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Human Immunodeficiency Virus Pre-Exposure Prophylaxis: Use of Emtricitabine/Tenofovir Alafenamide

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A B S T R A C T

Pre-exposure prophylaxis (PrEP) involves the use of antiretroviral medication in concert with safer sex practices to significantly reduce the risk of type 1 human immunodeficiency virus infection. In October 2019, daily use of emtricitabine/tenofovir alafenamide (FTC/TAF) 200 mg/25 mg was approved as a newer agent for PrEP to prevent HIV-1 infection in at-risk adults and adolescents. The purpose of this article is to: 1) provide an overview of the FTC/TAF regimen and its safety and efficacy profiles, 2) discuss indications and contraindications of FTC/TAF as PrEP, 3) provide a focused comparison of FTC/TDF with FTC/TAF, and 4) examine issues surrounding cost and accessibility in the United States.

The prevention of infection with type 1 human immunodeficiency virus (HIV-1) was revolutionized when the United States Food and Drug Administration approved once-daily use of oral antiretroviral medication as pre-exposure prophylaxis (PrEP).[1] Once-daily emtricitabine/tenofovir fumarate (FTC/TDF) 200 mg/300 mg (Truvada; Gilead, Foster City, CA) or once-daily emtricitabine/tenofovir alafenamide (FTC/TAF) 200 mg/25 mg (Descovy, Gilead), in concert with safer sex practices, reduces the risk of HIV-1 acquisition by approximately 99%, with only a very small number of infections (related to resistant HIV strains) occurring in those adherent to it.[2,3] FTC/TDF was approved for use as PrEP in 2012.[1] Research supporting FTC/TDF as efficacious is historically rooted in the 2010 Preexposure Prophylaxis Initiative (iPrEx) study.[1]

With detectable serum levels of the medication, participants in the iPrEx study had a 90% reduction in HIV transmission.[1] As data on the use of FTC/TDF for PrEP evolved, its efficacy was further supported. For example, the effectiveness of the regimen was found to be so high in immediate participants in the 2014 Pre-Exposure Prophylaxis to Prevent the Acquisition of HIV-1 Infection (PROUD) study, participants in the deferred arm of the study were promptly offered PrEP when early data supported its efficacy.[4]

Those enrolled in the PROUD study also showed no serious adverse events; the most common adverse events associated with the use of FTC/TDF for PrEP included nausea, headache, and arthralgia.[4] In 2018, the use of FTC/TDF for PrEP was expanded to include an indication for use in at-risk adolescents.[5] In October 2019, FTC/TAF 200 mg/25 mg (Descovy) was approved as a newer agent for once-daily use for PrEP in both high-risk adults and adolescents.[6] Two of the major benefits often associated with FTC/TAF compared with FTC/TDF are a lower incidence of renal toxicity and bone demineralization.[2,7,8]

This article provides an overview of the FTC/TAF regimen, discusses the indications and contraindications of FTC/TAF as PrEP, examines its safety and efficacy profiles (including adverse events and interactions), compares FTC/TAF with FTC/TDF, and examines issues surrounding cost and accessibility of these agents in the United States.

FTC/TAF for PrEP: Regimen, Safety Profile, and Efficacy

The implementation of FTC/TAF for PrEP in at-risk adolescents and adults involves prescribing a once-daily dose of FTC/TAF (Descovy) 200 mg/25 mg.[9,10] However, before this, the patient must be screened for HIV and have a documented negative screening result.[10] Because tenofovir prodrugs have been associated with renal impairment in both animal and human clinical trials, the patient's serum creatinine and creatinine clearance (CrCl) should be evaluated, in addition to evaluating the urine for the presence of glucosuria and proteinuria.[10] The regimen can be started only after ensuring the patient's CrCl is > 30 mL/min.[10]

The assessment of initial and ongoing phosphorus levels is essential for patients with chronic kidney disease.[10] Screening for hepatitis B virus (HBV) infection is also necessary before prescribing FTC/TAF for PrEP.[10] This is because exacerbations of HBV are possible with the discontinuation of FTC/TAF because of its ability to suppress HBV.[10-13]

After initiation, the patient's HIV serostatus should be ascertained every 3 months. If the patient develops symptoms suggestive of acute HIV infection (eg, fever, fatigue, lymphadenopathy,

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Table 1
Common P-glycoprotein (P-gp) Inhibitors[14] and Inducers[15]

P-gp Inhibitors[a]	Drug Class or Major Indication	P-gp Inducers	Drug Class or Major Indication
Clotrimazole	Topical broad-spectrum antifungal	Amprenavir	HIV PI
Dexamethasone	Glucocorticoid	Carbamazepine	Anticonvulsant
Digoxin	Cardiac glycoside	Dexamethasone	Glucocorticoid
Indinavir	HIV PI	Indinavir	HIV PI
Mifepristone	Cortisol receptor blocker	Mifepristone	Cortisol receptor blocker
Nifedipine	Dihydropyridine CCB	Nelfinavir	HIV PI
Reserpine	Antihypertensive	Nifedipine	Dihydropyridine calcium channel blocker
Ritonavir	HIV PI	Reserpine	Antihypertensive
Saquinavir	HIV PI	Rifampicin	Antimycobacterial
Verapamil	Nondihydropyridine CCB	Saquinavir	Serotonin uptake inhibitor
		Trazadone	Serotonin uptake inhibitor

