation PIs: • ↑ LDL-C, TC, and TG</td>
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<td></td>
<td>NNRTIs:</td>
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<td></td>
<td>• Lower incidence reported with NVP, RPV, and ETR than with EFV</td>
<td>Presentation NNRTIs: • ↑ LDL-C, TC, and HDL-C</td>
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## Table 15b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia

(Last updated April 16, 2019; last reviewed April 16, 2019)  (page 2 of 2)

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<td>Dyslipidemia, continued</td>
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- If there are minimal alterations in AST, ALT, and CK, monitor every 3 months–4 months during the first year and every 6 months thereafter (or as clinically indicated).
- Repeat FLP 4 weeks after increasing doses of antihyperlipidemic agents.

- Statin therapy should be considered for patients with elevated LDL-C levels. NHLBI provides recommendations for statin therapy in patients with specific LDL-C levels and risk factors. 
- Drug therapy can be considered in cases of severe hypertriglyceridemia (TG ≥500 mg/dL). 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.

### References


**Key to Acronyms:**
- ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; CK = creatine kinase; COBI = cobicistat; CVD = cardiovascular disease; DRV = darunavir; 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; LDL-C = low-density lipoprotein cholesterol; LFT = liver function test; 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; PUFA = polyunsaturated fatty acid; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglyceride


