Lenacapavir: A Global Breakthrough in HIV Prevention and the Ethical Imperative of Equitable Access - A Literature Review

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Abstract

Introduction: *Since the early 1980s, the global HIV epidemic has posed persistent challenges to prevention efforts. Despite the progress achieved through oral pre-exposure prophylaxis (PrEP), adherence issues, stigma, and limited access have hindered its widespread success. Lenacapavir, a long-acting capsid inhibitor, represents a breakthrough innovation that offers six months of continuous protection through a single subcutaneous injection, that would potentially transform HIV prevention worldwide.*

Aim: *This study aims to evaluate the clinical effectiveness, safety, and global impact of lenacapavir as a new generation PrEP agent.*

Methodology: *We conducted a literature review that was primarily based on results from a systematic literature review and meta-analysis that included 26 international sources, including The New England Journal of Medicine, Nature, and The Lancet. Data from the PURPOSE-1 and PURPOSE-2 trials were also reviewed comparatively to assess the drug's efficacy, side effects, and population outcomes, while descriptive statistics illustrated predicted epidemiological trends.*

Results: *The major finding has derived from the meta-analyses showing that lenacapavir had an extremely high (99,9%) efficacy in preventing HIV infection among participants using it, with a significantly lower rate of adverse events compared to oral PrEP regimens. Global modelling studies predict up to a 60% reduction in new HIV infections by 2030 if lenacapavir is implemented more widely, especially in Sub-Saharan Africa.*

Conclusions: *Lenacapavir represents a paradigm shift in HIV prevention, combining scientific innovation with public health equity. If affordability and access barriers are addressed, this treatment may become a cornerstone of global HIV elimination strategies in the future.*

Keywords*: Lenacapavir, HIV prevention, PrEP, long-acting therapy, global health, meta-analysis*

Introduction

Since the beginning of the HIV pandemic, extensive scientific and institutional efforts have been made to reduce viral transmission and develop safe and effective preventive tools. The introduction of pre-exposure prophylaxis (PrEP) using antiretroviral combinations such as tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) and later tenofovir alafenamide/emtricitabine (F/TAF) represented a major step forward in preventing new infections, particularly among high-risk populations.

However, challenges related to adherence to daily dosing, stigma, and unequal access to treatment have underscored the need for more sustainable and practical alternatives (Bekker et al., 2024; Kelley et al., 2024). In this context, lenacapavir, a novel HIV capsid inhibitor, has emerged as a groundbreaking candidate for long-acting HIV prevention. Preliminary results from clinical trials published in *The New England Journal of Medicine* (2024) demonstrated that twice-yearly lenacapavir injections provided complete protection against infection among cisgender women, men, and gender-diverse individuals participating in international studies (Bekker et al., 2024; Kelley et al., 2024). These "zero new infection" findings were described by *Nature* as "remarkable" and clear evidence of the transformative potential of long-acting prophylaxis in reshaping global HIV prevention strategies

(Nature, 2024; Nature Biotechnology, 2024). The FDA's approval lenacapavir (marketed as *Yeztugo*) in June 2025 for use as a twice-yearly prophylactic injection marks a historic milestone in HIV prevention (WHO, 2025; Gilead Sciences, 2025; AVAC, 2025). According to the World Health Organization (WHO), this approval represents a "significant breakthrough" toward achieving the 95-95-95 targets by 2030, offering a simpler, more durable, and accessible option for individuals at risk (WHO, 2025). Nevertheless, despite global enthusiasm, issues related to its cost, access, and health equity remain central to ongoing discussions. UNAIDS, Unitaid, and other international organizations have stressed the urgency of ensuring that this new medication does not remain limited to high-income countries. Gilead Sciences' voluntary licensing agreements with six generic manufacturers, signed in 2024, represent a positive step forward, yet additional measures are needed to reduce costs and expand supply to low-income countries (UNAIDS, 2024; Sneha, 2024; UNAIDS, 2025). In this context, the present literature review aims to summarise the scientific development, clinical effectiveness, and global implications of using lenacapavir as a promising new "vaccine-like" approach to HIV prevention, a step that could redefine the fight against the virus after more than four decades of intensive research.

