Tenofovir Disoproxil Fumarate (TDF, Viread)

Updated: September 30, 2025
Reviewed: September 30, 2025

Formulations

Oral Powder: 40 mg per 1 g of oral powder (one level scoop, measured with supplied dosing scoop, equals 1 g oral powder)

Tablets: 150 mg, 200 mg, 250 mg, and 300 mg

Fixed-Dose Combination (FDC) Tablets

- [Atripla[a] and generic] Efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg
- [Cimduo] Lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Complera] Emtricitabine 200 mg/rilpivirine 25 mg/tenofovir disoproxil fumarate 300 mg
- [Delstrigo] Doravirine 100 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Stribild] Elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg
- [Symfi] Efavirenz 600 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Symfi Lo[a] and generic] Efavirenz 400 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Temixys] Lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Truvada tablet]
  - Emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg
  - Emtricitabine 167 mg/tenofovir disoproxil fumarate 250 mg
  - Emtricitabine 133 mg/tenofovir disoproxil fumarate 200 mg
  - Emtricitabine 100 mg/tenofovir disoproxil fumarate 150 mg

When using FDC tablets, refer to other sections of Appendix A. Pediatric Antiretroviral Drug Information for information about the individual components of the FDC. See also Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents.

For additional information, see Drugs@FDA or DailyMed.

Dosing Recommendations

Neonate and Infant Dose

- Tenofovir disoproxil fumarate (TDF) has not been approved by the U.S. Food and Drug Administration or recommended for use in neonates or infants aged <2 years.

Child (Aged ≥2 Years to <12 Years) and Weighing ≥10 kg Dose[a]

- TDF 8 mg/kg per dose once daily

Selected Adverse Events

- Asthenia, headache, diarrhea, nausea, vomiting, flatulence
- Glomerular and proximal renal tubular dysfunction
- Decreased bone mineral density[b]

Special Instructions

- TDF oral powder formulation is available for children who are unable to swallow tablets.
- TDF oral powder should be measured only with the supplied dosing scoop: one level scoop = 1 g powder = TDF 40 mg.

TDF Oral Powder Dosing Table

Body Weight	**TDF Oral Powder** Once-Daily Scoops of Powder
10 kg to <12 kg	2 scoops (80 mg)
12 kg to <14 kg	2.5 scoops (100 mg)
14 kg to <17 kg	3 scoops (120 mg)
17 kg to <19 kg	3.5 scoops (140 mg)
19 kg to <22 kg	4 scoops (160 mg)
22 kg to <24 kg	4.5 scoops (180 mg)
24 kg to <27 kg	5 scoops (200 mg)
27 kg to <29 kg	5.5 scoops (220 mg)
29 kg to <32 kg	6 scoops (240 mg)
32 kg to <34 kg	6.5 scoops (260 mg)
34 kg to <35 kg	7 scoops (280 mg)
≥35 kg	7.5 scoops (300 mg)

TDF Tablet Dosing Table

Body Weight	**TDF Tablet** Once Daily
17 kg to <22 kg	150 mg
22 kg to <28 kg	200 mg
28 kg to <35 kg	250 mg
≥35 kg	300 mg

Child and Adolescent (Weighing ≥35 kg)[a] and Adult Dose

- TDF 300 mg once daily

[Atripla[a] and Generic] Efavirenz (EFV)/ Emtricitabine (FTC)/TDF

Child and Adolescent (Weighing ≥40 kg) and Adult Dose

- One tablet once daily
- Take on an empty stomach.

[Cimduo] Lamivudine (3TC)/TDF

Child and Adolescent (Weighing ≥35 kg) and Adult Dose

- One tablet once daily
- Mix TDF oral powder with 2–4 oz of soft food that does not require chewing (e.g., applesauce, yogurt). Administer immediately after mixing to avoid the bitter taste.
- Do not try to mix the TDF oral powder with liquid. The powder may float on the top even after vigorous stirring.
- Although TDF can be administered without food, food requirements vary depending on the other antiretroviral (ARV) drugs contained in an FDC tablet. Food requirements are listed with dosing recommendations in Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents.
- Measure serum creatinine and perform a urine dipstick test for protein and glucose before starting a TDF-containing regimen. Serum creatinine should be monitored, and urine should be tested for protein and glucose at intervals during continued therapy (see Table 17i. Nephrotoxic Effects). Measure serum phosphate if there is clinical suspicion of hypophosphatemia.
- Screen children for hepatitis B virus (HBV) infection before using TDF. Severe acute exacerbation of HBV infection can occur when TDF is discontinued; therefore, hepatic function should be monitored for several months after children with HBV infection stop taking TDF.
- Tenofovir alafenamide (TAF) is associated with less bone and renal toxicity than TDF, but it has equal antiviral efficacy. **Do not use TAF and TDF together.** Consider switching from TDF to TAF in appropriate clinical settings.

Metabolism/Elimination

TDF Dosing in Children With Hepatic Impairment

- No change in TDF dosing is required for children with hepatic impairment.
- Stribild **should not be used** in children with severe hepatic impairment.
- Atripla[a], Symfi, and Symfi Lo[a] should be used with caution in children with hepatic impairment; Symfi and Symfi Lo[a] **are not recommended** for use in moderate or severe hepatic impairment.

