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

**Last updated April 14, 2020; last reviewed April 14, 2020**

<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>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidemia</td>
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<tr>
<td>PIs:</td>
<td>All PIs, especially RTV-boosted PIs; lower incidence reported with DRV/r and ATV, with or without RTV.</td>
<td>Onset: As early as 2 weeks to months after beginning therapy</td>
<td>Reported frequency varies with specific ARV regimen, duration of ART, and the specific laboratory parameters used to diagnose lipid abnormalities.</td>
<td>Advanced-stage HIV disease, High-fat, high-cholesterol diet, Lack of exercise, Obesity, Hypertension, Smoking, Family history of dyslipidemia or premature ASCVD, Metabolic syndrome, Fat maldistribution</td>
<td>Prevention: Low-fat diet, Exercise, Smoking-prevention counseling, When possible, use ARVs associated with a lower prevalence of dyslipidemia. These include INSTIs and newer PIs (e.g., ATV, DRV).</td>
<td>Assess all patients for additional ASCVD risk factors. Patients with HIV are considered to be at moderate risk of ASCVD. 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 ≥ 250 mg/dL or TG is ≥ 500 mg/dL. If LDL-C is ≥ 130 mg/dL but &lt; 250 mg, or TG is ≥ 150 mg/dL but &lt; 500 mg/dL, the following staged treatment approach is recommended by the NHLBI guidelines: Implement diet, nutrition, and lifestyle management for 6–9 months. Consult with a dietician if one is available. If a 6-month 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.</td>
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<tr>
<td>NRTIs:</td>
<td>Lower incidence reported with TDF than with TAF.</td>
<td>Presentation PIs: t LDL-C, TC, and TG</td>
<td>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. Higher abnormal fasting serum lipids have been observed in ART-naïve adults who received EVG/c/FTC/TAF than in those who received EVG/c/FTC/TDF. Increase in serum lipids from baseline has also been noted in adolescents receiving EVG/c/FTC/TAF.</td>
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<tr>
<td>NNRTIs:</td>
<td>Lower incidence reported with NVP, RPV, and ETR than with EFV.</td>
<td>Prevention:</td>
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**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 April 14, 2020; last reviewed April 14, 2020) (page 2 of 2)

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<tr>
<td>Dyslipidemia, continued</td>
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- If there are minimal alterations in AST, ALT, and CK, 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.

- 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.

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**Key:**  
ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; ASCVD = atherosclerotic cardiovascular disease; AST = aspartate aminotransferase; ATV = atazanavir; CK = creatine kinase; COBI = cobicistat; 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; 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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**References**


Table 15c. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Gastrointestinal Effects  (Last updated April 16, 2019; last reviewed April 14, 2020)  (page 1 of 2)

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<td>Nausea/Vomiting</td>
<td>All ARV drugs, but most notably RTV-boosted PIs</td>
<td>Onset: • Early Presentation: • Nausea and emesis, both of which may be associated with anorexia and/or abdominal pain</td>
<td>Varies by ARV agent; generally &lt;15%</td>
<td>Unknown</td>
<td>Instruct patient to take PIs with food. Monitor for weight loss and ARV adherence.</td>
<td>Reassure patient that these adverse effects generally improve over time (usually in 6–8 weeks). Consider switching to ARV drugs with smaller tablet sizes (see Appendix A, Table 2). Provide supportive care. In extreme or persistent cases, use antiemetics or switch to another ARV regimen.</td>
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<tr>
<td>Diarrhea</td>
<td>All ARV drugs, but most notably RTV-boosted PIs</td>
<td>Onset: • Early Presentation: • More frequent bowel movements and stools that are generally soft</td>
<td>Varies by ARV agent; generally &lt;15%</td>
<td>Unknown</td>
<td>Monitor for weight loss and dehydration.</td>
<td>In prolonged or severe cases, exclude infectious or noninfectious (e.g., lactose intolerance) causes of diarrhea. Reassure patient that this adverse effect generally improves over time (usually in 6–8 weeks). Consider switching to another ARV regimen in persistent and severe cases. Treatment data in children are lacking; however, the following strategies may be useful when the ARV regimen cannot be changed: • Dietary modification • Using bulk-forming agents (e.g., psyllium) • Using antimotility agents (e.g., loperamide) • Using crofelemer, which is approved by the FDA to treat ART-associated diarrhea in adults aged ≥18 years; no pediatric data are available.</td>
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| Pancreatitis    | Rare, but may occur with NRTIs or RTV-boosted PIs | Onset:  
  • Any time, usually after months of therapy  
Presentation:  
  • Emesis, abdominal pain, elevated amylase and lipase levels (asymptomatic hyperamylasemia or elevated lipase do not in and of themselves indicate pancreatitis) | <2% in a recent case series | Use of concomitant medications that are associated with pancreatitis (e.g., TMP-SMX, pentamidine, ribavirin)  
  Hypertriglyceridemia  
  Advanced HIV infection  
  Previous episode of pancreatitis  
  Alcohol use | Measure serum amylase and lipase concentrations if persistent abdominal pain develops. | Discontinue offending agent and avoid reintroduction.  
Manage symptoms of acute episodes.  
If pancreatitis is associated with hypertriglyceridemia, consider using interventions to lower TG levels. |

**Key:** ART = antiretroviral therapy; ARV = antiretroviral; FDA = Food and Drug Administration; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RTV = ritonavir; TG = triglyceride; TMP-SMX = trimethoprim sulfamethoxazole

**References**


