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) (page 1 of 2)

<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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<td><strong>Dyslipidemia</strong></td>
<td><strong>Pis:</strong> • All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV with or without RTV. <strong>NRTIs:</strong> • Especially d4T • Lower incidence reported with TDF than TAF <strong>NNRTIs:</strong> • Lower incidence reported with NVP, RVP, and ETR than EFV</td>
<td><strong>Onset:</strong> • As early as 2 weeks to months after beginning therapy <strong>Presentation</strong> <strong>Pis:</strong> • ↑LDL-C, TC, and TG <strong>NNRTIs:</strong> • ↑LDL-C, TC, and HDL-C <strong>NRTIs:</strong> • ↑LDL-C, TC, and TG</td>
<td>Reported frequency varies with specific ARV regimen, duration of ART, and 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 in EVG/COBI/FTC/TAF vs. EVG/COBI/FTC/TDF regimen in studies of treatment-naive adults. Increase in serum lipids from baseline also 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 • Do not use d4T</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. 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. ART regimen changes can be considered. Discontinue d4T or substitute a PI-sparing regimen or PI-based regimen with a more favorable lipid profile. Consider lipid-lowering therapy in consultation with a lipid specialist if ≥6-month trial of lifestyle modification fails. 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. 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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Table 15b. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia
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<td>Dyslipidemia</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). • Repeat FLPS 4 weeks after increasing doses of antihyperlipidemic agents.</td>
<td>Statins such as pravastatin, atorvastatin, or rosuvastatin can be considered. 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. 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>
</tr>
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Adverse Effects: 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; INSTI = integrase 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; PUFA = polyunsaturated fatty acid; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglyceride

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

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31. Calza L, Colangeli V, Magistrelli E, et al. No correlation between statin exposure and incident diabetes mellitus in HIV-1-infected patients receiving combination

