Cost-Effectiveness of Lenacapavir Versus Oral and Injectable PrEP Options for HIV Prevention in the United States

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Conclusions

- Lenacapavir (LEN) has demonstrated efficacy and safety in the PURPOSE-1 and PURPOSE-2 trials as a pre-exposure prophylaxis (PrEP) option for human immunodeficiency virus (HIV) prevention in the US
- Compared with generic and branded oral PrEP and cabotegravir (CAB), LEN provides more quality-adjusted life years (QALYs) and equal-value life years (evLYs) at lower overall costs, supporting LEN as the dominant strategy
  - LEN's consistent dominance across nearly all scenarios supports its cost-effectiveness
- Findings from this analysis may inform payer and policy decision-making, supporting adoption of long-acting LEN as a high value intervention with strong HIV prevention potential
- Results support prioritizing LEN for populations disproportionately affected by HIV, particularly those facing adherence challenges to daily or more frequent dosing regimens
- As long-acting HIV prevention continues to evolve, LEN may play a pivotal role in reducing HIV incidence, avoiding the lifetime burden of HIV, and expanding the reach and impact of PrEP programs

Plain Language Summary

Lenacapavir (LEN) is a long-acting injectable (LAI) for prevention of HIV (PrEP). It has shown a good balance of benefits and cost versus oral pills and cabotegravir (another LAI). As an LAI, LEN may help patients stay on treatment which can lower HIV rates. This balance of benefit and cost may help payer and policy access decisions.

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Introduction

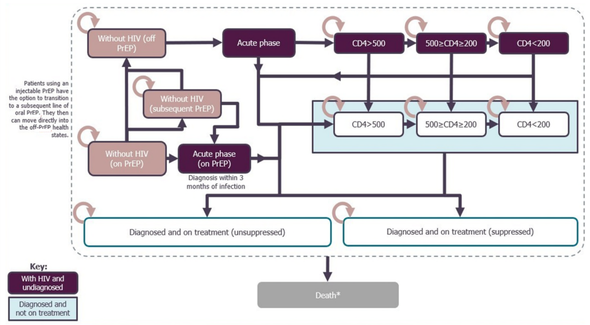
- Despite major advances in HIV treatment and prevention, the HIV epidemic persists globally and in the US[1,2]
- HIV prevention strategies, including treatment of people living with HIV and widespread PrEP use, are critical to meeting the US Ending the HIV Epidemic goal of 90% reduction in incident cases by 2030[3]
- Approved PrEP options include daily oral tenofovir disoproxil fumarate/ emtricitabine (TDF/FTC) and tenofovir alafenamide fumarate and emtricitabine (TAF/FTC), every-two-month injectable CAB, and twice-yearly injectable LEN[4-7]
- Among established PrEP modalities, US uptake remains suboptimal, with persistent sociodemographic inequities; LEN was only recently approved in 2025[7,8]
- Adherence and long-term persistence with daily oral PrEP are significant challenges; with only about one third of new users persisting at 12 months[9]
- The PURPOSE-1 and PURPOSE-2 trials demonstrated superior efficacy for LEN versus oral PrEP among cisgender women (CGW), men-who-have-sex-with-men (MSM), and transgender and non-binary persons (TGNB), with ≥99.9% of participants who received LEN remaining HIV-negative[10,11]
- This analysis evaluated the cost-effectiveness of LEN versus oral PrEP and injectable CAB for HIV prevention in US populations who benefit from PrEP

Methods

Model Structure

- A Markov model was developed to simulate HIV acquisition, persistence, and transmission over a 50-year time horizon from a US commercial healthcare payer perspective using quarterly cycles and 3% discounting (**Figure 1**)
- All individuals enter the model without HIV and initiate PrEP in the first cycle
- PrEP options include oral TAF/FTC, oral TDF/FTC (using generic and brand prices), injectable CAB, and long-acting LEN
- PrEP persistence was modeled using an exponential decay approach based on 1-year discontinuation rates
  - Half of those discontinuing injectable PrEP switch to an oral PrEP option (also subject to discontinuation)
- Individuals are assumed to have a greater likelihood of HIV acquisition for 10 years, after which remaining PrEP users transition off PrEP and revert to the lower background HIV risk of the general population.
- Once transitioned off PrEP, individuals do not re-initiate PrEP