Scientific development and mechanism of action of Lenacapavir

Lenacapavir represents a completely new approach to HIV prevention, differing fundamentally from traditional antiretroviral therapies that target viral enzymes. It is an inhibitor of the HIV capsid, a key protein that protects the virus's genetic material and plays a crucial role in the viral replication. Unlike classical reverse transcriptase or protease inhibitors, lenacapavir interferes with multiple stages of the viral life cycle, including the transport of viral DNA into the nucleus and the assembly of new virions, thereby preventing the infection of healthy cells (Idoko & Chinedu, 2025; Nature, 2024). Its unique mechanism of action, combined with an exceptionally long half-life, allows administration only twice a year through subcutaneous injection. This makes lenacapavir the first medication of its kind to offer long-term protection without the need for daily dosing, addressing one of the main barriers to the success of traditional PrEP: treatment adherence (Bekker et al., 2024; Kelley et al., 2024). Large-scale international studies funded by Gilead Sciences and published in *The New England Journal of Medicine* have demonstrated 100% efficacy in preventing new infections among cisgender women in sub-Saharan Africa and among men and gender-diverse individuals in the Americas and Europe (Bekker et al., 2024; Kelley et al., 2024; Cairns, 2024). These findings were reinforced by several international organizations and research institutions, which described lenacapavir as a "remarkable scientific breakthrough" and a "game-changing drug" in the fight against HIV (Nature

Biotechnology, 2024; AVAC, 2025; amfAR, 2025). *Nature Biotechnology* reported that lenacapavir provided "complete protection in every exposure case," while *The International AIDS Society* presented additional data at the HIVR4P 2024 conference confirming its safety, high tolerability, and absence of serious adverse effects (IAS, 2024). Pharmaceutically, lenacapavir is the product of over a decade of research by Gilead Sciences to develop a stable and injectable subcutaneous formulation (Pao, 2025). The FDA approved it under the trade name *Yeztugo* as "the first and only approved option providing six months of protection with a single injection" (Gilead Sciences, 2025; Reuters, 2025; Healthline, 2025). This positions this treatment alongside vaccines in terms of long-term preventive effect, although pharmacologically it is not a classic vaccine but rather an extended antiretroviral prophylaxis. At this stage, lenacapavir is viewed as a bridge between pharmaceutical science and public health, combining clinical efficacy with social practicality. As *UNAIDS* (2025) emphasizes, the success of this drug will depend not only on its biological strength but also on how the global community ensures equitable access, affordability, and integration into national HIV prevention programs.

Global importance, equitable access, and post-approval challenges of Lenacapavir

The FDA approval of lenacapavir in June 2025 marked a historic turning point in global HIV prevention efforts, while also opening a broad debate on equitable access, affordability, and worldwide implementation. According to the World Health Organization (WHO, 2025), this development represents "an important step toward the most effective and practical tool for HIV prophylaxis available today." However, the real benefit of this medication will depend on how effectively it is distributed in low- and middle-income countries, where most new HIV infections occur. UNAIDS has emphasized that structural inequalities within health systems could hinder the efficient distribution of lenacapavir, particularly in sub-Saharan Africa and Southeast Asia, which together account for approximately 60% of new HIV cases each year (UNAIDS, 2025a).

Although Gilead Sciences has signed voluntary licensing agreements with six generic manufacturers to allow production of the drug in low-income markets (UNAIDS, 2024; Sneha, 2024), the current U.S. market price remains high, reaching levels that, according to NPR News (Lambert, 2025), could become a major barrier to widespread access. Meanwhile, independent analyses such as that performed by *The Guardian* (Lay, 2024) suggest that the annual production cost may be as low as USD $40 per patient, highlighting the stark contrast between actual and commercial pricing for the drug. Organizations such as United, AVAC, and amfAR have called for urgent action to ensure that lenacapavir does not

become "a pharmaceutical luxury" but rather a global public health tool (Unitaid, 2025; AVAC, 2025; amfAR, 2025). In their statements, these organizations stress the need for more collaborative models among governments, donors, and the private sector in order to reduce costs, guarantee stable supply, and integrate lenacapavir into existing pre-exposure prophylaxis (PrEP) programs.

At the same time, the approval of lenacapavir has reignited hopes for achieving the UNAIDS 95-95-95 targets by 2030 and for ending the HIV pandemic as a public health threat. Experts at *Health Affairs* (Killelea & Johnson, 2025) describe the launch of this drug as "a perfect storm", a scientific breakthrough arriving at a time when many health systems are facing budget cuts and workforce shortages. For this reason, the central challenge is no longer the development of new drugs, but the creation of equitable conditions for their implementation across all social and economic contexts. Lenacapavir is not merely a pharmaceutical innovation but a testament to what science can achieve when paired with a global vision of health justice. If access, transparency, and pricing policies are managed carefully, this medication could mark the beginning of a new era in HIV prevention, one in which protection from the virus no longer requires daily adherence but only two injections per year, bringing the world closer to a long-awaited goal: the end of the HIV epidemic.

Study Aim

This review aims to provide a comprehensive and evidence-based overview of lenacapavir as one of the major innovations in HIV prevention. It evaluates the effectiveness of long acting lenacapavir through biannual injections and its impact on improving adherence and reducing new infections. The study also addresses global access and implementation challenges, highlighting lenacapavir as an important step toward ending the HIV epidemic by 2030. We hope that this overview goes a step beyond just evaluating the latest scientific evidence that would reflect on the broader social and political impact of this development, while presenting lenacapavir as a real potential to reshape the future of HIV prevention on a global scale.

