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

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

<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>
<td>Pls:</td>
<td></td>
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<tr>
<td></td>
<td>• All Pls, especially RTV-boosted Pls; lower incidence reported with DRV/r and ATV, with or without RTV.</td>
<td>Onset:</td>
<td>As early as 2 weeks to months after beginning therapy</td>
<td>Prevention Pls:</td>
<td>• LDL-C, TC, and TG</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>
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<td></td>
<td>NRTIs:</td>
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<td></td>
<td>• Lower incidence reported with TDF than with TAF.</td>
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<tr>
<td></td>
<td>NNRTIs:</td>
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<tr>
<td></td>
<td>• Lower incidence reported with NVP, RPV, and ETR than with EFV.</td>
<td>Presentation</td>
<td>Pls:</td>
<td>• LDL-C, TC, and TG</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>NRTIs:</td>
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<td></td>
<td>• Lower incidence reported with TDF than with TAF.</td>
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<td>• LDL-C, TC, and TG</td>
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<tr>
<td></td>
<td></td>
<td>Fat maldistribution</td>
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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)

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
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<th>Prevention/Monitoring</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidemia, continued</td>
<td></td>
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<td></td>
<td>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).</td>
<td>Repeat FLP 4 weeks after increasing doses of antihyperlipidemic agents.</td>
<td>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). * 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.</td>
</tr>
</tbody>
</table>

\* 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](https://www.nhlbi.nih.gov/guidelines).

**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

### References


### Table 15c. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Gastrointestinal Effects

_Last updated April 16, 2019; last reviewed April 14, 2020_

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
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<tbody>
<tr>
<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>
</tr>
</tbody>
</table>

- 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.

| Diarrhea | All ARV drugs, but most notably RTV-boosted PIs | Onset: • Early Presentation: • More frequent bowel movements and stools that are generally soft | Varies by ARV agent; generally <15% | Unknown | Monitor for weight loss and dehydration. | 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. |
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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**


