National Essential Medicines List Pharmacoeconomics and Budget impact analysis
Component: HIV infection

Date: 24 July 2025
Medication: Lenacapavir (injectable)
Indication: For the prevention of HIV infection in HIV negative individuals at risk of HIV acquisition

1 INTRODUCTION

This document is an annexure to the medicine review of injectable lenacapavir for HIV prevention in South Africa, comparing it to daily oral tenofovir disoproxil fumarate and emtricitabine (TDF/FTC), the current standard-of-care PrEP formulation. South Africa, with the world's largest HIV treatment and oral PrEP programs, still faces high HIV incidence among adolescent girls and young women (AGYW) and men who have sex with men (MSM), populations for whom lenacapavir for HIV prevention trials were conducted.

Lenacapavir demonstrated superior efficacy to TDF/FTC through two well-conducted randomized clinical trials, PURPOSE-1 and PURPOSE-2 [1,2]. PURPOSE-1, conducted at 28 sites in South Africa and Uganda, studied cisgender adolescent girls and young women (aged 16-26 years) over 4,821 person-years of follow-up [2]. There were zero HIV infections among 2,134 participants in the lenacapavir group, achieving 100% efficacy. PURPOSE-2, conducted across 88 sites in various countries including South Africa, evaluated lenacapavir in cisgender men and transgender and gender non-binary individuals who have sex with partners assigned male at birth (aged 16+ years) [1]. An interim analysis revealed a 96% reduction in HIV acquisition risk for lenacapavir users, with only two new HIV cases among 2,180 lenacapavir recipients compared to nine among 1,087 TDF/FTC recipients. Both trials were unblinded early due to lenacapavir meeting its efficacy endpoints.

While the originator company has issued voluntary licenses to six generic manufacturers, including in low- and middle-income countries (LMIC), there is currently no public price information for lenacapavir for any LMIC. Cheaper generic production will likely take several years to start, time that a country like South Africa will pay for in tens of thousands of avoidable infections. This report describes a cost-effectiveness analysis that compares the scaling up of lenacapavir compared to TDF/FTC, with varying assumptions for cost, coverage and duration. Our analysis also includes a threshold analysis with the aim of estimating the optimal price at which lenacapavir remains as cost-effective as TDF/FTC.

2 PHARMACOECONOMICS MODEL – METHODS AND SCENARIOS

This analysis uses Thembisa (version 4.8), a deterministic compartmental HIV transmission model of the South African HIV epidemic, to estimate the impact of the scale up of lenacapavir and TDF/FTC [3]. The model population is stratified by age, sex, sexual experience, sexual behavior, marital status, HIV testing

history, and male circumcision status. More detailed information about the model can be access at www.thembisa.org.

Lenacapavir and TDF/FTC scale-up were modeled over a 20-year horizon, starting from 2026, targeting all women (including AGYW, pregnant women, FSW), heterosexual men, and MSM. The baseline scenario was the current HIV programme, including the current TDF/FTC roll-out trajectory in South Africa, which has the following coverage levels for FSW (11%), MSM (10%), other women (1%, including 7% AGYW),and heterosexual men (0.2%) (Table 1). The scale-up scenarios modelled were:

- **TDF/FTC scale-up**: We assumed higher oral TDF/FTC initiation rates than at baseline, resulting in higher coverage levels for FSW (22%), MSM (21%), other women (3%, including 16% for AGYW, 41% for pregnant women), and heterosexual men (0.5%). Average duration on TDF/FTC was assumed to be 3 months (women, heterosexual men) and 6 months (MSM).
- **Conservative lenacapavir scale-up**: We assumed the same initiation rates as TDF/FTC scale-up, but an average duration of 6 months (women, heterosexual men) and 12 months (MSM). This resulted in coverages of 40% of FSW, 28% of MSM, 7% of other women (31% of AGYW, 41% of pregnant women), and 1% of heterosexual men.
- **Optimistic lenacapavir scale-up**: We doubled initiation rates compared to TDF/FTC scale-up and assumed longer use durations: 12 months (women, heterosexual men) and 24 months (MSM). These resulted in coverages of 65% FSW, 49% MSM, 14% other women (51% AGYW, 54% pregnant women), and 3% heterosexual men.