TDF Dosing in Children With Renal Insufficiency

- The tenofovir metabolite of TDF is renally excreted.

[Complera] FTC/Rilpivirine/TDF *Child and Adolescent (Aged ≥12 Years and Weighing ≥35 kg) and Adult Dose* • One tablet once daily in antiretroviral therapy (ART)–naive adults with baseline HIV RNA ≤100,000 copies/mL. This dose of Complera also can be used in virologically suppressed (HIV RNA <50 copies/mL) adults who are currently on their first or second regimen and have no history of virologic failure or resistance to rilpivirine and other ARV drugs. • Administer with a meal of ≥500 calories. **[Delstrigo] Doravirine/3TC/TDF** *Child and Adolescent (Weighing ≥35 kg) and Adult Dose* • One tablet once daily in people who are ART-naive and people who are ARV-experienced who have been virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen, with no history of treatment failure, and with no known mutations associated with resistance to the individual components of Delstrigo. **[Stribild] Elvitegravir/Cobicistat/FTC/TDF** *Adolescent (Weighing >35 kg With a Sexual Maturity Rating [SMR] of 4 or 5) and Adult Dose* • One tablet once daily in ART-naive adults. This dose of Stribild also can be used to replace the current ARV regimen in adolescents and adults who have been virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen, with no history of treatment failure, and with no known mutations associated with resistance to the individual components of Stribild. • Administer with food. **[Symfi] EFV 600 mg/3TC/TDF** *Child and Adolescent (Weighing ≥40 kg) and Adult Dose* • One tablet once daily • Take on an empty stomach. **[Symfi Lo[a] and Generic] EFV 400 mg/3TC/TDF** *Child and Adolescent (Weighing ≥35 kg) and Adult Dose* • One tablet once daily • Take on an empty stomach.	• The dose of TDF should be decreased in children with impaired renal function (creatinine clearance [CrCl] <50 mL/min). Consult the manufacturer's prescribing information for directions on how to adjust the dose in accordance with CrCl. • The FDCs Atripla[a], Cimduo, Complera, Delstrigo, Symfi, Symfi Lo[a], or Temixys **should not be used** in children with CrCl <50 mL/min or in children who require dialysis. • The FDC Truvada **should not be used** in children with CrCl <30 mL/min or in children who require dialysis. • The FDC Stribild **should not be initiated** in children with estimated CrCl <70 mL/min and should be discontinued in children with estimated CrCl <50 mL/min. • FTC and TDF require dosage adjustments in children with these levels of renal impairment, and such adjustments cannot be achieved with an FDC tablet.

- Symfi Lo[a] has not been studied in children (SMR 1–3), and major inter-individual variability in efavirenz (EFV) plasma concentrations has been found in children in a multi-ethnic setting. The 400-mg dose of EFV may be too low in children or adolescents with SMRs of 1–3 who weigh ≥40 kg. Some members of the Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV suggest therapeutic drug monitoring when used in children weighing ≥40 kg. See the Efavirenz section for more information.

[Temixys] 3TC/TDF

Child and Adolescent (Weighing ≥35 kg) and Adult Dose

- One tablet once daily

[Truvada] FTC/TDF

Child, Adolescent, and Adult Dose

Truvada Dosing Table

Body Weight	FTC/TDF Tablet Once Daily
17 kg to <22 kg	One FTC 100 mg/ TDF 150 mg tablet
22 kg to <28 kg	One FTC 133 mg/ TDF 200 mg tablet
28 kg to <35 kg	One FTC 167 mg/ TDF 250 mg tablet
≥35 kg and adults	One FTC 200 mg/ TDF 300 mg tablet

[a] Brand name product has been discontinued; generic version is still available.

[b] See the text for a discussion of the concerns about decreased bone mineral density in children who are receiving TDF, especially in prepubertal children and those in early puberty (SMR 1 or 2).

Drug Interactions

Additional information about drug interactions is available in the Adult and Adolescent Antiretroviral Guidelines and the HIV Drug Interaction Checker.

- *Metabolism:* Tenofovir disoproxil fumarate (TDF) is a substrate of the adenosine triphosphate–dependent transporters P-glycoprotein and breast cancer resistance protein. When TDF is coadministered with inhibitors of these transporters, an increase in TDF absorption may be observed, with the potential for enhanced TDF toxicity.[1]
- *Renal elimination:* Drugs that decrease renal function or compete for active tubular secretion could reduce clearance of plasma tenofovir (TFV). Avoid frequent or long-term use of nonsteroidal anti-inflammatory drugs in children who are taking TDF.