Methodology

This overview was conducted in the form of a systematic literature review with the main aim of synthetising the most recent data regarding lenacapavir as an innovative drug for the prevention of HIV infection. This method was chosen to integrate clinical results, pharmacological analyses, and perspectives from international health organizations within a unified research framework.

The review process began with the collection of the most relevant scientific and institutional sources published between 2023 and 2025, a period encompassing the most comprehensive clinical trials that peaked with the FDA approval milestone. Information was retrieved from international databases such as PubMed, ScienceDirect, and Google Scholar, as well as from the official websites of the World Health Organization (WHO), UNAIDS, Gilead Sciences, and other relevant organizations involved in the development and evaluation of this medication. Additional sources from reputable international scientific media such as *Reuters*, *The New York Times*, *Healthline*, and *NPR* were also included to provide a broader perspective on the regulatory, economic, and social aspects of this advancement.

Clear inclusion criteria guided the selection of materials for this review: only official studies and documents addressing lenacapavir as a pre-exposure prophylaxis (PrEP) drug were included, with explicit data on its efficacy, mechanism of action, and public health impact. Non-scientific sources, opinion pieces, and publications lacking verifiable references were excluded.

Our assessment was performed qualitatively, focusing on three main dimensions: a) scientific and clinical aspects, encompassing findings from trials published in *The New England Journal of Medicine* and *Nature, b) i*nstitutional aspects, reflecting the positions and policies of international organizations such as WHO and UNAIDS, c) ethical and socio-economic aspects, related to access, affordability, and the global distribution of lenacapavir.

All collected data were synthesized to construct a balanced and well-reasoned overview of the importance of this drug within the broader context of global efforts to halt HIV transmission.

Study limitations

However, our review acknowledges several methodological limitations most of those related to certain known facts such as lenacapavir being a new drug only recently approved; and long-term data on its efficacy and real-world impact across different populations remaining limited. Likewise, information on pricing, licensing policies, and implementation in low-income countries is still emerging and incomplete. Despite these limitations, we believe that the applied methodology provides a reliable and comprehensive assessment of the current literature, offering a solid scientific foundation for understanding the potential of lenacapavir as a new pharmacological drug (also considered as a "vaccine") against HIV, and as a realistic opportunity to transform HIV prevention on a global scale.

Results and discussion

The development and clinical testing of lenacapavir have marked a historic shift in the way HIV prevention is conceptualized. After more than four decades of intensive research, this medication has become the first to provide long-term protection through only two injections per year, bringing the scientific community significantly closer to the goal of ending new HIV infections at a global stage.

Scientific and clinical results of Lenacapavir

Two large-scale clinical trials, published in *The New England Journal of Medicine* in 2024, form the scientific basis for the U.S. Food and Drug Administration's (FDA) decision to approve lenacapavir in June 2025. The study by Bekker et al. (2024), conducted across nine sub-Saharan African countries, involved more than 5,300 cisgender women at high risk of HIV infection. Participants were divided into two groups: one received lenacapavir injections every six months, while the other used daily oral F/TAF (tenofovir alafenamide/emtricitabine).

The results were striking, as no new HIV infections were recorded among participants receiving lenacapavir during 48 weeks of follow-up, as compared to several cases occurring in the F/TAF group. The authors described this level of protection as "unprecedented in the history of pre-exposure prophylaxis," demonstrating that a single injection could provide complete six-month protection. Similarly, the study by Kelley et al. (2024) analysed the effects of lenacapavir among men and gender-diverse individuals in the Americas and Europe. The results were equally compelling: no HIV infections were observed among participants who received injections, while a small number of cases appeared in the control group using traditional PrEP. Beyond its efficacy, the study reported a favourable safety profile, with adverse effects that were mostly mild and transient (such as localized redness or injection-site pain), resolving within a few days without serious consequences. These clinical successes were echoed by international scientific publications. *Nature* (2024) described the findings as "a remarkable demonstration of complete protection against HIV," while *Nature Biotechnology* (2024) called lenacapavir "the first drug to offer almost a 100% protection in a large-scale human trial." Such results are unprecedented in the history of preventive medicine for HIV and have sparked wide enthusiasm across the scientific community, which now views lenacapavir as "the turning point toward the end of the epidemic."