Under lenacapavir scenarios, for TDF/FTC we assume no further scale-up, using the same initiation rates as the baseline scenario. Tail protection for lenacapavir, referring to the period during which drug levels remain high enough to offer some continued protection against HIV after the primary dosing effect has waned, was considered to be an average of 6 months after the initial 6 months' protection, based on early pharmacokinetic data [2]. All scenarios and key assumptions are detailed in Table 1 below.

3 CLINICAL INPUTS AND COSTS

Effectiveness

TDF/FTC effectiveness, accounting for both efficacy and adherence, is assumed to be 85% for MSM, and 65% for heterosexual men and women [4–6]. **Lenacapavir effectiveness** was assumed to be 99% in all populations [1,2].

Costs

Costs were analysed from the perspective of the provider, the South African government, and reported in 2025 South African Rand (ZAR). The exchange rate used was ZAR 18.60 = 1 USD, based on reported exchange rates from the Reserve Bank from Jan-May 2025 [7].

The **average cost of PrEP provision was estimated using an ingredients-based approach,** with the cost dependent on the duration assumed**.** Briefly, PrEP is provided in primary healthcare clinics and includes repeat rapid HIV testing, counselling, provision of condoms, syndromic screening for sexual lytransmitted infections with treatment referral, adherence counselling, training, outreach, mobilisation, and monitoring and evaluation costs. The cost of TDF/FTC (drug only) is R64.85 per month [8].

Lenacapavir provision costs were structured similarly to the current oral TDF/FTC programme, but included more professional nurse time for injection administration, and excluded lab monitoring (creatinine and alanine transaminase testing) as these are not required with lenacapavir. In terms of dosing, a client requires two 1.5ml (927mg total) lenacapavir injections at initiation and 6-monthly thereafter, plus two 300mg lenacapavir tablets at initiation and day 2 each (1200mg total) as a loading dose. Since a local price for lenacapavir in South Africa is unknown, our initial analysis assumed it be $100 per person per year (PPPY), or R1,860, for 4 injections and including the cost of the initial loading dose, based on a recent cost-of-goods analysis [9]. To note, Hill et al (2024) estimated that this price could decrease to $40 (or R744) PPPY once a global volume of 10 million treatment-years has been reached, and an updated estimate from the same group, still under peer-review, suggests that even lower pricing is possible: $35-$46 PPPY, and $25 PPPY once a committed demand of 5-10 million people globally has been reached [10]. Important to note is that the models do not account for drug interaction-related dose adjustments, or for additional loading doses which may be required if clients come late for their next injection visit.

Table 1. Key assumptions on duration, coverage, effectiveness and cost of lenacapavir and TDF/FTC

	Baseline *(current TDF/FTC trajectory)*	**TDF/FTC scale-up**	**Lenacapavir conservative scale-up** *Same initiation rates as TDF/FTC scale-up, 6-12m duration*	**Lenacapavir optimistic scale-up** *Higher initiation rates than TDF/FTC scale-up, 12-24m duration*	**Source**
Coverage scenarios *(% coverage in population)*					
Coverage of TDF/FTC	11% FSW 10% MSM 7% AGYW 0% pregnant women 0.2% heterosexual men	22% FSW 21% MSM 16% AGYW 41% pregnant women 0.5% heterosexual men	6% FSW 7% MSM 5% AGYW 0% pregnant women 0.2% heterosexual men	3% FSW 4% MSM 3% AGYW 0% pregnant women 0.2% heterosexual men	[3] for baseline initiation rates, relative uptake between populations; other initiation rates assumed
Coverage of injectable lenacapavir	0% all populations		40% FSW 28% MSM 31% AGYW 41% pregnant women 1% heterosexual men	65% FSW 49% MSM 51% AGYW 54% pregnant women 3% heterosexual men	Assumed same or double initiation rates as TDF/FTC scale-up