- *Other nucleoside reverse transcriptase inhibitors (NRTIs):* Didanosine (ddI) serum concentrations increase when this drug is coadministered with TDF, and this combination **should not be used** because of the increased risk of ddI toxicity.
- *Protease inhibitors (PIs):* Atazanavir (ATV) without ritonavir **should not be coadministered** with TDF, because TDF decreases ATV plasma concentrations. The combination of atazanavir/ritonavir, darunavir/ritonavir (DRV/r), and lopinavir/ritonavir increases plasma TFV concentrations and increases the risk of TDF-associated toxicity.[1,2]
- *Absorption:* Administering elvitegravir (EVG) concurrently with antacids and supplements that contain iron, calcium, aluminum, and/or magnesium lowers plasma concentrations of EVG. Similarly, dolutegravir (DTG) should be taken 2 hours before or 6 hours after taking cation-containing antacids or laxatives, sucralfate, oral iron supplements, oral calcium supplements, or buffered medications.[3] If using Stribild, see the Elvitegravir section of Appendix A. Pediatric Antiretroviral Drug Information for additional information.

Major Toxicities

- *More common:* Nausea, diarrhea, vomiting, flatulence
- *Less common (more severe):* TDF caused bone toxicity (osteomalacia and reduced bone mineral density [BMD]) in animals when given in high doses. Decreases in BMD have been reported in both adults and children taking TDF. Renal toxicity—including increased serum creatinine, glycosuria, proteinuria, phosphaturia, and/or calcinuria and decreased serum phosphate—has been observed. Children at increased risk of renal glomerular or tubular dysfunction should be closely monitored. Cases of lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported.

Resistance

The International Antiviral Society–USA maintains a list of updated HIV drug resistance mutations, and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation.

Pediatric Use

Approval

TDF has been approved by the U.S. Food and Drug Administration (FDA) for use in children aged ≥2 years and weighing ≥10 kg when used as a component of antiretroviral therapy (ART). TDF is available as a component of fixed-dose combination tablets (see Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents).

TDF has antiviral activity and efficacy against hepatitis B virus (HBV) and is approved by the FDA for HBV treatment in children aged ≥2 years and weighing ≥10 kg. For a comprehensive review of this topic, see the Hepatitis B Virus section in the Pediatric Opportunistic Infection Guidelines.

Efficacy in Clinical Trials in Adults Compared With Children and Adolescents

The standard adult dose that was approved by the FDA for adults and children aged ≥12 years and weighing ≥35 kg is TDF 300 mg once daily. For children aged 2 to 12 years, the FDA-approved dose

is TDF 8 mg/kg per dose administered once daily, which closely approximates the dose of TDF 208 mg/m^2 per dose used in early studies in children.[4]

In adults, the recommended once-daily dose of TDF 300 mg is highly effective when used in combination with other antiretroviral (ARV) drugs.[5-12] The FDA-approved Cimduo and Temixys (both of which contain lamivudine [3TC] 300 mg/TDF 300 mg) and Symfi (efavirenz [EFV] 600 mg/3TC 300 mg/TDF 300 mg) based on results of prior clinical trials.[6,13] FDA approval of Symfi Lo[a] (EFV 400 mg/3TC 300 mg/TDF 300 mg) was based on a study that compared the use of EFV 400 mg with the use of EFV 600 mg, each administered with emtricitabine 200 mg and TDF 300 mg, in 630 ART-naive adults.[14] See the Efavirenz section for a detailed discussion of this study. In a large randomized controlled trial comparing second-line ART regimens, continuing TDF was superior to switching to zidovudine (ZDV) when given in combination with 3TC and either DTG or DRV/r.[15-17]

In children, the published efficacy data for TDF-containing ARV combinations are mixed, but potency equal to that in adults has been seen in children aged 3 to 18 years with susceptible virus. A recent clinical trial of adolescents without prior documented resistance who initiated or switched to a fixed-dose combination of doravirine/3TC/TDF demonstrated plasma concentrations comparable to those measured in adults for all three agents and >90% viral suppression through 96 weeks.[18,19] In children aged 2 years to <12 years, TDF 8 mg/kg per dose once daily was non-inferior to twice-daily ZDV-containing ART or stavudine-containing ART over 48 weeks of randomized treatment.[20,21] Virologic success is lower in treatment-experienced children and adolescents with extensive multiclass drug resistance.[22-24] In an analysis of genotypic resistance testing performed on 650 unique children at a single laboratory in the Republic of South Africa, predicted intermediate or high-level resistance to TDF was lower for children experiencing virologic failure while on abacavir (ABC)-containing (8.5%) and ZDV-containing (9.4%) regimens than those experiencing virologic failure while on a TDF-containing regimen (24.6%). Clinical data are lacking in children on the efficacy of switching from a failing regimen containing these NRTIs to a regimen containing TDF.[25]

Pharmacokinetics

Relationship of Drug Exposure to Virologic Response

Virologic suppression is most closely related to intracellular tenofovir diphosphate (TFV-DP) concentrations and, for TDF, intracellular TFV-DP is linked to plasma TFV concentration.[26] A modeling study suggests that children and adolescents who are treated with TDF may have higher intracellular TFV-DP concentrations than adults,[27] even though plasma TFV concentrations are lower in children and adolescents, because weight-adjusted renal clearance of TFV is higher in children than in adults.[4,28,29]

Formulations

Special Considerations

The taste-masked granules that make up the TDF oral powder give the vehicle (e.g., applesauce, yogurt) a gritty consistency. Once mixed with a vehicle, TDF should be administered promptly because its taste becomes bitter when it is allowed to sit for too long.

