Briefing Note

Managing Tenofovir Alafenamide (TAF) Demand

Date published: 11 July 2024

Background and Purpose

HIV treatment that contains tenofovir alafenamide, or TAF, is recommended by the World Health Organization (WHO) for use in special circumstances for adults and adolescents or people with established osteoporosis and/or impaired kidney function. TAF may also be used as an alternative regimen for children weighing at least 25kg.[1]

Until 2024, Global Fund-financed TAF procurement has been limited.[2] However, an increasing number of Global Fund-supported countries are considering TAF adoption and procurement of larger quantities than anticipated by WHO recommendations.

In light of clinical, market, and programmatic complexities related to TAFp, the Global Fund has developed this document to describe the key considerations pertaining to adoption and procurement of TAF-based products by Principal Recipients (PRs) using Global Fund resources.

Key Considerations

The Global Fund supports TAF procurement provided it considers the clinical, market, and programmatic complexities associated with the product.

[1] "Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach," Guidance, World Health Organization, last updated July 16, 2021, https://www.who.int/publications/i/item/9789240031593

[2] As of June 2024, 11 countries have procured TAF-based products though the Global Fund Pooled Procurement Mechanism (PPM) with total spend having been a fraction of overall ARV procurements. Global Fund financed procurement outside of the PPM has been limited, per reporting to the Global Fund Price & Quality Report.

1.1 Clinical

TAF and tenofovir disoproxil fumarate (TDF), with dolutegravir (DTG) and lamivudine (3TC) or emtricitabine (FTC), are equally effective in achieving viral load suppression among people living with HIV (PLHIV).[3] But, as outlined by the WHO guidelines, there are some differences in side effect profile. TAF is favored in cases of renal insufficiency and established osteoporosis. However, there is some recent evidence that TAF with DTG may be associated with increased weight gain, hypercholesterolemia, and hypertension.[4] TAF appears safe to use in pregnancy, but it is contraindicated with rifampin, a TB co-treatment.

1.2 Market

The latest Global Fund Pooled Procurement Mechanism (PPM) reference prices for TAF-based products and TLD, a fixed dose combination of TDF/3TC/DTG, are summarized in Table 1 below.[5]

TAF-based products are >30% more expensive than TLD. Thus, decisions related to TAF can have a large impact on grant budgets and could affect the scale-up of HIV treatment coverage.[6] Illustratively, US$1 million can treat 2,242 PLHIV annually with TLD (90 pack) compared to 1,388 with TAFED (30 pack).

Table 1. Global Fund PPM reference prices for TLD and TAF-based products

Product[7]	Pack Size	Q2 2024 PPM Reference Price List (Ex-Works, US$)	Comment
TLD	30	$37.20	**TAF-based products are >30% more expensive than TLD.** US$1 million can treat 2,242 PLHIV annually with TLD (90 pack) compared to 1,388 with TAFED (30 pack).
	90	$37.16	
	180	$37	
TAFED*	30	$60**	
TAFLD*		$57**	

*TAFED and TAFLD are also available in 90 and 180 pack sizes; pricing for these multi-month dispensing options will be confirmed once demand is available but is expected to be proportional to 30 pack offering; **Potential for lower price at higher volumes given lower amount of active pharmaceutical ingredient (API) needed.

The Global Fund list of quality assured suppliers for TAF-based formulations can be found here.

