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

<table>
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<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
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<th>Risk Factors</th>
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| Osteopenia and Osteoporosis | Any ART regimen | Onset:  
Specific Agents of Concern:  
• TDF, especially when used in a regimen that includes a boosting agent (i.e., RTV, COBI)  
• PIs, especially LPV/r | BMD z Score Less Than -2.0:  
<10% in U.S. cohorts  
Approximately 20% to 30% in international cohorts | Longer duration and greater severity of HIV disease  
Vitamin D insufficiency/deficiency  
Delayed growth or pubertal delay  
Low BMI  
Lipodystrophy  
Non-black race  
Smoking  
Prolonged systemic corticosteroid use  
Medroxyprogesterone use  
Lack of weight-bearing exercise | Prevention:  
• Ensure that the patient has sufficient intake and levels of both calcium and vitamin D  
• Encourage weight-bearing exercise.  
• Minimize modifiable risk factors (e.g., smoking, low BMI, use of steroids or medroxyprogesterone).  
• Use TAF instead of TDF whenever possible.  
• Use TDF with EFV or an un-boosted INSTI.  
• When using TDF in a regimen, consider supplementing with vitamin D3 at a daily dose of 1,000–4,000 IU.  
Monitoring:  
• Assess nutritional intake (calcium, vitamin D, and total calories).  
• Strongly consider measuring serum 25-OH-vitamin D levels, particularly in patients who are taking ARV drugs of concern.a  
• Obtain a DXA.b | Same options as for prevention.  
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).  
Treat patient with vitamin D3 to raise serum 25-OH-vitamin D concentrations to >30 ng/mL. Vitamin D3 levels should be monitored in patients who are receiving a daily dose of vitamin D3 >4,000 IU.  
The role of bisphosphonates in managing osteopenia and osteoporosis in children with HIV has not been established. |

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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