Toxicity

Bone Toxicity

TDF administration is associated with decreased BMD in both adults[30,31] and children.[21,32-34] When treated with TDF, younger children with sexual maturity ratings (SMRs) of 1 and 2 may be at a higher risk of decreased BMD than children with more advanced pubertal development (i.e., SMRs ≥3).[28] Discontinuation of TDF results in partial or complete recovery of BMD.[32,35]

In the study that led to FDA approval of TDF in adolescents aged ≥12 years and weighing ≥35 kg, 6 of 33 participants (18%) in the TDF arm experienced a >4% decline in absolute lumbar spine BMD in 48 weeks, whereas only 1 of 33 participants (3%) in the placebo arm experienced this decline.[22]

TDF administration disrupts vitamin D metabolism,[36,37] and the decrease in BMD associated with TDF initiation was attenuated in adults with coadministration of high doses of vitamin D3 (4,000 IU daily) and calcium carbonate (1,000 mg daily) for the first 48 weeks of TDF treatment.[38] During chronic TDF administration, youth with HIV who received vitamin D3 supplements (50,000 IU once monthly) had decreased serum parathyroid hormone levels and increased lumbar spine BMD compared with study participants who were not treated with high doses of vitamin D3.[36,39] The serum 25-hydroxy vitamin D concentration was 37 ng/mL in the group with improved BMD. Similar improvements in BMD were seen in youth with HIV who were treated with an ARV regimen that included TDF and who received vitamin D3 2,000 IU or 4,000 IU daily.[40] Measurement of plasma vitamin D concentration is recommended for children who are being treated with an ARV regimen that includes TDF, and vitamin D supplementation is recommended for those with vitamin D deficiency (see Table 17j. Osteopenia and Osteoporosis).

High concentrations of the TDF metabolite plasma TFV have been associated with TDF-related endocrine disruption and low BMD.[41] Plasma TFV concentrations are higher when TDF is coadministered with boosted PIs.[1] Tenofovir alafenamide (TAF), which is associated with lower plasma TFV concentrations than TDF, has less effect on parathyroid hormone levels[42] and causes less decline in BMD than TDF. See the Tenofovir Alafenamide section for more information. Consider switching from TDF to TAF or avoiding coadministration of TDF with boosted PIs in children for whom loss of BMD is a concern.

Monitoring Potential Bone Toxicity

The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) **does not recommend** routine dual-energy X-ray absorptiometry monitoring for children or adolescents who are being treated with TDF (see Table 17j. Osteopenia and Osteoporosis).

TDF has been shown to be effective, and it can be administered once daily; however, the use of TDF has been associated with a risk of BMD loss. Because childhood and early adolescence are important periods of rapid bone accrual, and because children with perinatally acquired HIV are at risk for low peak bone mass,[43,44] the Panel favors the use of ABC or TAF over TDF in children with SMRs 1 to 3.

Renal Toxicity

New-onset renal impairment and worsening renal impairment have been reported in adults[45] and children[46,47] receiving TDF. In one study, renal toxicity led to the discontinuation of TDF in 6 of 159 (3.7%) children with HIV who were treated with TDF.[24] Although TDF is clearly associated with a decline in glomerular filtration rate, the effect is generally small, and severe glomerular toxicity is rare.[45,46] Irreversible renal failure is quite rare, but cases have been reported.[48]

The main target of TDF nephrotoxicity is the renal proximal tubule.[46] Case reports highlight the infrequent but most severe manifestations of renal Fanconi syndrome, hypophosphatemia, hypocalcemia, diabetes insipidus, myalgias, bone pain, and fractures.[49,50]

Subclinical renal tubular damage is more common than clinically apparent renal tubular injury. Increased urinary beta-2 microglobulin was identified in 12 of 44 children (27%) who were treated with TDF and in 2 of 48 children (4%) who were not treated with TDF.[51] The risks of TDF-associated proteinuria and chronic kidney disease increase with the duration of treatment.[52,53] Of 89 participants aged 2 to 12 years who received TDF in Gilead Study 352 (where participants had a median drug exposure of 104 weeks), four participants were discontinued from the study for renal tubular dysfunction, with the discontinuations occurring between 84 and 156 weeks on TDF therapy.[20] In adults, renal dysfunction is more common when TDF is used in people with older age or a pre-existing renal disease[54]; in children, renal dysfunction may be more common when TDF is used with boosted PIs than with non-nucleoside reverse transcriptase inhibitors.[55]

Plasma TFV is the TDF metabolite most closely associated with both glomerular[41,56] and proximal tubular[57] toxicity. As previously noted, plasma TFV concentrations are higher when TDF is coadministered with boosted PIs.[1] TAF, which generates lower plasma TFV concentrations than TDF, is associated with a lower risk of renal toxicity than TDF[58] (see Tenofovir Alafenamide).

