**Box 1: Important Clinical Considerations With Either TDF/FTC or TAF/FTC as Initial ART [a]**

☑ **If the patient is at risk for chronic kidney disease (e.g., age >40 years, with hypertension, diabetes, or preexisting mild kidney disease):** The greater possibility of kidney disease among individuals who have risk factors is an essential component of the risk-benefit discussion and shared decision-making regarding initiation of tenofovir-containing regimens.

- Higher rates of renal dysfunction have been reported in individuals taking TDF in conjunction with RTV- and COBI-containing regimens [Pilkington, et al. 2020; Hill, et al. 2018; Cuzin, et al. 2017; Ryom, et al. 2013; Goicoechea, et al. 2008].
- For people at low risk for kidney disease, TDF, when not combined with a regimen that contains a pharmacokinetic booster (RTV or COBI), appears to have similar renal safety to TAF [Pilkington, et al. 2020; Hill, et al. 2018].
- TAF has fewer adverse effects on renal function and is associated with lower rates of proteinuria than TDF [Mills, et al. 2016; Pozniak, et al. 2016; Sax, et al. 2015].
- TDF/FTC should be initiated only in individuals with CrCl ≥50 mL/min.
- TAF/FTC should be initiated only in individuals with CrCl ≥30 mL/min.

☑ **If the patient has osteopenia, osteomalacia, or osteoporosis:**

- The risk of bone loss in individuals with preexisting risk factors or documented osteopenia, osteomalacia, or osteoporosis is an important component of the risk-benefit discussion and shared decision-making regarding initiation of TDF/FTC or TAF/FTC.
- TDF is associated with osteomalacia and decreases in bone mineral density [McComsey, et al. 2011; Stellbrink, et al. 2010; Perrot, et al. 2009].
- TAF/FTC is preferred for people with osteoporosis.

☑ **If the patient has concerns about weight gain, hyperlipidemia, or metabolic disorders:**

- Greater weight gain has been observed with initiation of TAF than TDF and with a switch from TDF to TAF, especially in conjunction with INSTIs [Łomiak, et al. 2021; Surial, et al. 2021; Bourgi(a), et al. 2020; Bourgi(b), et al. 2020; Calmy, et al. 2020; Lake, et al. 2020; Sax, et al. 2020; Venter, et al. 2020; Venter, et al. 2019].
- TDF is associated with lower lipid levels than TAF [Souza, et al. 2013].

☑ **If the patient is an adolescent or youth:** There is limited data on bone safety in adolescents taking TAF/FTC. However, given the more favorable bone biomarkers of TAF versus TDF, TAF may have an advantage in adolescents who have not achieved bone maturation. Because this advantage is theoretical and not currently supported with clinical data, a clear recommendation cannot be made at this time.

☑ **If the patient is pregnant or attempting to conceive:**

- Information about the potential benefits and risks of taking tenofovir-containing regimens during pregnancy is an essential component of shared decision-making regarding risk reduction.
- Due to the greater experience with TDF in this population, TDF/FTC is the preferred dual NRTI backbone for use as HIV treatment during pregnancy [b].
- Prospectively report information regarding the use of ART medications during pregnancy to the Antiretroviral Pregnancy Registry.

☑ **If the patient has active chronic HBV:**

- TDF, TAF, and FTC are active against HBV. TDF and TAF are considered equally effective against HBV [c].
- Discontinuation of TDF/FTC or TAF/FTC in patients with chronic HBV requires close monitoring for rebound HBV viremia.

**Abbreviations:** 3TC, lamivudine; ART, antiretroviral therapy; COBI, cobicistat; CrCl, creatinine clearance; DHHS, U.S. Department of Health and Human Services; FDA, U.S. Food and Drug Administration; FTC, emtricitabine; HBV, hepatitis B virus; INSTI, integrase strand transfer inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

**Notes:**

a. Consider safety, cost, and access when choosing between use of TDF/FTC or TAF/FTC.
b. Refer to DHHS Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
c. TDF and TAF are approved by the FDA as treatment for HBV. FTC is also active against HBV but is not FDA-approved for HBV treatment. TDF or TAF in combination with FTC or 3TC, which is FDA-approved for HBV treatment and is molecularly similar to FTC, is commonly used in patients with HIV/HBV coinfection as part of an antiretroviral regimen to treat both infections.

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