Table 17b. 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	**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.	Advanced 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 ARV drugs, such as INSTIs, and to a lesser extent, newer PIs (e.g., ATV, DRV), is associated with a lower prevalence of dyslipidemia. • When considering a TDF-based or TAF-based regimen, the lipid-lowering beneficial effect of TDF should be weighed against its potential for increased renal and bone toxicities. **Monitoring**[a] • Obtain fasting (or non-fasting) lipid profile (TC, HDL-C, non-HDL-C, LDL-C, and TG) twice (>2 weeks but ≤3 months apart) and average these results. Monitor every 6 months (for abnormal results) or every 12 months (for normal results).	Assess all patients for additional ASCVD risk factors. Patients with HIV are considered to be at moderate risk for 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. The lipid-lowering effect of an ARV regimen switch on LDL-C is less pronounced than with statin therapy but may be enough to re-establish a healthy lipid profile. Refer patients to a lipid specialist early if LDL-C is ≥250 mg/dL or TG is ≥500 mg/dL.

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
	INSTIs • EVG/c	**NNRTIs** • ↑ LDL-C, TC, and HDL-C	Pooled dyslipidemia prevalence of 39.5% and an incidence of 32% (191 per 1,000 person-years) reported in a meta-analysis and a review of a large consortium of prospective observational cohorts, respectively.		• 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 every 6 months thereafter (or as clinically indicated). • Repeat FLP 4 weeks after increasing doses of antihyperlipidemic agents.	If LDL-C is ≥130 mg/dL but <250 mg or TG is ≥100 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. • 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 guidelines provide recommendations for statin therapy in patients with specific LDL-C levels and risk factors.[b] Concurrent substitution—preferably to ARV drugs 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.

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
						• Drug therapy can be considered in cases of severe hypertriglyceridemia (TG ≥500 mg/dL). Fibrates (gemfibrozil and fenofibrate) may be used. Refer to Statin Therapy in People With HIV in the Adult and Adolescent Guidelines for additional recommendations on statin therapy for people with HIV who are aged <40 years.[c] 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.

[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.

[c] Statin Therapy in People With HIV in the Adult and Adolescent Guidelines states the following: "There are insufficient data to inform whether risk enhancers, such as HIV-related factors, would favor statin therapy among people under 40 years of age. However, some younger people with HIV may be at increased ASCVD risk—particularly those with a very long duration of HIV infection (e.g., due to perinatal exposure)."

Key to Symbol:
↑ = increase

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; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides

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