Table 15b. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Dyslipidemia

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Dyslipidemia	**PIs** • All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV, with or without RTV **NRTIs** • Lower incidence reported with TDF than with TAF **NNRTIs** • Lower incidence reported with NVP, RPV, and ETR than with EFV **INSTIs** EVG/c	**Onset** • As early as 2 weeks to months after beginning therapy **Presentation** *PIs* • ↑ LDL-C, TC, and TG *NRTIs* • ↑ LDL-C, TC, and TG. Significant increase in plasma lipid values was observed in adults switching from TDF to TAF, regardless of third agent or presence of a boosting agent.	Reported frequency varies with specific ARV regimen, duration of ART, and the specific laboratory parameters used to diagnose lipid abnormalities. 10% to 20% of young children receiving LPV/r will have lipid abnormalities. 40% to 75% of older children and adolescents with prolonged ART history will have lipid abnormalities. Pooled dyslipidemia prevalence of 39.5% and an incidence of 32% (191 per 1,000 person-years)	Advanced-stage HIV disease High-fat, high-cholesterol diet Sedentary lifestyle Obesity Hypertension Smoking Family history of dyslipidemia or premature ASCVD Metabolic syndrome Fat maldistribution	**Prevention** • Low-fat diet • Exercise • Smoking-prevention counseling • Use of ARVs associated with a lower prevalence of dyslipidemia, such as INSTIs and, to a lesser extent, newer PIs (e.g., ATV, DRV). • When considering a TDF-based or a TAF-based regimen, the lipid-lowering beneficial effect of TDF should be weighed against its potential for increased renal and bone toxicities. **Monitoring**[a] *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). Monitor FLP every 6 months (for	Assess all patients for additional ASCVD risk factors. Patients with HIV are considered to be at moderate risk of ASCVD.[b] ARV regimen changes should be considered, especially when the patient is receiving older PIs (e.g., LPV/r) and/or RTV boosting. Switching to 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 with statin therapy. Refer patients to a lipid specialist early if LDL-C is ≥250 mg/dL or TG is ≥500 mg/dL. If LDL-C is ≥130 mg/dL but <250 mg or TG is ≥150 mg/dL but <500 mg/dL, the following staged treatment approach is recommended by the NHLBI guidelines:[b] • Implement diet, nutrition, and lifestyle management for 6–9 months. Consult with a dietician if one is available.

		NNRTIs • ↑ LDL-C, TC, and HDL-C	reported in a recent meta-analysis and a recent review of a large consortium of prospective observational cohorts, respectively.		abnormal results) or every 12 months (for normal results). *Children (Aged ≥2 Years) without Lipid Abnormalities or Additional Risk Factors* • Obtain nonfasting screening lipid profiles at entry into care and then every 6–12 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 weeks, 8 weeks, and 3 months after starting lipid therapy. • If minimal alterations in AST, ALT, and CK are indicated, monitor every 3–4 months during the first year and	• If a 6- 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. • 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] Concurrent substitution—preferably to ARVs with no inhibitory or inducing effect on CYP3A4 or OATP1B1 (e.g., INSTI)—also should be considered as appropriate to limit drug–drug interaction potential. • 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 who are receiving ART are unclear. However, persistent dyslipidemia in children may lead to premature ASCVD.

					every 6 months thereafter (or as clinically indicated). • Repeat FLP 4 weeks after increasing doses of antihyperlipidemic agents.	

[a] Because of the burden of collecting fasting blood samples, some practitioners routinely measure cholesterol and TG 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 (PDF).

Key: ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; ASCVD = atherosclerotic cardiovascular disease; AST = aspartate aminotransferase; ATV = atazanavir; CK = creatine kinase; COBI = cobicistat; CYP3A4 = cytochrome P450 3A4; DRV = darunavir; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FLP = fasting lipid profile; 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; OATP1B1 = organic anion transporter polypeptide 1B1; PI = protease inhibitor; PUFA = polyunsaturated fatty acid; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides

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