Figure 1. Model Structure



*Transition to the death state is possible from all states

Abbreviations: CD4, cluster of differentiation four; HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis

HIV Acquisition and Progression

- HIV acquisition probability determined transmission risk each cycle
  - To account for onward HIV transmission, a multiplier was applied assuming 0.92 additional transmissions per novel HIV acquisition[12]
- Individuals who recently acquired HIV enter a one-cycle acute phase, stratified by HIV acquisition on versus off PrEP
  - HIV testing was assumed for PrEP users, consistent with US Prescribing Information;[4-7] HIV acquisition on PrEP was assumed to be diagnosed within 3 months
  - HIV acquisition off PrEP may remain undiagnosed
- HIV health states were stratified by diagnosis status; only diagnosed individuals receive treatment
- Mortality could occur from all states, with rates varying by HIV status; individuals without HIV follow age- and sex-specific general mortality

Methods (cont'd)

Model Inputs

- Starting age was set at 16 years, consistent with the minimum eligibility age of participants in the PURPOSE-1 & 2 trials[10,11]
- Clinical inputs were sourced from the PURPOSE-1, PURPOSE-2, HPTN 083, and HPTN 084 trials[10,11,13,14]
- Costs included drug acquisition, drug administration, monitoring, HIV testing, adverse events, HIV management, and mortality, and were sourced from the NAVLIN by EVERSANA database[16] and published literature,[16-20] expressed as 2026 USD
- PrEP dosing schedules were based on US Prescribing Information[4-7]

Outcomes and Analyses

- MSM/TGNB and CGW were modeled separately, with results reported as a weighted population; evLYs, QALYs, and pair-wise incremental cost-effectiveness ratios (ICERs) were calculated
- A probabilistic sensitivity analysis was conducted using 2,000 iterations to account for the joint uncertainty of the underlying parameter estimates
- Scenario analyses were conducted to assess the impact of key model inputs and assumptions including (1) MSM/TGNB and CGW subgroups (2) no discounting, (3) median starting ages from PURPOSE-1 & 2,[10,11] (4) dynamic risk approach for onward transmission,[21] (5) no onward transmission, (6) using the upper bound of the 95% confidence interval for HIV incidence for LEN and CAB, to examine uncertainty around incidence estimates, (7) 25-year time horizon, and (8) 30 year HIV-risk duration

Results

Primary Results

- Over a 50-year time horizon in the weighted MSM/TGNB and CGW population, LEN strongly dominated (more effective, less costly than comparator) both CAB and branded and generic daily oral PrEP, generating more QALYs (+0.07 to +0.39) and evLYs (+0.05 to +0.24) at a lower cost (-$6,978 to -$41,358) (**Table 1**)

Table 1. Primary Results (Weighted MSM/TGNB and CGW Populations)

	LEN	TAF/FTC	TDF/FTC	TDF/FTC (generic)	CAB
Total Costs[a]	$356,045	$397,403	$392,621	$375,039	$363,023
Total evLYs	24.467	24.227	24.230	24.230	24.422
Total QALYs	20.988	20.599	20.604	20.604	20.916
Incremental Costs		-$41,358	-$36,576	-$18,994	-$6,978
Incremental evLYs		0.241	0.238	0.238	0.045
Incremental QALYs		0.389	0.384	0.384	0.073
ICER (Cost/evLY)		**LEN Dominant**	**LEN Dominant**	**LEN Dominant**	**LEN Dominant**
ICER (Cost/QALY)		**LEN Dominant**	**LEN Dominant**	**LEN Dominant**	**LEN Dominant**