CCB = calcium channel blocker; HIV = human immunodeficiency virus; PI = protease inhibitor.
[a] Note that some of the medications listed are classified as both P-gp inhibitors and inducers.

myalgia, or rash), the regimen should be converted to a comprehensive HIV management program until a negative serostatus can be confirmed through screening.[10] HIV screening should also accompany any diagnosis of a sexually transmitted infection (STI) while the patient remains on the regimen.[10] Continuous assessment of renal function should be performed while the patient remains on the regimen; this could be assessed in conjunction with HIV serostatus every 3 months or when clinically indicated.[10,14] Medications that may reduce renal function (eg, nonsteroidal anti-inflammatory drugs) or compete with active tubular secretion (eg, probenecid and fluoroquinolones) should not be administered simultaneously with FTC/TAF.[10,14] This is because of the consequent risk for increasing concentrations of FTC and, thus, opportunities for associated adverse events.[10,14]

The most common adverse events, which occurred in approximately 2% of participants in PrEP clinical trials, include diarrhea, nausea, headache, fatigue, and abdominal pain.[10,14] Upon initiation of the regimen, "start-up" symptoms of diarrhea, nausea, and vomiting may occur initially, but they usually abate within 3 months of therapy.[2] Cases of lactic acidosis with severe hepatomegaly with steatosis have been reported with the use of FTC, a component of FTC/TAF.[10,14]

FTC/TAF should be immediately stopped if the patient has laboratory findings confirming lactic acidosis or clinical findings such as hepatomegaly and/or steatosis.[10,14] Pharmacologic agents that inhibit P-glycoprotein (P-gp) may increase concentrations of TAF (and risk for adverse events), whereas those that induce P-gp may decrease concentrations of TAF (and regimen efficacy).[10,14] Examples of common P-gp inhibitors[15] and inducers[16] are provided in Table 1. Table 2 reviews initial laboratory analyses, ongoing monitoring, precautions, adverse events, and drug interactions.

Although the efficacy of FTC/TAF as PrEP for HIV-1 has been found to be approximately 99%,[2] proper adherence to the once-daily regimen is vital to achieve this, emphasizing that the relationship between adherence and efficacy is a significant patient education point.[10] In addition, because PrEP does not protect against other STIs, it is imperative to counsel patients on STI reduction strategies, including consistent and proper use of condoms, open discussion of HIV serostatus and HIV-1 viremic status with sex partners, and self-employment of other harm reduction approaches.[10]

Indications and Contraindications of FTC/TAF as PrEP

FTC/TAF is specifically indicated as PrEP in adults and adolescents (over the age of 13)[9] considered to be at risk of sexually acquired HIV-1 infection.[10] These risk factors include those that are behavioral, biological, or epidemiologic.[10] Behavioral risks include condomless sex (also referred to as *barebacking*),[11] self-identification as being at higher risk for HIV infection, or having sexual partners of unknown HIV-1 viremic status. Biological risk includes diagnosis of past or current STIs, whereas epidemiologic risks involve sexual activity in a high-prevalence area or network.[10]

FTC/TAF is not indicated for females at risk for HIV-1 acquisition through vaginal sex.[10] In addition, it is vital for clinicians to confirm a negative HIV serostatus before initiating FTC/TAF as PrEP because drug-resistant HIV-1 variants have been identified.[10] Consequently, FTC/TAF is contraindicated in persons who are HIV infected or have an unknown HIV serostatus.[10]

FTC/TAF and FTC/TDF: A Focused Comparison

Although FTC/TAF is a newer agent for PrEP, it is noninferior to FTC/TDF in preventing HIV-1 infections.[2] Although FTC/TAF has been associated with lower incidences of associated renal toxicity and bone demineralization as adverse events,[2,7,8] the overall incidence of both with the use of FTC/TDF is low.[17,18] Research has shown small but statistically significant decreases in bone mineral density that stabilizes after 24 weeks of FTC/TDF treatment.[17]

Similarly, data suggest FTC/TDF as being associated with a low incidence of a very mild and nonprogressive decrease in CrCl in some users.[18] However, this has been found to be reversible and managed with routine serum creatinine monitoring.[18] FTC/TDF has been supported for use in everyone at risk for HIV-1 infection compared with FTC/TAF, which is supported for use in gay and bisexual men and transwomen who have sex with men.[2]

A small amount of weight loss has been associated with the use of FTC/TDF compared with a small amount of weight gain with FTC/TAF.[2] Variation in the effects of these agents on lipids has also been reported. The use of FTC/TDF may decrease high-density lipoprotein, low-density lipoprotein, and total cholesterol values minimally; small increases in low-density lipoproteins and triglycerides have been observed with the use of FTC/TAF.[2,19] Table 3 summarizes the major differences between FTC/TDF and FTC/TAF.[2,17-21]

Cost and Accessibility of PrEP in the United States

Without insurance or cost support from drug manufacturer assistance programs, both FTC/TDF and FTC/TAF could be considered expensive. Estimates indicate both medications cost approximately $1,845 per month.[2] However, Gilead, the manufacturer of FTC/TDF (sold under the brand name Truvada) and FTC/TAF (sold under the brand name Descovy), offers assistance programs to help patients offset the costs for both medications.