	Baseline *(current TDF/FTC trajectory)*	TDF/FTC scale-up	Lenacapavir conservative scale-up *Same initiation rates as TDF/FTC scale-up, 6-12m duration*	Lenacapavir optimistic scale-up *Higher initiation rates than TDF/FTC scale-up, 12-24m duration*	Source
Duration of protection, including tail protection (months)	3m (women, heterosexual men) 6m (MSM)		6m (+6m tail) (women, heterosexual men) 12m (+6m tail) (MSM)	12m (+6m tail protection) (women, heterosexual men) 24m (+6m tail) (MSM)	[2,11]
Effectiveness in preventing HIV infection	65% (women, heterosexual men) 85% (MSM)		99% (all populations)		[1,2,4–6,12,13]
Cost of provision of PrEP (per person initiated in ZAR) **					
TDF/FTC	R1,050 (women, heterosexual men), R1,319 (MSM)				HE²RO HIV unit cost model
Injectable lenacapavir	N/A		R1,463-R1,459 (women, heterosexual men), R2,518 (MSM)	R2,550-R2,541 (women, heterosexual men), R4,682 (MSM)	

***Full service cost presented includes costs for staff, HIV and laboratory testing, drugs, consumables and overheads. TDF/FTC price for drug only = R64.85 per month; assumed price for lenacapavir (drug only, includes cost of loading dose) = $100 or R1,860 PPPY.*

Cost effectiveness

Cost effectiveness was estimated over a 20-year time horizon (2026-2045) as incremental cost per HIV infection averted and incremental cost per life year saved. Threshold prices for lenacapavir were estimated to determine the price point at which it would be as cost-effective as further scaling up TDF/FTC. Prices for injections and loading dose tablets were calculated separately, proportionally allocated based on the ratio of active pharmaceutical ingredient (API) in each formulation: 927mg lenacapavir per injection vs 1200mg loading dose.

Sensitivity analysis

A probabilistic sensitivity analysis was conducted to assess the uncertainty of 58 parameters in the model, including PrEP-specific parameters such as effectiveness of TDF/FTC and lenacapavir, tail protection of lenacapavir and reduced condom use while on either PrEP type, and consisted of 1,000 Monte Carlo simulations sampled data from predetermined distributions for all parameters. Median estimates of the threshold price with 2.5th and 97.5th percentiles.

4 RESULTS

Epidemiological impact

Our optimistic lenacapavir scenario averted up to 52,200 HIV infections per year over the modelled period, while our conservative lenacapavir scenario averted up to 33,000 infections per year. In comparison, TDF/FTC scale-up averted a maximum of 8,600 infections per year. Over 20 years combined, lenacapavir scenarios averted 20%-32% of new HIV infections over baseline compared to 5% with TDF/FTC scale-up.

Costs, cost-effectiveness and price threshold estimates

Assuming a price for lenacapavir of $100/R1,860 PPPY, total HIV programme costs would increase by 5%-17% over 2026-2045, depending on uptake and duration. In comparison, TDF/FTC scale-up at current prices will increase the cost of the HIV programme by 3% over the same period (Table 2). The incremental cost-effectiveness ratios (ICERs) of oral TDF/FTC scale-up were R177,691/HIV infection averted and R139,303/life year saved over baseline. At an assumed price of $100 PPPY, lenacapavir would be more cost-effective than oral TDF/FTC scale-up, even at higher uptake and duration, with R74,392-R147,232/HIV infection averted across scenarios and R60,388-R118,229/life year saved. In terms of averting disability-adjusted life years (DALYs), cost-effectiveness for scaling up the different PrEP modalities were R29,729/DALY averted (oral TDF/FTC), R27,567/DALY averted (conservative lenacapavir scale-up), and R64,087/DALY averted (optimistic lenacapavir scale-up).

