



Briefing Note

Cost and Supply Security Benefits of Using Tenofovir Disoproxil Fumarate + Lamivudine (TDF/3TC) for Oral Pre-exposure Prophylaxis (PrEP)

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Purpose

Describe key benefits and considerations for using tenofovir disoproxil fumarate/lamivudine (TDF/3TC) for oral PrEP in national programs. Countries are encouraged to consider this information and utilize it to inform decision making.

Background

Access to oral pre-exposure prophylaxis (PrEP) for HIV prevention is growing rapidly globally. In alignment with WHO guidelines, countries with oral PrEP programming utilize TDF in combination with either emtricitabine (FTC) or 3TC. While some countries have policies which allow for either TDF/FTC or TDF/3TC to be utilized for oral PrEP, many countries have policies that rely solely on the use of one or the other. For countries that exclusively utilize TDF/FTC, there exists an opportunity for the program to realize a range of benefits by switching to primarily using TDF/3TC for oral PrEP.

WHO recommends that oral PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.¹ WHO considers FTC and 3TC as equivalent and interchangeable for use in HIV prevention and treatment.^{2,3,4} FTC and 3TC are nucleoside reverse transcriptase inhibitors, with similar chemical structure and very similar activity, safety, and

¹ World Health Organization, *Guideline on When to Start Antiretroviral Therapy and on Pre-exposure Prophylaxis for HIV* (Geneva, 2015), Available: <https://www.who.int/publications/i/item/9789241509565>

² World Health Organization, *Technical Update on Treatment Optimization: Pharmacological Equivalence and Clinical Interchangeability of Lamivudine and Emtricitabine: A review of Current Literature* (Geneva, 2012), Available: <https://www.who.int/publications/i/item/9789241503815>

³ Ford, N, et al., "Comparative Efficacy of Lamivudine and Emtricitabine: A Systematic Review and Meta-analysis of Randomized Trials," *PLoS One* 8 no. 11 (2013): e79981. Available: <https://doi.org/10.1371/journal.pone.0079981>

⁴ World Health Organization, *Appropriate medicines: options for pre-exposure prophylaxis* (Geneva, 2018), Available: <https://www.who.int/publications/i/item/WHO-CDS-HIV-18.22>

resistance profiles. This means that either TDF/FTC or TDF/3TC may be used for oral PrEP, and both have been listed on the WHO essential medicines list.^{5,6,7}

Expected Cost-savings with TDF/3TC vs TDF/FTC for Oral PrEP

Fixed dose combinations of TDF/FTC and TDF/3TC vary in price due to a range of factors, including generic accessibility and product procurement volumes. Many low- and middle-income countries source oral PrEP through the Global Fund to Fight AIDS, Tuberculosis, and Malaria and the President’s Emergency for AIDS Relief (PEPFAR), implemented by United States Agency for International Development, which periodically publish reference prices for products procured through them.

The Global Fund (Q4 2023) and PEPFAR Reference Prices (January 2024) for 30 tablet packs of TDF/FTC and TDF/3TC are as follows:

	TDF/FTC	TDF/3TC	% Savings with TDF/3TC
Global Fund ⁸	\$3.80	\$3.20	16%
PEPFAR ⁹	\$3.75	\$3.09	18%

At the current price, procuring TDF/3TC rather than TDF/FTC at scale could result in significant savings at the country and global level while delivering equivalent HIV prevention.

While prices are subject to change, the current cost-savings are important to consider in country and program decision making.

Savings could be directed to support wider PrEP scale-up, implementation of person-centered innovative service delivery models, adoption of new PrEP products, and/or other programmatic priorities. Lower pricing will improve cost-effectiveness, support longer-term domestic financing and sustainability, and may help lower private sector prices. This could increase the number of people that are able and willing to self-fund oral PrEP.

Programmatic Considerations of Using TDF/3TC for Oral PrEP

Countries with policies that only allow for the use of TDF/FTC for oral PrEP are encouraged to consider adopting TDF/3TC as an option for oral PrEP. To implement this change, countries may need to assess and address any local regulatory and policy barriers to the

⁵ World Health Organization, *Appropriate Medicines: Options for Pre-exposure Prophylaxis* (Geneva, 2018), Available: <https://www.who.int/publications/i/item/WHO-CDS-HIV-18.22>

⁶ World Health Organization, *Model List of Essential Medicines – 23rd List* (Geneva, 2023), Available: <https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02>

⁷ World Health Organization, *HIV Prevention: What the TDF/3TC? The Rationale and the Evidence for TDF/3TC in PrEP*, (Geneva, 2019), Available: <https://www.who.int/news-room/events/detail/2019/02/27/default-calendar/hiv-prevention-what-the-tdf-3tc-the-rationale-and-the-evidence-for-tdf-3tc-in-prep>

⁸ The Global Fund to Fight AIDS, Tuberculosis and Malaria, *Pooled Procurement Mechanism Reference Pricing: ARVs* (Geneva, Q4 2023), Available: https://www.theglobalfund.org/media/5813/ppm_arvreferencepricing_table_en.pdf

⁹ Chemonics International Incorporated, *USAID GHSC-PSM e-Catalog* (Washington, D.C., January 2024), Available: <https://www.ghsupplychain.org/for-suppliers/products>

use of TDF/3TC as PrEP. This may involve working with drug manufacturers or distributors for registration of TDF/3TC. Countries will also need to consider their existing and future procurement contracts and other supply chain dynamics, such as any required changes in stock management processes.

Supply Security Benefits of Including Both TDF/3TC and TDF/FTC in Guidelines for Oral PrEP

Countries are encouraged to have both TDF/FTC and TDF/3TC approved for use as oral PrEP. Globally, both formulations have a sufficient number of suppliers to meet demand. Given the interchangeability of these formulations for PrEP, doing so will make supply chains more flexible and can help to ensure continuity of PrEP access if there are stock outs or unforeseen market challenges and pricing changes occur, as either drug can be used.

TDF/3TC and TDF/FTC have differences in tablet size, color, and packaging. Before and during any product substitution, it is important that both providers and clients are equipped with the knowledge they need to understand and have confidence in the substitution.

Technical circulars for providers that outline changes and guidance for addressing changes with their clients are likely needed. Proactive awareness raising activities by civil society and other stakeholders, ideally including community-led components, educational materials, and counseling, are also likely needed to inform clients.

Key messages for clients and providers may include:

- TDF/FTC and TDF/3TC are equally effective for oral PrEP. Both drug combinations are recommended by the WHO.
- TDF/FTC and TDF/3TC are considered clinically equivalent and interchangeable and are equally effective at preventing HIV.

There are a range of benefits that countries might experience by including TDF/3TC as an option for use as oral PrEP and by moving toward TDF/3TC as the optimal choice for oral PrEP. National programs, PEPFAR implementing partners, Global Fund Principal Recipients and others can reach out to their WHO, PEPFAR, and Global Fund points of contact for questions.