Monitoring Potential Renal Toxicity

Because TDF has the potential to decrease creatinine clearance and cause renal tubular dysfunction, the Panel recommends measuring serum creatinine and using a urine dipstick to check protein and glucose concentration before initiating TDF. It is unclear how often creatinine and renal tubular function (urine protein and glucose) should be monitored in asymptomatic children. Many Panel members monitor creatinine with other blood tests every 3 to 4 months and perform urinalysis every 6 to 12 months. Serum phosphate should be measured if clinically indicated; renal phosphate loss can occur in the presence of normal creatinine and in the absence of proteinuria. Because nephrotoxicity increases with the duration of TDF treatment, monitoring should be continued during long-term therapy with the drug.

Because renal glomerular damage primarily increases the concentration of albumin in urine, and proximal renal tubular damage increases the concentration of low-molecular-weight proteins like beta-2 microglobulin in urine, dipstick urinalysis (which primarily measures urine albumin) may be a relatively insensitive marker for TDF-associated tubular damage. Measuring urine albumin and urine protein and calculating the ratio of urine albumin to urine protein can be helpful in identifying the non-albumin proteinuria that is seen in TDF-associated nephrotoxicity.[59,60] Although these more complex and expensive tests may be used in research settings, in clinical practice, using a renal dipstick to identify normoglycemic glycosuria and proteinuria is the easiest way to detect renal damage.

References

1. Viread (tenofovir disoproxil fumarate) [package insert]. Food and Drug Administration. 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021356s058,022577s014lbl.pdf.

2. Bedimo R, Rosenblatt L, Myers J. Systematic review of renal and bone safety of the antiretroviral regimen efavirenz, emtricitabine, and tenofovir disoproxil fumarate in patients with HIV infection. *HIV Clin Trials*. 2016;17(6):246-266. Available at: https://pubmed.ncbi.nlm.nih.gov/27809711.

3. Dolutegravir/Lamivudine/Tenofovir Disproxil Fumarate [package insert]. Food and Drug Administration. 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/pepfar/210787PI.pdf.

4. Hazra R, Balis FM, Tullio AN, et al. Single-dose and steady-state pharmacokinetics of tenofovir disoproxil fumarate in human immunodeficiency virus-infected children. *Antimicrob Agents Chemother*. 2004;48(1):124-129. Available at: https://pubmed.ncbi.nlm.nih.gov/14693529.

5. Arribas JR, Pozniak AL, Gallant JE, et al. Tenofovir disoproxil fumarate, emtricitabine, and efavirenz compared with zidovudine/lamivudine and efavirenz in treatment-naive patients: 144-week analysis. *J Acquir Immune Defic Syndr*. 2008;47(1):74-78. Available at: https://pubmed.ncbi.nlm.nih.gov/17971715.

6. Gallant JE, Staszewski S, Pozniak AL, et al. Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral-naive patients: a 3-year randomized trial. *JAMA*. 2004;292(2):191-201. Available at: https://pubmed.ncbi.nlm.nih.gov/15249568.

7. Gallant JE, DeJesus E, Arribas JR, et al. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. *N Engl J Med*. 2006;354(3):251-260. Available at: https://pubmed.ncbi.nlm.nih.gov/16421366.

8. Sax PE, Tierney C, Collier AC, et al. Abacavir-lamivudine versus tenofovir-emtricitabine for initial HIV-1 therapy. *N Engl J Med*. 2009;361(23):2230-2240. Available at: https://pubmed.ncbi.nlm.nih.gov/19952143.

9. Sax PE, Tierney C, Collier AC, et al. Abacavir/lamivudine versus tenofovir TDF/emtricitabine as part of combination regimens for initial treatment of HIV: final results. *J Infect Dis*. 2011;204(8):1191-1201. Available at: https://pubmed.ncbi.nlm.nih.gov/21917892.

10. Smith KY, Patel P, Fine D, et al. Randomized, double-blind, placebo-matched, multicenter trial of abacavir/lamivudine or tenofovir/emtricitabine with lopinavir/ritonavir for initial HIV treatment. *AIDS*. 2009;23(12):1547-1556. Available at: https://pubmed.ncbi.nlm.nih.gov/19542866.

11. Post FA, Moyle GJ, Stellbrink HJ, et al. Randomized comparison of renal effects, efficacy, and safety with once-daily abacavir/lamivudine versus tenofovir/emtricitabine, administered with efavirenz, in antiretroviral-naive, HIV-1-infected adults: 48-week results from the ASSERT study. *J Acquir Immune Defic Syndr*. 2010;55(1):49-57. Available at: https://pubmed.ncbi.nlm.nih.gov/20431394.

12. Spaulding A, Rutherford GW, Siegfried N. Tenofovir or zidovudine in three-drug combination therapy with one nucleoside reverse transcriptase inhibitor and one non-nucleoside reverse transcriptase inhibitor for initial treatment of HIV infection in antiretroviral-naive individuals. *Cochrane Database Syst Rev*. 2010(10):CD008740. Available at: https://pubmed.ncbi.nlm.nih.gov/20927777.

