

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	<p>PIs:</p> <ul style="list-style-type: none"> All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV, with or without RTV. <p>NRTIs:</p> <ul style="list-style-type: none"> Lower incidence reported with TDF than with TAF. <p>NNRTIs:</p> <ul style="list-style-type: none"> Lower incidence reported with NVP, RPV, and ETR than with EFV. 	<p>Onset:</p> <ul style="list-style-type: none"> As early as 2 weeks to months after beginning therapy <p>Presentation</p> <p><i>PIs:</i></p> <ul style="list-style-type: none"> ↑ LDL-C, TC, and TG <p><i>NRTIs:</i></p> <ul style="list-style-type: none"> ↑ 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. <p><i>NNRTIs:</i></p> <ul style="list-style-type: none"> ↑ LDL-C, TC, and HDL-C 	<p>Reported frequency varies with specific ARV regimen, duration of ART, and the specific laboratory parameters used to diagnose lipid abnormalities.</p> <p>10% to 20% of young children receiving LPV/r will have lipid abnormalities.</p> <p>40% to 75% of older children and adolescents with prolonged ART history will have lipid abnormalities.</p> <p>Pooled dyslipidemia prevalence of 39.5% reported in a recent meta-analysis.</p> <p>Increase in serum lipids from baseline has also been noted in adolescents receiving EVG/c/FTC/TAF.</p>	<p>Advanced-stage HIV disease</p> <p>High-fat, high-cholesterol diet</p> <p>Lack of exercise</p> <p>Obesity</p> <p>Hypertension</p> <p>Smoking</p> <p>Family history of dyslipidemia or premature ASCVD</p> <p>Metabolic syndrome</p> <p>Fat maldistribution</p>	<p>Prevention:</p> <ul style="list-style-type: none"> Low-fat diet Exercise Smoking-prevention counseling Use ARVs associated with a lower prevalence of dyslipidemia, these include INSTIs and newer PIs (e.g., ATV, DRV). When considering a TDF-based or a TAF-based regimen, lipid-lowering beneficial effect of TDF should be weighed against its potential for increased renal and bone toxicities. <p>Monitoring^a</p> <p><i>Adolescents and Adults:</i></p> <ul style="list-style-type: none"> 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 abnormal results) or every 12 months (for normal results). <p><i>Children (Aged ≥2 Years) without Lipid Abnormalities or Additional Risk Factors:</i></p> <ul style="list-style-type: none"> 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. <p><i>Children with Lipid Abnormalities and/or Additional Risk Factors:</i></p> <ul style="list-style-type: none"> Obtain 12-hour FLP before initiating or changing therapy and every 6 months thereafter (more often if indicated). <p><i>Children Receiving Lipid-Lowering Therapy with Statins or Fibrates:</i></p>	<p>Assess all patients for additional ASCVD risk factors. Patients with HIV are considered to be at moderate risk of ASCVD.^b</p> <p>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.</p> <p>Refer patients to a lipid specialist early if LDL-C is ≥250 mg/dL or TG is ≥500 mg/dL.</p> <p>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</p> <ul style="list-style-type: none"> 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 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

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Dyslipidemia, continued					<ul style="list-style-type: none"> 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. 	<p>on CYP3A4 or OATP1B1 (e.g., INSTI)—also should be considered as appropriate to limit drug-drug interaction potential^a</p> <ul style="list-style-type: none"> 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. <p>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.</p>

^a Given 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](#).

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; FTC = emtricitabine; 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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