As of November 2020, Gilead's assistance copay program for the commercially insured covers up to $7,200 in copays per year with

Table 2
Emtricitabine/Tenofovir Alafenamide Prescribing (200 mg/25 mg Orally Daily) and Monitoring Principles[10,12-14]

Initial Laboratory Analyses	Ongoing Monitoring	Precautions	Adverse Events Drug Interactions
Negative HIV antibody screening Serum creatinine CrCl (> 30 mL/min) Urine: glucosuria proteinuria HBV Those with CKD: phosphorus	Negative HIV antibody screening[a] Serum creatinine[a] CrCl (> 30 mL/min)[a] Negative HIV antibody screening with any new STI diagnosis	Development of symptoms suggestive of acute HIV infection: 1) convert to comprehensive HIV regimen program until 2) negative HIV serostatus is confirmed. Avoid medications that may reduce renal function or compete with active tubular secretion	Diarrhea P-gp inhibitors Nausea P-gp inducers Headache Fatigue Abdominal pain Lactic acidosis Steatosis

CKD = chronic kidney disease; CrCl = creatinine clearance; HBV = hepatitis B virus; HIV = human immunodeficiency virus; P-gp = P-glycoprotein; STI = sexually transmitted infection.
[a] Monitor every 3 months.

Table 3
Major Differences Between Emtricitabine/Tenofovir Fumarate (FTC/TDF) and Emtricitabine/Tenofovir Alafenamide (FTC/TAF)[2,16-20]

General Characteristics	FTC/TDF	FTC/TAF
Approval date	2012	2019
Brand name	Truvada	Descovy
Tablet shape	Capsular	Rectangular
Tablet color	Blue	Blue
Tablet imprint	Gilead/701	Gilead/225
Tablet size	19 mm	13 mm
Regimen	200 mg/300 mg once daily	200 mg/25 mg once daily
Indicated for HIV-1 PrEP for	Populations at risk	Gay and bisexual men, transwomen who have sex with men
Cost without insurance	$1,845/month	$1,845/month
Generic	Available	Not available
Assistance	Available	Available
Efficacy data	FTC/TDF	FTC/TAF
HIV-1 prevention efficacy	> 99%	> 99%
Safety data	FTC/TDF	FTC/TAF
Common adverse events	Low (diarrhea, nausea, vomiting; usually improves within 3 months of treatment)	Low (diarrhea, nausea, vomiting; usually improves within 3 months of treatment)
Bone mineral density	Low risk, stabilizes at 24 weeks of treatment	Lower risk of adverse events
Renal toxicity	Low risk, nonprogressive, reversible with routine serum creatinine monitoring	Lower risk of adverse renal events
Weight changes	Possible small degree of weight loss	Possible small degree of gain
Serum lipids	Possible small decrease in HDL, LDL, and total cholesterol	Possible small increase in LDL and triglycerides

Abbreviations: FTC, emtricitabine; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TAF, tenofovir alafenamide; TDF, tenofovir fumarate.

no monthly limit for both agents.[22] Gilead also offers several options to assist patients who are uninsured in obtaining these medications.[23] Providers can find more information on the assistance programs offered by Gilead on the company's website.[24] Finally, providers should consult their local health departments to determine any accessibility assistance or other PrEP resources offered.[25]

Summary and Conclusion

PrEP is making inroads in the global prevention of HIV-1 infection.[1] The once-daily regimen of FTC/TDF 200 mg/300 mg or FTC/TAF 200 mg/25 mg has been shown to prevent HIV-1 infection by approximately 99% in both at-risk adults and adolescents.[2] Although the PrEP regimen using FTC/TDF has been established since 2012, the regimen using FTC/TAF is newer, gaining FDA approval in 2019.[6] Clinicians should be familiar with the indications and contraindications of FTC/TAF as PrEP, details regarding the appropriate and safe prescribing and initiation of the regimen, its efficacy and safety profile (including adverse events and interactions), and required ongoing monitoring.

Providers must also be able to articulate the differences between FTC/TDF and FTC/TAF. Although both regimens are costly without insurance, nurse practitioners, physicians, and physician assistants should have a working knowledge of the resources available to help patients better afford and access PrEP. These resources include those offered by the drugs' manufacturer, in addition to local and state health departments. Coupled with the use of safer sex practices, PrEP can substantially and universally impact the HIV pandemic. Nurse practitioners can play an important role as patient and public health advocates in reaching the vulnerable populations disproportionately at risk for HIV-1 infection and implement PrEP as an essential preventative tool in these individuals.

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