



## **Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection**

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 7/11/2017

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

**Table 13j. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Osteopenia and Osteoporosis** (Last updated April 27, 2017; last reviewed April 27, 2017)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
<b>Osteopenia and Osteoporosis</b>	Any ART regimen  <u>Specific Agents of Possible Concern:</u> • TDF • PIs, especially LPV/r	<u>Onset:</u> • Any age; decrease in BMD usually seen early after initiation of ART.  <u>Presentation:</u> • Most commonly asymptomatic  • Rarely presents as osteoporosis; a clinical diagnosis defined by evidence of bone fragility (e.g., fracture with minimal trauma).	<u>BMD z Score Less Than -2.0:</u> • <10% in U.S. cohorts  • Approximately 20% to 30% in international cohorts	Longer duration and greater severity of HIV disease Growth or pubertal delay Low BMI Lipodystrophy Non-black race Smoking Prolonged systemic corticosteroid use Medroxyprogesterone use Limited weight-bearing exercise	<u>Prevention:</u> • Ensure sufficient calcium intake and vitamin D sufficiency. • Encourage weight-bearing exercise. • Minimize modifiable risk factors (e.g., smoking, low BMI, use of steroids or medroxyprogesterone).  <u>Monitoring:</u> • Assess nutritional intake (calcium, vitamin D, and total calories). • Consider measuring serum 25-OH-vitamin D level. <sup>a</sup> • DXA. <sup>b</sup>	Same options as for prevention.  Consider change in ARV regimen (e.g., changing TDF to TAF).  Role of bisphosphonates not established in children with HIV infection.

<sup>a</sup> Some experts would periodically measure 25-OH-vitamin D, especially in urban youth with HIV infection, because in that population, the prevalence of vitamin D insufficiency is high.

<sup>b</sup> Until more data are available about the long-term effects of TDF on bone mineral acquisition in childhood, some experts would obtain a DXA at baseline and every 6 to 12 months for prepubertal children and children in early puberty who are initiating treatment with TDF. DXA could also be considered in adolescent women on TDF and medroxyprogesterone and in children with indications 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; DXA = dual-energy x-ray absorptiometry; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; TDF = tenofovir disoproxil fumarate, TAF= tenofovir alafenamide

## References

### Osteopenia and Osteoporosis

- Gafni RI, Hazra R, Reynolds JC, et al. Tenofovir disoproxil fumarate and an optimized background regimen of antiretroviral agents as salvage therapy: impact on bone mineral density in HIV-infected children. *Pediatrics*. 2006;118(3):e711-718. Available at <http://www.ncbi.nlm.nih.gov/pubmed/16923923>.
- Jacobson DL, Lindsey JC, Gordon CM, et al. Total body and spinal bone mineral density across Tanner stage in perinatally HIV-infected and uninfected children and youth in PACTG 1045. *AIDS*. 2010;24(5):687-696. Available at <http://www.ncbi.nlm.nih.gov/pubmed/20168204>.
- Jacobson DL, Spiegelman D, Duggan C, et al. Predictors of bone mineral density in human immunodeficiency virus-1 infected children. *Journal of Pediatric Gastroenterology and Nutrition*. 2005;41(3):339-346. Available at <http://www.ncbi.nlm.nih.gov/pubmed/16131991>.
- Kalkwarf HJ, Zemel BS, Gilsanz V, et al. The bone mineral density in childhood study: bone mineral content and density according to age, sex, and race. *J Clin Endocrin Metab*. 2007;92(6):2087-2099. Available at <http://www.ncbi.nlm.nih.gov/pubmed/17311856>.
- Bachrach LK, Sills IN, Section on E. Clinical report-bone densitometry in children and adolescents. *Pediatrics*. 2011;127(1):189-194. Available at <http://www.ncbi.nlm.nih.gov/pubmed/21187316>.