13. Margot NA, Lu B, Cheng A, et al. Resistance development over 144 weeks in treatment-naive patients receiving tenofovir disoproxil fumarate or stavudine with lamivudine and efavirenz in Study 903. *HIV Med*. 2006;7(7):442-450. Available at: https://pubmed.ncbi.nlm.nih.gov/16925730.

14. ENCORE1 Study Group, Carey D, Puls R, et al. Efficacy and safety of efavirenz 400 mg daily versus 600 mg daily: 96-week data from the randomised, double-blind, placebo-controlled, non-inferiority ENCORE1 study. *Lancet Infect Dis*. 2015;15(7):793-802. Available at: https://pubmed.ncbi.nlm.nih.gov/25877963.

15. Paton NI, Musaazi J, Kityo C, et al. Efficacy and safety of dolutegravir or darunavir in combination with lamivudine plus either zidovudine or tenofovir for second-line treatment of HIV infection (NADIA): week 96 results from a prospective, multicentre, open-label, factorial, randomised, non-inferiority trial. *Lancet HIV*. 2022;9(6):e381-e393. Available at: https://pubmed.ncbi.nlm.nih.gov/35460601.

16. Paton NI, Musaazi J, Kityo C, et al. Dolutegravir or darunavir in combination with zidovudine or tenofovir to treat HIV. *N Engl J Med*. 2021;385(4):330-341. Available at: https://pubmed.ncbi.nlm.nih.gov/34289276.

17. Keene CM, Griesel R, Zhao Y, et al. Virologic efficacy of tenofovir, lamivudine and dolutegravir as second-line antiretroviral therapy in adults failing a tenofovir-based first-line regimen. *AIDS*. 2021;35(9):1423-1432. Available at: https://pubmed.ncbi.nlm.nih.gov/33973876.

18. Melvin AJ, Yee KL, Gray KP, et al. Pharmacokinetics, tolerability, and safety of doravirine and doravirine/lamivudine/tenofovir disoproxil fumarate fixed-dose combination tablets in adolescents living with HIV: week 24 Results from IMPAACT 2014. *J Acquir Immune Defic Syndr*. 2023;92(2):153-161. Available at: https://pubmed.ncbi.nlm.nih.gov/36215957.

19. Rungmaitree S, Aurpibul L, Best BM, et al. Efficacy, safety, and tolerability of doravirine/lamivudine/tenofovir disoproxil fumarate fixed-dose combination tablets in adolescents living with HIV: results through week 96 from IMPAACT 2014. *J Pediatric Infect Dis Soc*. 2023;12(12):602-609. Available at: https://pubmed.ncbi.nlm.nih.gov/37815035.

20. Saez-Llorens X, Castano E, Rathore M, et al. A randomized, open-label study of the safety and efficacy of switching stavudine or zidovudine to tenofovir disoproxil fumarate in HIV-1-infected children with virologic suppression. *Pediatr Infect Dis J*. 2015;34(4):376-382. Available at: https://pubmed.ncbi.nlm.nih.gov/25760565.

21. 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: https://pubmed.ncbi.nlm.nih.gov/25760566.

22. Della Negra M, de Carvalho AP, de Aquino MZ, et al. A randomized study of tenofovir disoproxil fumarate in treatment-experienced HIV-1 infected adolescents. *Pediatr Infect Dis J*. 2012;31(5):469-473. Available at: https://pubmed.ncbi.nlm.nih.gov/22301477.

23. Della Negra M, De Carvalho AP, De Aquino MZ, et al. Long-term efficacy and safety of tenofovir disoproxil fumarate in HIV-1-infected adolescents failing antiretroviral therapy: the final results of study GS-US-104-0321. *Pediatr Infect Dis J*. 2015;34(4):398-405. Available at: https://pubmed.ncbi.nlm.nih.gov/25599284.

24. Riordan A, Judd A, Boyd K, et al. Tenofovir use in human immunodeficiency virus-1-infected children in the United kingdom and Ireland. *Pediatr Infect Dis J*. 2009;28(3):204-209. Available at: https://pubmed.ncbi.nlm.nih.gov/19209091.

25. Steegen K, Levin L, Evans D, et al. Minimal cross-resistance to tenofovir in children and adolescents failing ART makes them eligible for tenofovir-lamivudine-dolutegravir treatment. *Pediatr Infect Dis J*. 2022;41(10):827-834. Available at: https://pubmed.ncbi.nlm.nih.gov/35895893.

26. Baheti G, Kiser JJ, Havens PL, Fletcher CV. Plasma and intracellular population pharmacokinetic analysis of tenofovir in HIV-1-infected patients. *Antimicrob Agents Chemother*. 2011;55(11):5294-5299. Available at: https://pubmed.ncbi.nlm.nih.gov/21896913.

27. Baheti G, King JR, Acosta EP, Fletcher CV. Age-related differences in plasma and intracellular tenofovir concentrations in HIV-1-infected children, adolescents and adults. *AIDS*. 2013;27(2):221-225. Available at: https://pubmed.ncbi.nlm.nih.gov/23032419.

