Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 17b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia (page 1 of 2) (Last updated November 1, 2012; last reviewed November 1, 2012)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention / Monitoring	Management
Dyslipidemia	PIs: All PIs; lower incidence with ATV and DRV NRTIs: Especially d4T NNRTIs: RPV < EFV	Onset: Weeks to months after beginning therapy Presentation: *PIs:* ↑LDL-C, TC, and TG *NNRTIs:* ↑LDL-C, TC, and HDL-C *NRTIs:* ↑LDL-C, TC, and TG	20%–50% of children receiving ART will have lipoprotein abnormalities.	HIV infection High-fat, high-cholesterol diet Lack of exercise Obesity Hypertension Smoking Family history of dyslipidemia or premature CVD Metabolic syndrome	Prevention: Low-fat diet, exercise, no smoking Monitoring: *Adolescents and adults:* Obtain fasting (12-hour) TC, HDL-C, non-HDL-C, LDL-C, and TG before initiating or changing ART, then every 6 months, and thereafter, every 6–12 months. *Children (aged ≥2 years) without lipid abnormalities or additional risk factors:* Obtain non-fasting screening lipid profiles before initiating or changing therapy and then, if levels are stable, 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 fasting (12-hour) TC, HDL-C, TG, and LDL-C before initiating or changing therapy and every 6 months thereafter (or more often if indicated). *Children receiving lipid-lowering therapy with statins or fibrates:* Obtain fasting (12-hour) lipid profiles, LFTs, and CK before initiating lipid therapy and at 4 weeks and 8 weeks after starting lipid therapy. If minimal alterations in AST, ALT, and CK, repeat tests every 3 months. Also repeat tests 4 weeks after increasing doses of antihyperlipidemic agents.	Counsel lifestyle modification (low-fat diet, exercise, smoking cessation) for adequate trial period (3–6 months). Switch to a new ART regimen less likely to cause lipid abnormalities.[a] Pharmacologic Management: Initiate drug therapy promptly in patients with TG ≥500 mg/dL: Statins such as pravastatin, atorvastatin, or rosuvastatin.[b] Ezetimibe may be considered in addition to statins.[c] Fibrates (gemfibrozil and fenofibrate) and N-3 PUFAs derived from fish oils may be used as alternative agents for adults with ↑TG but are not approved for use in children. No consensus as to what LDL-C should prompt treatment in children receiving ARVs.[d] HIV-infected patients are considered to be at moderate risk of CVD. Assessment of additional risk factors should be done in all patients.[e] *High-risk patients:* Goal LDL-C ≤100 mg/dL. *Moderate-risk patients:* Goal LDL-C ≤130 mg/dL. *At-risk patients:* Goal LDL-C ≤160 mg/dL.

Table 17b. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Dyslipidemia (page 2 of 2) (Last updated November 1, 2012; last reviewed November 1, 2012)

[a] The risks of new treatment-related toxicities and virologic failure that could occur with changes in therapy must be weighed against the potential risk of drug interactions and toxicities associated with the use of lipid-lowering agents.

[b] Statins (HMG-CoA reductase inhibitors) are contraindicated in pregnancy (potentially teratogenic) and should not be used in patients who may become pregnant. Serious toxicities include hepatotoxicity, skeletal muscle toxicity, and rhabdomyolysis. Experience with statins is limited to children >6 years of age.

[c] In general, recommend using in boys aged ≥10 years and in girls preferably after onset of menses. Treatment with statins in children ≤10 years of age is limited to those with severe primary hyperlipidemia, a high-risk condition, or evident CVD, all under the care of a lipid specialist. Multiple drug interactions exist between ARVs and statins (exception pravastatin, which is not dependent on CYP3A4 for metabolism). Pravastatin (Pravachol®), atorvastatin (Lipitor®), rosuvastatin (Crestor®), fluvastatin (Lescol®), and ezetimide (Zetia®) are approved for use in children ≥10 years of age.

[d] The long-term risks of lipid abnormalities in children receiving ART are unclear. However, persistent dyslipidemia in children is likely to lead to premature CVD.

[e] Refer to NHLBI guidelines at http://www.nhlbi.nih.gov/guidelines/cvd_ped/summary.htm#chap9.

Key to Acronyms: ALT = alanine transaminase, ARV = antiretroviral, AST = aspartate aminotransferase, ATV = atazanavir, ART = antiretroviral therapy, CK = creatine kinase, CVD = cardiovascular disease, d4T = stavudine, EFV = efavirenz, HDL-C = high-density lipoprotein cholesterol, non-HDL-C= non-high-density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, LFT = liver function tests, NNRTI = non-nucleoside reverse transcriptase inhibitor, NRTI = nucleoside reverse transcriptase inhibitor, PI = protease inhibitor, PUFA = polyunsaturated fatty acid, RPV = rilpivirine, TC = total cholesterol, TG = triglycerides

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