Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
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<tbody>
<tr>
<td>Dyslipidemia</td>
<td>Pls:</td>
<td>• All Pls, especially RTV-boosted Pls; 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>Advanced-stage HIV disease</td>
<td>Prevention: • Low-fat diet</td>
<td>Assess all patients for additional CVD risk factors. Patients living with HIV are considered to be at moderate risk of CVD. (^a) ART regimen changes should be considered, especially when the patient is receiving older Pls (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.</td>
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<td>NRTIs:</td>
<td>• Lower incidence with TDF than with TAF.</td>
<td>Presentation Pls: • ↑ LDL-C, TC, and TG.</td>
<td>High-fat, high-cholesterol diet</td>
<td>Monitoring(^a) 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>
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<td>NNRTIs:</td>
<td>• Lower incidence reported with NVP, RPV, and ETR than with EFV.</td>
<td>Presentation: Pls: • ↑ LDL-C, TC, and HDL-C.</td>
<td>Lack of exercise</td>
<td>When possible, use ARVs associated with a lower prevalence of dyslipidemia. These include INSTIs and newer Pls (e.g., ATV, DRV).</td>
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<td>NRTIs:</td>
<td>• Lower incidence reported with NVP, RPV, and ETR than with EFV.</td>
<td>Presentation: Pls: • ↑ LDL-C, TC, and TG.</td>
<td>Obesity</td>
<td>Prevention: • Low-fat diet, exercise, smoking-prevention counseling</td>
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<td>Presentation: Pls: • ↑ LDL-C, TC, and TG.</td>
<td>Hypertension</td>
<td>Monitoring(^a) 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>
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<td>Prevention: • Low-fat diet, exercise, smoking-prevention counseling</td>
<td>Smoking</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 Pls (e.g., ATV, DRV).</td>
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<td>Prevention: • Low-fat diet, exercise, smoking-prevention counseling</td>
<td>Family history of dyslipidemia or premature CVD</td>
<td>Monitoring(^a) 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>
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<td>Prevention: • Low-fat diet, exercise, smoking-prevention counseling</td>
<td>Metabolic syndrome</td>
<td>Monitoring(^a) 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>
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<td>Prevention: • Low-fat diet, exercise, smoking-prevention counseling</td>
<td>Fat maldistribution</td>
<td>Monitoring(^a) 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>
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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</td>
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<td>• 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.¹&lt;br&gt;• Drug therapy can be considered in cases of severe hypertriglyceridemia (TG &gt;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.</td>
</tr>
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</table>

¹ 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.

² Refer to the NHLBI guidelines: Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents.

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; PReSA = polyunsaturated fatty acid; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglyceride

References


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