Table 15j. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Osteopenia and Osteoporosis

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/ Monitoring	Management
Osteopenia and Osteoporosis	Any ARV regimen **Specific Agents of Concern** • TDF, especially when used in a regimen that includes a boosting agent (i.e., RTV, COBI) • PIs (LPV, ATV>DRV) • EFV	**Onset** • Any age; decrease in BMD is usually seen soon after initiating ART. **Presentation** • Usually asymptomatic • Rarely presents as osteoporosis, a clinical diagnosis defined by evidence of bone fragility (e.g., a fracture with minimal trauma).	**BMD *z score* Less Than −2.0** • <10% in U.S. cohorts • Approximately 10% to 20% in international cohorts	• Longer duration and greater severity of HIV disease • Detectable viral load • Vitamin D insufficiency/deficiency • Delayed growth or pubertal delay • Low BMI • Lipodystrophy • 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 RPV or an unboosted INSTI. • When using TDF or EFV in a regimen, consider measuring vitamin D levels and supplementing with vitamin D3 if deficiency is identified. **Monitoring** • Assess nutritional intake (calcium, vitamin D, and total calories). • Consider measuring serum 25-OH-vitamin D levels, particularly in patients who are taking ARV drugs of concern.[a] • DXA is rarely indicated.[b]	• Same options as for prevention. • Consider changing the ARV regimen (e.g., switching from TDF to TAF, and/or from LPV/r to RPV or an unboosted INSTI whenever possible). • Supplement with vitamin D3 to raise serum 25-OH-vitamin D concentrations to >30 ng/mL. There is no clear benefit to administering daily supplemental vitamin D3 doses that are >4,000 IU. If patients are receiving a daily dose of vitamin D3 that is >4,000 IU, consider monitoring levels of 25-OH-vitamin D. • An increase in BMD was seen in one trial that evaluated the use of alendronate in youth with HIV and low BMD. However, the role of bisphosphonates in managing osteopenia and osteoporosis in children with HIV has not been established.

[a] Drugs of greatest concern are TDF and EFV. Some experts measure 25-OH-vitamin D in children with HIV with additional risk factors, including living at high latitudes, sun avoidance, low dietary intake, and obesity (U.S. Preventive Services Task Force 2021 guidelines).

[b] DXA scanning is not routinely recommended for children and youth who are being treated with TDF. DXA scanning can be considered for children and youth who are receiving additional medications which also affect bone density or have non-HIV related conditions for which DXA scans may be indicated (such as cerebral palsy).

Key: 25-OH-vitamin D = 25-hydroxy vitamin D; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; BMD = bone mineral density; BMI = body mass index; COBI = cobicistat; DRV = darunavir; DXA = dual-energy x-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; IU = international unit; LPV = lopinavir; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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