Under the conservative scenario, the price of lenacapavir would need to be R1,985 PPPY for four injections (or R496 per one 1.5ml injection) and R1,285 for the 1200mg loading dose (R321 per 300mg tablet) to be as cost-effective as TDF/FTC scale-up in terms of incremental cost per life year saved. Under the optimistic scenario, the threshold price decreases to R1,366 PPPY (R342 per one 1.5ml injection) and R884 for the 1200mg loading dose (R221 per 300mg tablet). Results comparing cost-effectiveness per HIV infection averted produced similar price thresholds.

Table 2. Effect and cost-effectiveness of oral TDF/FTC and long-acting injectable lenacapavir scale-up compared with baseline, over a 20-year period (2026–45)

	Total cost of the HIV programme		Incremental cost effectiveness			New HIV infections		Life years lost due to AIDS		Disability-adjusted life year (DALY)	
Scenario	**Cost (billions, ZAR)**	**Incremental cost over baseline, %**	**Cost per infection averted (ZAR)**	**Cost per life year saved (ZAR)**	**Cost per DALY averted (ZAR)**	**Number (millions)**	**% averted over baseline**	**Number (millions)**	**% saved over baseline**	**Number (millions)**	**% averted over baseline**
Baseline	R729	-	-	-		2.63	-	18.75	-	23.75	-
Oral TDF/FTC scale up	R752	3%	R177,691	R139,303	R29,729	2.50	5%	18.59	1%	23.01	3%
Lenacapavir (assumed drug price $100/PPPY)											
Conservative: same initiation rates as TDF/FTC; 6-12m duration	R768	5%	R74,392	R60,388	R27,567	2.11	20%	18.11	3%	22.35	6%
Optimistic: higher initiation rates than TDF/FTC, 12-24m duration	R854	17%	R147,232	R118,229	R64,087	1.78	32%	17.69	6%	21.81	8%

Abbreviations: DALY = disability-adjusted life year; TDF/FTC = tenofovir/emtricitabine, ZAR = South African Rand, PPPY=per person per year

Sensitivity analyses and their impact on the threshold price

Accounting for model uncertainty, lenacapavir still showed a substantial impact on the percentage of new HIV infections averted over baseline (95% UB: 17.1%-19.8% for conservative 6-12-month duration; 28.6%-33.8% for optimistic 12-24-month duration), exceeding TDF/FTC (UB 4.6%-4.9%) (Table 3).

Table 3: Uncertainty ranges around the impact of TDF/FTC and lenacapavir over a 20-year time horizon (2026-2045); based on a probabilistic sensitivity analysis

Estimates represented are the median estimate with 2.5th and 97.5th percentiles in brackets.

	New HIV infections		Life years lost due to AIDS	
Scenario	**Number (millions)**	**% averted over baseline**	**Number (millions)**	**% saved over baseline**
Baseline	2.56 (1.83-3.64)	-	18.52 (16.61-20.94)	-
Oral *TDF/FTC* scale up	2.44 (1.74-3.46)	4.8% (4.6%-4.9%)	18.37 (16.49-20.74)	0.8% (0.7%-1.0%)
Lenacapavir				
Conservative: same initiation rates as TDF/FTC, 6-12m duration	2.07 (1.51-2.92)	19.4% (17.1%-19.8%)	17.90 (16.23-20.05)	3.3% (2.3%-4.2%)
Optimistic: higher initiation rates than TDF/FTC, 12-24m duration	1.75 (1.30-2.41)	31.7% (28.6%-33.8%)	17.49 (15.95-19.45)	5.6% (4.0%-7.1%)

Price thresholds varied substantially once the uncertainty in model parameters was accounted for. For a conservative uptake of lenacapavir, with 6-12-month duration and same initiation rates as TDF/FTC, the injection price ranged between R1,217 and R3,313 PPPY (R304-R828/injection), and loading dose R788-R2,144 per person initiated for 4x300mg tablets (Table 4). For an optimistic uptake of lenacapavir, with higher initiation rates and 12-24-month duration, these thresholds ranged between R963 and R2,114 PPPY for injections (R241-R528/injection) and R623-R1,368 per loading dose per initiation (4x300mg tablets).

