What can modelling tell us about the scale-up of lenacapavir for PrEP?
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Key Messages

- Even once countries reach 95-95-95 goals for testing, treatment and viral suppression, there will still be a gap that needs to be filled by primary prevention.
- PrEP programs, including injectable lenacapavir, can contribute to incidence decline.
- The more programs can identify and deliver LEN to people at greatest risk of infection, the more cost-effective LEN programs can be.
- Delivering up to 6 million person-years of protection in the first three years of introduction could avert up to 100,000 new HIV infections, out of an anticipated 3 million.
- Although a modest contribution to the total in three years, this accelerated introduction is needed to build a more substantial and impactful market over time and can contribute significantly to global targets.

Injectable lenacapavir (LEN) for pre-exposure prophylaxis (PrEP) is an antiretroviral drug developed by Gilead Sciences to be administered every six months as two subcutaneous injections, with an oral loading dose of four tablets over two days to provide initial protection. In clinical trials, LEN was found to be safe to use and resulted in 96-100% protection against HIV acquisition. In June 2025, the US Food and Drug Administration issue the first approval for LEN to be used as an HIV prevention option, with approvals in other countries expected to follow imminently. WHO is expected to issue guidelines for LEN for PrEP in July 2025. While the price of LEN in low- and middle-income countries (LMIC) has not been publicly confirmed by Gilead, it is expected to be around $100 per person per year (PPPY) at launch, with prices dropping as volumes increase and with the introduction of generic versions by 2027.

Mathematical modelling can help project the expected impact and cost-effectiveness of LEN and inform policy decisions prior to rollout. Modelling on LEN has focused on answering the following questions thus far:

1. **What is the anticipated impact of LEN for PrEP, in the context of current product availability announcements?**

The Global Fund and the President's Emergency Plan for AIDS Relief (PEPFAR) publicly announced in December 2024, in conjunction with the Children's Investment Fund Foundation (CIFF) and the Gates Foundation, an ambition to provide access to LEN for at least 2 million person-years of protection over three years. Two models, EMOD-HIV and Goals, investigated the impact of providing between 1 to 6 million person-years (PY) of LEN over three years, when delivered strategically to populations and locations with high HIV incidence risk. Provision of 1 million PY was found to avert between 22,000-39,000 new infections over 3 years in South Africa, while 6 million PY could avert up to 103,000 new infections over the same period when used among populations with high incidence in South Africa, the Philippines, and Eswatini. These estimates are a small proportion of total expected new HIV infections over this period (~3 million) but would be a necessary first step before building a more substantial market over time.

2. What is the potential impact of LEN for PrEP with increased population coverage?

When LEN is delivered to a small, well-targeted proportion of the population, new infections can be averted with greater efficiency. A larger impact can be achieved when a higher proportion of the population is reached, but with diminishing efficiency (i.e., more PY of LEN would be required to avert an infection). For example, in generalized epidemics in the African region, the EMOD-HIV model found that offering LEN to 5% of adults, prioritized by location and risk behaviour, would avert 25-35% of new infections over 10 years, depending on the setting. If offered to 20% of all adults, LEN could avert between 50-70% of expected new infections over this period. In a concentrated epidemic in the Philippines, an analysis using the Goals model found that offering LEN to key populations, including men who have sex with men, transgender women, sex workers, and people who inject drugs, would avert ~45% of new infections with ~60% ley population coverage (equivalent to ~2% total adult population coverage).

3. What is the maximum LEN for PrEP could cost while still being cost-effective?

Two studies using the EMOD-HIV model investigated the maximum price per dose for LEN in South Africa, Western Kenya, and Zimbabwe. One study found that the maximum price PPPY – when isolated to the price of the drug only – would be $212 in South Africa, $42 in Zimbabwe, and $34 in western Kenya. A second EMOD-HIV study including the fully-loaded cost of delivering LEN, including commodities and delivery costs, found that the price of LEN PPPY could be up to $106 in South Africa, $30 in Zimbabwe, and $16 in western Kenya.

One study using the Thembisa model in South Africa found that LEN could cost a maximum of $225 PPPY to be cost-effective compared to expanded oral PrEP. LEN was found to have a greater projected impact than both expanded oral PrEP and long-acting injectable cabotegravir due to its higher effectiveness, assumed increased uptake, and assumed longer duration of effective use.

Cost-effectiveness was found to decrease in both models when total adult population coverage increased, although expanded use of LEN resulted in a higher overall impact.

4. What are price thresholds for LEN to provide net savings on future treatment costs?

An analysis using the Goals model found that providing LEN would be cost-saving in the context of lifelong antiretroviral therapy (ART). At a lifetime cost of $5,000 per person for ART (including drugs, hospitalizations, and health system costs), providing LEN to populations with incidence of greater than 1% would be cost-saving if the total price of LEN was $40-60 PPPY (including commodities and delivery). If the price of LEN was lower, LEN use could be expanded to populations and locations with lower incidence and still be cost-saving. This perspective is solely financial, however, and does not consider value generated to improved health outcomes (e.g. productivity or wellbeing gains) accrued from averted infections.