6. Lima LR, Silva RC, Giuliano Ide C, Sakuno T, Brincas SM, Carvalho AP. Bone mass in children and adolescents infected with human immunodeficiency virus. *Jornal de pediatria*. 2013;89(1):91-99. Available at <http://www.ncbi.nlm.nih.gov/pubmed/23544816>.
7. Puthanakit T, Saksawad R, Bunupuradah T, et al. Prevalence and risk factors of low bone mineral density among perinatally HIV-infected Thai adolescents receiving antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2012;61(4):477-483. Available at <http://www.ncbi.nlm.nih.gov/pubmed/22918157>.
8. Siberry GK, Li H, Jacobson D, Pediatric ACTGCS. Fracture risk by HIV infection status in perinatally HIV-exposed children. *AIDS Res Hum Retroviruses*. 2012;28(3):247-250. Available at <http://www.ncbi.nlm.nih.gov/pubmed/22471877>.
9. DiMeglio LA, Wang J, Siberry GK, et al. Bone mineral density in children and adolescents with perinatal HIV infection. *AIDS*. 2013;27(2):211-220. Available at <http://www.ncbi.nlm.nih.gov/pubmed/23032412>.
10. Bunders MJ, Frinking O, Scherpbier HJ, et al. Bone mineral density increases in HIV-infected children treated with long-term combination antiretroviral therapy. *Clin Infect Dis*. 2013;56(4):583-586. Available at <http://www.ncbi.nlm.nih.gov/pubmed/23097583>.
11. Huang JS, Hughes MD, Riddler SA, Haubrich RH, AIDS Clinical Trials Group AST. Bone mineral density effects of randomized regimen and nucleoside reverse transcriptase inhibitor selection from ACTG A5142. *HIV Clin Trials*. 2013;14(5):224-234. Available at <http://www.ncbi.nlm.nih.gov/pubmed/24144899>.
12. Puthanakit T, Siberry GK. Bone health in children and adolescents with perinatal HIV infection. *J Int AIDS Soc*. 2013;16:18575. Available at <http://www.ncbi.nlm.nih.gov/pubmed/23782476>.
13. Aurpibul L, Cressey TR, Sricharoenchai S, et al. Efficacy, safety and pharmacokinetics of tenofovir disoproxil fumarate in virologic-suppressed HIV-infected children using weight-band dosing. *Pediatr Infect Dis J*. 2015;34(4):392-397. Available at <http://www.ncbi.nlm.nih.gov/pubmed/25760566>.
14. Overton ET, Chan ES, Brown TT, et al. Vitamin D and Calcium Attenuate Bone Loss With Antiretroviral Therapy Initiation: A Randomized Trial. *Ann Intern Med*. 2015;162(12):815-824. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26075752>.
15. Ross AC. The 2011 report on dietary reference intakes for calcium and vitamin D. *Public Health Nutr*. 2011;14(5):938-939. Available at <http://www.ncbi.nlm.nih.gov/pubmed/21492489>.
16. Mirani G, Williams PL, Chernoff M, et al. Changing trends in complications and mortality rates among US youth and young adults with HIV infection in the Era of Combination Antiretroviral Therapy. *Clin Infect Dis*. 2015;61(12):1850-1861. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26270680>.
17. Eckard AR, Mora S. Bone health in HIV-infected children and adolescents. *Curr Opin HIV AIDS*. 2016;11(3):294-300. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26890208>.
18. Okonkwo RI, Weidmann AE, Effa EE. Renal and bone adverse effects of a tenofovir-based regimen in the treatment of HIV-infected children: a systematic review. *Drug Safety*. 2016;39(3):209-218. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26692394>.
19. Palchetti CZ, Szejnfeld VL, de Menezes Succi RC, et al. Impaired bone mineral accrual in prepubertal HIV-infected children: a cohort study. *Braz J Infect Dis*. 2015;19(6):623-630. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26477385>.
20. Mills A, Arribas JR, Andrade-Villanueva J, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multicentre, open-label, phase 3, non-inferiority study. *Lancet Infect Dis*. 2016;16(1):43-52. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26538525>.
21. Tebas P, Kumar P, Hicks C, et al. Greater change in bone turnover markers for efavirenz/emtricitabine/tenofovir disoproxil fumarate versus dolutegravir + abacavir/lamivudine in antiretroviral therapy-naïve adults over 144 weeks. *AIDS*. 2015;29(18):2459-2464. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26355674>.
22. Kizito H, Gaur A, Prasitsuebsai W, et al. Changes in renal laboratory parameters and bone mineral density in treatment-naïve HIV-1-infected adolescents initiating therapy with INSTI-based single-tablet regimens containing tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF). Presented at: The 21st International AIDS Conference. 2016. Durban, South Africa.