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 16, 2019; last reviewed April 16, 2019)*  
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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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</table>
| **Dyslipidemia** | **PIs:**  
  • All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV with or without RTV.  
  **NRTIs:**  
  • Lower incidence with TDF than with TAF  
  **NNRTIs:**  
  • Lower incidence reported with NVP, RPV, and ETR than with EFV | **Onset:**  
  • As early as 2 weeks to months after beginning therapy  
  **Presentation:**  
  **PIs:**  
  • ↑ LDL-C, TC, and TG  
  **NRTIs:**  
  • ↑ LDL-C, TC, and TG  
  **NNRTIs:**  
  • ↑ LDL-C, TC, and TG | **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 been observed 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.** | **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  
  • When possible, use ARVs associated with a lower prevalence of dyslipidemia. These include INSTIs and newer PIs (e.g., ATV, DRV).** | **Assess all patients for additional CVD risk factors. Patients living with HIV are considered to be at moderate risk of CVD.** |
| **Adolescents and Adults:**  
  • Obtain FLP (TC, HDL-C, non-HDL-C, LDL-C, and TG) twice (>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. | **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.** |
| **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. | **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 <250 mg/dL or TG is ≥150 mg/dL but <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. | **Assess all patients for additional CVD risk factors. Patients living with HIV are considered to be at moderate risk of CVD.** |  |
### 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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- 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.\(^b\)
- 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.

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\(^a\) 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.

\(^b\) 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
- PUFAs = polyunsaturated fatty acids
- RPV = rilpivirine
- RTV = ritonavir
- TAF = tenofovir alafenamide
- TC = total cholesterol
- TDF = tenofovir disoproxil fumarate
- TG = triglyceride

**References**