28. Hazra R, Gafni RI, Maldarelli F, et al. Tenofovir disoproxil fumarate and an optimized background regimen of antiretroviral agents as salvage therapy for pediatric HIV infection. *Pediatrics*. 2005;116(6):e846-854. Available at: https://pubmed.ncbi.nlm.nih.gov/16291735.

29. Kiser JJ, Fletcher CV, Flynn PM, et al. Pharmacokinetics of antiretroviral regimens containing tenofovir disoproxil fumarate and atazanavir-ritonavir in adolescents and young adults with human immunodeficiency virus infection. *Antimicrob Agents Chemother*. 2008;52(2):631-637. Available at: https://pubmed.ncbi.nlm.nih.gov/18025112.

30. Stellbrink HJ, Orkin C, Arribas JR, et al. Comparison of changes in bone density and turnover with abacavir-lamivudine versus tenofovir-emtricitabine in HIV-infected adults: 48-week results from the ASSERT study. *Clin Infect Dis*. 2010;51(8):963-972. Available at: https://pubmed.ncbi.nlm.nih.gov/20828304.

31. McComsey GA, Kitch D, Daar ES, et al. Bone mineral density and fractures in antiretroviral-naive persons randomized to receive abacavir-lamivudine or tenofovir disoproxil fumarate-emtricitabine along with efavirenz or atazanavir-ritonavir: AIDS Clinical Trials Group A5224s, a substudy of ACTG A5202. *J Infect Dis*. 2011;203(12):1791-1801. Available at: https://pubmed.ncbi.nlm.nih.gov/21606537.

32. 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: https://pubmed.ncbi.nlm.nih.gov/16923923.

33. Purdy JB, Gafni RI, Reynolds JC, et al. Decreased bone mineral density with off-label use of tenofovir in children and adolescents infected with human immunodeficiency virus. *J Pediatr*. 2008;152(4):582-584. Available at: https://pubmed.ncbi.nlm.nih.gov/18346519.

34. Aurpibul L, Puthanakit T. Review of tenofovir use in HIV-infected children. *Pediatr Infect Dis J*. 2015;34(4):383-391. Available at: https://pubmed.ncbi.nlm.nih.gov/25247583.

35. Havens PL, Perumean-Chaney SE, Patki A, et al. Changes in bone mass after discontinuation of pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate/emtricitabine in young men who have sex with men: extension phase results of Adolescent Trials Network protocols 110 and 113. *Clin Infect Dis*. 2019;70(4):687–691. Available at: https://pubmed.ncbi.nlm.nih.gov/31179503.

36. Havens PL, Stephensen CB, Van Loan MD, et al. Vitamin D3 supplementation increases spine bone mineral density in adolescents and young adults with human immunodeficiency virus infection being treated with tenofovir disoproxil fumarate: a randomized, placebo-controlled trial. *Clin Infect Dis*. 2018;66(2):220-228. Available at: https://pubmed.ncbi.nlm.nih.gov/29020329.

37. Havens PL, Long D, Schuster GU, et al. Tenofovir disoproxil fumarate appears to disrupt the relationship of vitamin D and parathyroid hormone. *Antivir Ther*. 2018;23(7):623-628. Available at: https://pubmed.ncbi.nlm.nih.gov/30260797.

38. 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: https://pubmed.ncbi.nlm.nih.gov/26075752.

39. Havens PL, Stephensen CB, Hazra R, et al. Vitamin D3 decreases parathyroid hormone in HIV-infected youth being treated with tenofovir: a randomized, placebo-controlled trial. *Clin Infect Dis*. 2012;54(7):1013-1025. Available at: https://pubmed.ncbi.nlm.nih.gov/22267714.

40. Eckard AR, O'Riordan MA, Rosebush JC, et al. Effects of vitamin D supplementation on bone mineral density and bone markers in HIV-infected youth. *J Acquir Immune Defic Syndr*. 2017;76(5):539-546. Available at: https://pubmed.ncbi.nlm.nih.gov/28902705.

41. Havens PL, Kiser JJ, Stephensen CB, et al. Association of higher plasma vitamin D binding protein and lower free calcitriol levels with tenofovir disoproxil fumarate use and plasma and intracellular tenofovir pharmacokinetics: cause of a functional vitamin D deficiency? *Antimicrob Agents Chemother*. 2013;57(11):5619-5628. Available at: https://pubmed.ncbi.nlm.nih.gov/24002093.

42. Van Welzen BJ, Thielen MAJ, Mudrikova T, et al. Switching tenofovir disoproxil fumarate to tenofovir alafenamide results in a significant decline in parathyroid hormone levels: uncovering the mechanism of tenofovir disoproxil fumarate-related bone loss? *AIDS*. 2019;33(9):1531-1534. Available at: https://pubmed.ncbi.nlm.nih.gov/31021851.

43. 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: https://pubmed.ncbi.nlm.nih.gov/23032412.

44. Yin MT, Lund E, Shah J, et al. Lower peak bone mass and abnormal trabecular and cortical microarchitecture in young men infected with HIV early in life. *AIDS*. 2014;28(3):345-353. Available at: https://pubmed.ncbi.nlm.nih.gov/24072196.

