Table 13b. 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>
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| Dyslipidemia    | PIs:            | Onset: As early as 2 weeks to months after beginning therapy | Reported frequency varies with specific ARV regimen, duration of ART and specific laboratory parameters used to diagnose lipid abnormalities. | Advanced-stage HIV disease | Prevention: | 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.  
Counsel on lifestyle modification, dietary interventions (e.g., a diet low in saturated fat, cholesterol, and refined sugars particularly in case of ↑TG, elimination of transfat, physical activity, smoking cessation) for an adequate trial period (3–6 months). Consider consultation with dietician. | ART regimen changes can be considered. Discontinue d4T or substitute a PI-sparing regimen or PI-based regimen with a more favorable lipid profile. |
|                 | • All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV with or without RTV. | Presentation PIs: ↑LDL-C, TC, and TG | 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  
Increase in serum lipids from baseline noted in adolescents receiving EVG/COBI/FTC/TAF | High-fat, high-cholesterol diet  
Lack of exercise  
Obesity  
Hypertension  
Smoking  
Family history of dyslipidemia or premature CVD  
Metabolic syndrome  
Fat maldistribution | Counseling and 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). | 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. |
|                 | NNRTIs:         | Presentation NNRTIs: ↑LDL-C, TC, and HDL-C | 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  
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|                 | NRTIs:          | Monitoring a | 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.  
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|                 | • Especially d4T | Monitoring a | Prevention: Low-fat diet  
• Exercise  
• Smoking-prevention counseling  
Avoid d4T  
Monitoring: Adolescents and Adults:  
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The minimal goal of therapy should be to achieve and maintain a LDL-C value below 130 mg/dL, while maintaining viral control. |
|                 | • EFV > NVP, RPV, and ETR | Monitoring a | 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.  
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### Table 13b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia
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<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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**Statins such as pravastatin, atorvastatin, or rosuvastatin can be considered.** 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.** Statins may also increase the risk of insulin resistance and diabetes mellitus. Risks must be weighed against potential benefits. Cholesterol absorption inhibitors (e.g., ezetimibe) can be considered as alternative.

**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.

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**Key to Acronyms:** ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; CCK = 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