[3] Note: TAF-based regimens for HIV treatment can contain either emtricitabine (FTC or 'E') or lamivudine (3TC or 'L'). 3TC and FTC are interchangeable for treatment given their similar clinical efficacy. TLD products procured are exclusively 3TC-containing whereas both FTC (TAFED) and 3TC (TAFLD) contain products for TAF are available and procured by countries.
[4] A Hill, M Mirchandani, B Simmons, S Sokhela, F Venter. Long-term risks of clinical obesity in the ADVANCE, NAMSAL and VISEND trials. HIV Glasgow, 2022. https://hivglasgow.org/wp-content/uploads/2023/01/P149_Hill_Andrew.pdf
[5] "Pooled procurement mechanism reference pricing: ARVs, version Q2 2024', the Global Fund, April 2024, https://www.theglobalfund.org/media/5813/ppm_arvreferencepricing_table_en.pdf
[6] "Pooled procurement mechanism reference pricing: ARVs, version Q2 2024', the Global Fund, April 2024, https://www.theglobalfund.org/media/5813/ppm_arvreferencepricing_table_en.pdf
[7] TLD = tenofovir disoproxil fumarate (TDF), lamivudine (3TC), dolutegravir (DTG); TAFED = TAF, emtricitabine (FTC), DTG; TAFLD = TAF, 3TC, DTG

1.3 Programmatic

TAF-based products ensure equitable treatment for PLHIV who are not able to take TLD**.** Further, smaller pills and bottle sizes of TAF products is preferrable for both those taking treatment and for supply chains.

Introducing TAF-based products will increase the complexity of delivering first-line regimens for PLHIV. This will require a dedicated plan which should consider an update or revision to in-country guidelines, healthcare worker trainings, including TAF into national and sub-national supply chain systems, quantification and forecasting, product registration, demand generation and community engagement. There may also be increased risks of stock-outs given the expanded reliance on three first-line regimens and products (TLD, TAFED or TAFLD, and efavirenz-containing TLE) that will need to be managed through national and sub-national monitoring.

1.4 Partner support

As mentioned in their Fiscal Year 2024 Country and Regional Operational Plan (COP) guidance, PEPFAR "currently recommends the use of TAF containing regimens only in individuals with renal insufficiency and osteoporotic bone disease. Widespread procurement is not recommended."[8]

The WHO is planning a review of benefits of TAF versus TDF in HIV regimens for its 2025 HIV guidelines update. The WHO is also conducting a values and preferences survey of community groups in preparation of the 2025 HIV guidelines update.

The table in the annex summarizes the benefits and limitations of TAF-based products.

Recommended Country Actions

The Global Fund recommends HIV programs interested in adopting and procuring TAF-based products to work with the WHO when evaluating existing guidelines and emerging evidence from global studies, as well as national programmatic data.

PRs interested in ordering TAF-based products are encouraged to notify their Global Fund Country Team before submitting their first requisition on Wambo.org to ensure alignment on a PR-supported transition to TAF. PRs are also suggested to align with their respective Global Fund Country Team to ensure that there is an implementation plan for TAF that reflects national HIV treatment guidelines, an informed quantification based on programmatic data, and efforts to capacitate healthcare workers to provide a new HIV treatment for PLHIV. Any changes in procurement plans that affect the Global Fund Health Product Management Templates (HPMTs) should be managed through routine grant-related processes.

[8] "FY 2024 Technical Considerations", PEPFAR https://www.state.gov/wp-content/uploads/2023/02/FY-2024-PEPFAR-Technical-Considerations.pdf

Annex

Table 2. Overview: Benefits and limitations of TAF-based products for HIV treatment

Benefits	Limitations
Clinical	
• Alternative regimen for adults and adolescents with established osteoporosis and/or impaired kidney function. • Can be used in children weighing at least 25kg due to lower bone density effects than TDF. • Appears safe to use in pregnancy.	• Recent evidence that TAF (with DTG) may be associated with increased weight gain, hypercholesterolemia, and hypertension. • Contraindicated with rifampin (TB co-treatment).
Programmatic	
• Ensures equitable treatment for PLHIV not able to take TLD. • Smaller pill and bottle size.	• Currently only 30 pack size products are commercialized (however this may change with demand). • Increase program complexity with alternative regimen options to be provided. • Potential increase in stock-out risks given reliance on three first-line products (TLD, TLE, TAFED or TAFLD).
Market	
• Potential for lower price at higher volumes given lower amount of API needed.[9]	• TAF-based products are currently >30% more expensive than TLD.

[9] "TAF Product Profile", Clinton Health Access Initiative (CHAI), May 2024