[a] Total costs include costs associated with drug acquisition, drug administration, monitoring, HIV testing, adverse events, HIV management, and mortality

Note: MSM/TGNB represented 76% of the total population, and CGW accounted for 24%; results represent outcomes for a single weighted patient

Abbreviations: CAB, cabotegravir; CGW, cis-gender women; LEN, lenacapavir; ICER, incremental cost-effectiveness ratio; evLY, equal value life year; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; QALY, quality adjusted life year; TAF/FTC, tenofovir alafenamide fumarate and emtricitabine; TDF/FTC, tenofovir disoproxil fumarate and emtricitabine; TGNB, transgender and non-binary

Probabilistic Sensitivity Analysis Results

- Results of the probabilistic sensitivity analysis were consistent with the primary results for the weighted MSM/TGNB and CGW population. LEN was dominant versus CAB and generic and branded daily oral PrEP options
- Using the Institute for Clinical and Economic Review's willingness-to-pay threshold of $100,000 per QALY,[22] the probability of LEN being the most cost-effective PrEP was 77% for MSM/TGNB and 63% for CGW

Table 2. Scenario Analysis Results (ICER [Cost/QALY])

	TAF/FTC	TDF/FTC	TDF/FTC (generic)	CAB
MSM/TGNB subgroup	Dominant	Dominant	Dominant	Dominant
CGW subgroup	Dominant	Dominant	Dominant	Dominant
0% discount rate	Dominant	Dominant	Dominant	Dominant
Start age: MSM/TGNB: 29 yrs; CGW: 21 yrs	Dominant	Dominant	Dominant	Dominant
Dynamic onward transmission risk	Dominant	Dominant	Dominant	Dominant
No onward transmission	Dominant	$15,508	$93,227	$23,280
HIV incidence: 95% upper CI estimates	Dominant	Dominant	Dominant	Dominant
25-year time horizon	Dominant	Dominant	$45,262	Dominant
30-year risk	Dominant	Dominant	$28,219	Dominant

Abbreviations: CAB, cabotegravir; CGW, cis-gender women; CI, confidence interval; HIV, human immunodeficiency virus; ICER, incremental cost-effectiveness ratio; MSM, men who have sex with men; QALY, quality adjusted life year; TAF/FTC, tenofovir alafenamide fumarate and emtricitabine; TDF/FTC, tenofovir disoproxil fumarate and emtricitabine; TGNB, transgender and non-binary

Scenario Analysis Results

- LEN remained dominant across all but three scenarios (**Table 2**)
  - In the scenario with no onward HIV transmission, limiting the analysis to the direct effects of PrEP on the user, LEN was dominant versus TAF/FTC and more effective but not dominant compared with branded and generic TDF/FTC and CAB (ICERs ranging from $15,508 to $93,227 per QALY)
  - With a duration of HIV risk of 30 years, LEN remained dominant versus all comparators except generic oral PrEP (ICER: $28,219 per QALY)
  - Similarly, LEN was dominant versus all comparators but generic oral PrEP when the time horizon was reduced to 25 years (ICER: $45,262 per QALY)
  - Using a willingness-to-pay threshold of $100,000 per QALY, LEN is still considered cost-effective versus all comparators across all scenarios

Limitations

- The analysis relied on several simplifying assumptions that may not fully reflect real-world PrEP use patterns or HIV progression
  - Equal PrEP persistence was assumed for LEN and CAB, which may overestimate CAB persistence given its more frequent dosing schedule
  - The cohort Markov model could not track time spent in health states, assuming PrEP use until discontinuation, HIV acquisition, or death, simplifying real-world start-stop patterns
  - Incidence rates were sourced directly from randomized controlled trials, which represent the best available evidence for LEN at this time; future analyses should incorporate real-world evidence as it becomes available
  - HIV progression was modeled with simplified states that, while not fully reflective of clinical practice, aligned with published transition probabilities