Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 15j. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Osteopenia and Osteoporosis *(Last updated April 16, 2019; last reviewed April 16, 2019)*

<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>Osteopenia and Osteoporosis</td>
<td>Any ART regimen</td>
<td>Onset: • Any age; decrease in BMD is usually seen soon after initiation of ART.</td>
<td>BMD z Score Less Than -2.0: • &lt;10% in U.S. cohorts</td>
<td>Longer duration and greater severity of HIV disease</td>
<td>• Ensure that the patient has sufficient intake and levels of both calcium and vitamin D</td>
<td>Same options as for prevention.</td>
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<tr>
<td>Specific Agents of Concern:</td>
<td>• TDF, especially when used in a regimen that includes a boosting agent (i.e., RTV, COBI)</td>
<td>Presentation: • Usually asymptomatic • Rarely presents as osteoporosis, a clinical diagnosis defined by evidence of bone fragility (e.g., fracture with minimal trauma)</td>
<td>Approximately 20% to 30% in international cohorts</td>
<td>Vitamin D insufficiency/deficiency</td>
<td>• Encourage weight-bearing exercise.</td>
<td>Consider changing the ARV regimen (e.g., switching from TDF to TAF, and/or from LPV/r to EFV or an un-boosted INSTI whenever possible).</td>
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<tr>
<td></td>
<td>• PIs, especially LPV/r</td>
<td>Delayed growth or pubertal delay</td>
<td>Low BMI</td>
<td>Delayed growth or pubertal delay</td>
<td>• Minimize modifiable risk factors (e.g., smoking, low BMI, use of steroids or medroxyprogesterone).</td>
<td>Treat patient with vitamin D3 to raise serum 25-OH-vitamin D concentrations to &gt;30 ng/mL. Vitamin D3 levels should be monitored in patients who are receiving a daily dose of vitamin D3 &gt;4,000 IU.</td>
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<td></td>
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<td>Lipodystrophy</td>
<td>Non-black race</td>
<td>Lipodystrophy</td>
<td>• Use TAF instead of TDF whenever possible.</td>
<td>The role of bisphosphonates in managing osteopenia and osteoporosis in children with HIV has not been established.</td>
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<td></td>
<td></td>
<td>Smoking</td>
<td>Prolonged systemic corticosteroid use</td>
<td>Non-black race</td>
<td>• Use TDF with EFV or an unboosted INSTI.</td>
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<tr>
<td></td>
<td></td>
<td>Medroxyprogesterone use</td>
<td>Smoking</td>
<td>Smoking</td>
<td>• When using TDF in a regimen, consider supplementing with vitamin D3 at a daily dose of 1,000–4,000 IU</td>
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<tr>
<td></td>
<td></td>
<td>Lack of weight-bearing exercise</td>
<td>Prolonged systemic corticosteroid use</td>
<td>Prolonged systemic corticosteroid use</td>
<td>Monitoring: • Assess nutritional intake (calcium, vitamin D, and total calories).</td>
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<td></td>
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<td></td>
<td>Medroxyprogesterone use</td>
<td>Medroxyprogesterone use</td>
<td>• Strongly consider measuring serum 25-OH-vitamin D levels, particularly in patients who are taking ARV drugs of concern.a</td>
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<td></td>
<td>Lack of weight-bearing exercise</td>
<td>Lack of weight-bearing exercise</td>
<td>• Obtain a DXA.b</td>
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</tbody>
</table>

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*a Some experts periodically measure 25-OH-vitamin D. This is especially important in children and adolescents with HIV who live in urban areas; the prevalence of vitamin D insufficiency is high in that population.*

*b Until more data are available on the long-term effects of TDF on bone mineral acquisition in childhood, DXA scanning is not usually recommended for children who are being treated with TDF. Obtaining a DXA could be considered for adolescent women who are receiving TDF and medroxyprogesterone and for children with indications that are not uniquely related to HIV infection (such as cerebral palsy).*

**Key to Acronyms:** ART = antiretroviral therapy; ARV = antiretroviral; BMD = bone mineral density; BMI = body mass index; COBI = cobicistat; DXA = dual-energy x-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; IU = international unit; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate.
References