Table 4: Uncertainty lower and upper bound price thresholds, compared to TDF/FTC scale up cost-effectiveness, over the 20-year period, based on a probabilistic sensitivity analysis

Lenacapavir scenario	**Cost of injections per person per year (ZAR)** (4x 1.5ml 463mg injections per year)	**Cost per loading dose per initiation (ZAR)** (4x 300mg tablets per initiation)
Conservative: same initiation rates as TDF/FTC, 6-12m duration	R1,217 - R3,313	R788 - R2,144
Optimistic: higher initiation rates than TDF/FTC, 12-24m duration	R963 - R2,114	R623 - R1,368

5 Published Health Economics

There are a limited number of published cost-effectiveness studies on lenacapavir for HIV prevention. Existing cost-effectiveness analyses of lenacapavir for HIV prevention highlight its potential to significantly reduce HIV incidence, while mentioning critical challenges related to affordability and access. A modeling analysis for Eastern and Southern Africa, including South Africa, Zimbabwe, and western Kenya, projected that lenacapavir could avert 12.3%-18.0% of infections over 10 years at a coverage of 1.6%-4.0% of the population, with maximum per-dose prices ranging from $16.58 in western Kenya to $106.28 in South Africa when compared to a cost-effectiveness threshold of <US$500 per disability-adjusted life-year averted in 2021 USD [14]. If adjusting these estimates for inflation using South African consumer price index figures and above-mentioned exchange rates for 2025, these would be equivalent to R4,888 PPPY in 2025. In a higher coverage scenario, prices would need to be lower still to maintain cost-effectiveness, emphasizing that widespread impact is contingent on reduced costs [14]. Another modeling study evaluating lenacapavir impact and cost-effectiveness for South Africa found that it would significantly reduce HIV acquisitions, by 22% with 5% coverage of populations groups prioritized by HIV risk, and up to 35% with 20% risk-prioritized coverage [15]. To be cost-effective under a threshold of US$500 per disability-adjusted life-year averted, the price per person per year for 5% risk-prioritized coverage is $105.98 PPPY (95% confidence interval $97.64-$114.42) (the equivalent price in 2025 ZAR would be R2,437 PPPY). This maximum annual cost decreases with higher coverage, reaching $45.91 PPPY (95% confidence interval $43.58-$48.29) for 20% risk-prioritized coverage (the equivalent price in 2025 ZAR would be R1,056 PPPY).

While lenacapavir is sold at a very high price in high income countries (currently ~$28,000 annually for treatment in the United States), cost-of-goods analyses suggest generic versions could be manufactured for as little as $25-$100 per person per year, particularly with large-scale uptake [9,10].

6 Budget Impact Analysis

The cost of lenacapavir for the South African market is currently unknown, and the expected volume/uptake is also uncertain. Consequently, we present budget impacts based on our optimistic and conservative lenacapavir scenarios, using their threshold prices based on cost-effectiveness relative to TDF/FTC scale-up. Under the conservative scenario, the price threshold was R496 per one 1.5ml injection (2 are required per visit) and R321 per 300mg loading dose tablet (4 tablets are required per initiation). Under the optimistic scenario, the price threshold was R342 per one 1.5ml 463mg injection (2 required per visit, R1,366 PPPY) and R221 per 300mg tablet (i.e. R884 for 4 tablets per person initiated).

Under a conservative scenario, we can expect between 590,000 and 1.35 million initiates per year, requiring between 1.23-2.88 million doses per year (Table 5). At a threshold price of R496 per injection and R321 per 300mg loading dose tablet, this would cost between R1.74 billion and R4.02 billion annually, including the cost of the drugs and service provision. This would result in a 5-11% increase in the annual HIV programme budget over the next 5 years, after accounting for the effect of reduced HIV infections and ART need.