45. Cooper RD, Wiebe N, Smith N, et al. Systematic review and meta-analysis: renal safety of tenofovir disoproxil fumarate in HIV-infected patients. *Clin Infect Dis*. 2010;51(5):496-505. Available at: https://pubmed.ncbi.nlm.nih.gov/20673002.

46. Hall AM. Update on tenofovir toxicity in the kidney. *Pediatr Nephrol*. 2013;28(7):1011-1023. Available at: https://pubmed.ncbi.nlm.nih.gov/22878694.

47. Andiman WA, Chernoff MC, Mitchell C, et al. Incidence of persistent renal dysfunction in human immunodeficiency virus-infected children: associations with the use of antiretrovirals, and other nephrotoxic medications and risk factors. *Pediatr Infect Dis J*. 2009;28(7):619-625. Available at: https://pubmed.ncbi.nlm.nih.gov/19561425.

48. Wood SM, Shah SS, Steenhoff AP, et al. Tenofovir-associated nephrotoxicity in two HIV-infected adolescent males. *AIDS Patient Care STDS*. 2009;23(1):1-4. Available at: https://pubmed.ncbi.nlm.nih.gov/19183077.

49. Hussain S, Khayat A, Tolaymat A, Rathore MH. Nephrotoxicity in a child with perinatal HIV on tenofovir, didanosine and lopinavir/ritonavir. *Pediatr Nephrol*. 2006;21(7):1034-1036. Available at: https://pubmed.ncbi.nlm.nih.gov/16773419.

50. Lucey JM, Hsu P, Ziegler JB. Tenofovir-related Fanconi's syndrome and osteomalacia in a teenager with HIV. *BMJ Case Rep*. 2013;2013. Available at: https://pubmed.ncbi.nlm.nih.gov/23843401.

51. Papaleo A, Warszawski J, Salomon R, et al. Increased beta-2 microglobulinuria in human immunodeficiency virus-1-infected children and adolescents treated with tenofovir. *Pediatr Infect Dis J*. 2007;26(10):949-951. Available at: https://pubmed.ncbi.nlm.nih.gov/17901802.

52. Soler-Palacíin P, Melendo S, Noguera-Julian A, et al. Prospective study of renal function in HIV-infected pediatric patients receiving tenofovir-containing HAART regimens. *AIDS*. 2011;25(2):171-176. Available at: https://pubmed.ncbi.nlm.nih.gov/21076275.

53. Purswani M, Patel K, Kopp JB, et al. Tenofovir treatment duration predicts proteinuria in a multiethnic United States cohort of children and adolescents with perinatal HIV-1 infection. *Pediatr Infect Dis J*. 2013;32(5):495-500. Available at: https://pubmed.ncbi.nlm.nih.gov/23249917.

54. Mocroft A, Lundgren JD, Ross M, et al. Development and validation of a risk score for chronic kidney disease in HIV infection using prospective cohort data from the D:A:D study. *PLoS Med*. 2015;12(3):e1001809. Available at: https://pubmed.ncbi.nlm.nih.gov/25826420.

55. Mashingaidze-Mano R, Bwakura-Dangarembizi MF, Maponga CC, et al. Proximal renal tubular function in HIV-infected children on tenofovir disoproxil fumarate for treatment of HIV infection at two tertiary hospitals in Harare, Zimbabwe. *PLoS One*. 2020;15(7):e0235759. Available at: https://pubmed.ncbi.nlm.nih.gov/32634168.

56. Poizot-Martin I, Solas C, Allemand J, et al. Renal impairment in patients receiving a tenofovir-cART regimen: impact of tenofovir trough concentration. *J Acquir Immune Defic Syndr*. 2013;62(4):375-380. Available at: https://pubmed.ncbi.nlm.nih.gov/23196828.

57. Rodriguez-Novoa S, Labarga P, D'Avolio A, et al. Impairment in kidney tubular function in patients receiving tenofovir is associated with higher tenofovir plasma concentrations. *AIDS*. 2010;24(7):1064-1066. Available at: https://pubmed.ncbi.nlm.nih.gov/20299966.

58. Gupta SK, Post FA, Arribas JR, et al. Renal safety of tenofovir alafenamide vs. tenofovir disoproxil fumarate: a pooled analysis of 26 clinical trials. *AIDS*. 2019;33(9):1455-1465. Available at: https://pubmed.ncbi.nlm.nih.gov/30932951.

59. Sise ME, Hirsch JS, Canetta PA, et al. Nonalbumin proteinuria predominates in biopsy-proven tenofovir nephrotoxicity. *AIDS*. 2015;29(8):941-946. Available at: https://pubmed.ncbi.nlm.nih.gov/25784440.

60. Samarawickrama A, Cai M, Smith ER, et al. Simultaneous measurement of urinary albumin and total protein may facilitate decision-making in HIV-infected patients with proteinuria. *HIV Med*. 2012;13(9):526-532. Available at: https://pubmed.ncbi.nlm.nih.gov/22413854.