Under an optimistic scenario, we can expect between 910,000 and 2.07 million initiates per year, requiring between 3.80-8.75 million doses per year (Table 5). At a threshold price of R342 per injection and R221

per 300mg loading dose tablet, this would cost between R1.98 billion and R4.52 billion annually, including the cost of the drugs and service provision. This would result in a 6-13% increase in the annual HIV programme budget over the next 5 years, after accounting for the effect of reduced HIV infections and ART need.

Table 5. Cost of lenacapavir provision from 2025/2026-2029/30, for conservative and optimistic scale-up scenarios

Conservative lenacapavir scale-up, same initiation rates as TDF/FTC, 6-12-month duration					
	2025/26	**2026/27**	**2027/28**	**2028/29**	**2029/30**
Number people initiated (millions)	0.59	0.78	0.97	1.15	1.35
Number doses required (millions)	0.61	0.82	1.03	1.23	1.44
Total cost (2025 ZAR, billions)	**1.74**	**2.32**	**2.88**	**3.43**	**4.02**
Scenario description and assumptions: *Coverage: 40% FSW, 28% MSM, 7% women (31% AGYW, 41% pregnant women), 1% heterosexual men* *Duration: 6mo (women, non-MSM); 12mo (MSM)* *Cost of drugs: R496/1.5ml 463mg injection (dose: 2 injections/visit); R321 per 300mg loading dose tablet (4 required/initiation)* *Total cost of provision (including drugs) per person initiated: R2,896-R2,900 (women, heterosexual men); R4,022 (MSM)*					
Optimistic lenacapavir scale-up, higher initiation rates than TDF/FTC, 12-24-month duration					
	2025/26	**2026/27**	**2027/28**	**2028/29**	**2029/30**
Number people initiated (millions)	0.91	1.23	1.52	1.78	2.07
Number doses required (millions)	1.90	2.59	3.20	3.76	4.37
Total cost (2025 ZAR, billions)	**1.98**	**2.69**	**3.31**	**3.89**	**4.52**
Scenario description and assumptions: *Coverage: 65% FSW, 49% MSM, 14% women (51% AGYW, 54% pregnant women), 3% heterosexual men* *Duration: 12mo (women, non-MSM); 24mo (MSM)* *Cost of drugs: R342/1.5ml 463mg injection (dose: 2 injections/visit); R221 per 300mg loading dose tablet (4 required/initiation)* *Total cost of provision (including drugs) per person initiated: R2,953-R2,963 (women, heterosexual men); R4,566 (MSM)*					

7 CONCLUSION

Lenacapavir will have a significant impact in reducing HIV infections, by between 20%-32% over baseline, compared to oral TDF/FTC, which even at scaled up levels will only reduce HIV infections by 5%. This is a higher impact than any other HIV prevention intervention studied in consecutive HIV Investment Case analyses since 2015. It is second only to the preventative impact of 95% ART uptake [16]. Lenacapavir can be as cost-effective as further scaling up oral PrEP with TDF/FTC if its price ranges between R342-R496 per injection and R221-R321 per 300mg loading dose tablet, depending on the uptake and duration assumptions. Accounting for uncertainty in the model, these prices ranged from R241 to R828 per 1.5ml injection and from R623 to R2,144 for the loading dose (4x300mg tablets). As the cost-of-goods analyses cited under Hill (2024) and Fortunak (2025) have shown, the price of lenacapavir will depend on the volume of the global market [9,10], most of which will be in South Africa as home to the largest population at risk of HIV acquisition [17].

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Conflicts of interest: LJ has no conflicts of interests related to lenacapavir.

Version	Date	Reviewer(s)	Conclusion
First	14 July 2025	Lise Jamieson	Lenacapavir is projected to significantly reduce HIV infections by 20-32% over baseline, outperforming oral TDF/FTC's 5% reduction, even at scaled-up levels. To achieve comparable cost-effectiveness to TDF/FTC in the same population, lenacapavir's price would need to be between R342-R496 per injection and R221-R321 per 300mg loading dose tablet, depending on uptake and duration.