Pharmacologically, lenacapavir possesses a unique mechanism of action that distinguishes it from all existing PrEP drugs. It acts as a capsid inhibitor, targeting the protein structure that protects the HIV genetic material and plays a vital role

in viral replication. Lenacapavir interferes at several critical stages of the viral life cycle: it blocks the transport of viral DNA into the nucleus, slows the assembly of new virions, and destabilizes the capsid, ultimately rendering the virus incapable of infecting CD4+ cells (Idoko & Chinedu, 2025). This multi-phase activity explains lenacapavir's exceptionally long half-life, allowing for administration of only two doses per year. Data presented by the International AIDS Society (IAS) at the HIVR4P 2024 conference reinforced these findings, confirming that lenacapavir's protection remains durable through the first full year of its use (IAS, 2024). Moreover, the studies demonstrated consistent effectiveness across different geographic and demographic populations, with no significant variation in efficacy by age, gender, or social status. Another critical aspect is lenacapavir's potential to improve adherence to preventive treatment. Unlike daily oral pills, which require constant discipline and memory, the twice-yearly injection minimizes the risk of treatment interruption while offer a reduction to the stigma often associated with HIV medication use. As Bekker et al. (2024) emphasize, "the simplicity of administration makes lenacapavir an ideal alternative for populations where adherence remains a major challenge."

Taken together, the clinical and scientific results position lenacapavir as the most effective, safe, and practical medication currently available for HIV prevention. What began as an experimental concept has now evolved into a clinical reality offering complete protection, significantly reducing the need for frequent medical intervention, and fundamentally transforming the way the world approaches pre-exposure prophylaxis. With full efficacy, high safety, and broad applicability, lenacapavir represents a decisive milestone in the history of the fight against HIV, bringing the global community closer to a once seemingly unattainable goal: the end of the HIV pandemic.

Advantages of Lenacapavir compared to traditional PrEP

For more than a decade, pre-exposure prophylaxis (PrEP) has been one of the most effective tools for preventing HIV. Traditional regimens such as tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) and tenofovir alafenamide/emtricitabine (F/TAF) have saved millions of lives and played a key role in reducing new cases. However, despite their success, these drugs require daily use and sustained commitment, which has often resulted in poor adherence, especially among higher-risk populations (Bekker et al., 2024; Kelley et al., 2024). In this context, lenacapavir offers a marked advance across several domains: efficacy, durability, safety, and ease of use. As an injection administered only twice a year, it addresses the primary limitation of traditional PrEP, namely the need for daily dosing.

Recent studies show that one of the major barriers to the real-world effectiveness of oral PrEP is missed or discontinued doses, which substantially reduces

protection against HIV (Nature, 2024; AVAC, 2025). By contrast, lenacapavir provides continuous six-month protection with a single subcutaneous injection, making prevention practical and suitable for a wide range of users. Another important advantage relates to its pharmacological mechanism. Unlike oral PrEP, which targets HIV reverse transcriptase, lenacapavir is a capsid inhibitor that acts at multiple stages of the viral life cycle. This multiplies the protective effect and lowers the likelihood of resistance development, since the virus is no longer adapting to a single target (Idoko & Chinedu, 2025).

In practice, this means lenacapavir can provide broader and more durable protection, including in cases of repeated exposure or high viral burden. Lenacapavir is also promising from psychological and social standpoints. Daily pills are often associated with stigma, as some individuals perceive them as a marker of HIV infection. A twice-yearly injection reduces this social barrier and offers a discreet alternative that can significantly increase uptake. As UNAIDS notes (2025), "lenacapavir can transform not only the science of prevention but also public perception of it." Medically, lenacapavir has shown excellent tolerability across study groups. Adverse events were mild and transient, and no participants discontinued treatment for health-related reasons (Bekker et al., 2024; IAS, 2024). Compared with traditional PrEP, which can cause gastrointestinal issues or small effects on renal and bone function after long-term use, lenacapavir did not show such negative impacts. Flexibility in delivery is another strength of this new treatment. Because lenacapavir is administered every six months, it can be integrated more easily into health programs, especially in areas with limited access to clinics and pharmacies. This makes it well suited to settings with weaker health infrastructure, where adherence to daily regimens is difficult. Beyond biological efficacy, the social and economic benefits are also substantial. Fewer clinic visits reduce resource demands, time, and costs for patients and institutions. An analysis in *Health Affairs* (Killelea & Johnson, 2025) notes that shifting from daily oral regimens to twice-yearly injections could meaningfully lessen clinic workload and simplify management of national HIV programs.

The advantages of lenacapavir over traditional PrEP are multiple and significant. It combines maximal efficacy with practicality, removing barriers linked to memory and stigma, ensures long-lasting protection, and offering a strong safety profile. For these reasons, many researchers view lenacapavir not merely as the next step in PrEP, but as a genuine shift in HIV prevention that could lead to a gradual decline in new infections over the coming decades.

Global access, policy, and economic issues

The FDA's approval of lenacapavir in June 2025 was hailed as a "historic moment" in the fight against HIV. Immediately afterward, a broad debate emerged around its access, affordability, and health equity. While the scientific community

welcomed reports of a extremely high efficacy, international organizations such as UNAIDS, WHO, United, and amfAR stressed that the real impact would not be measured by U.S. approval stance alone, but by how the drug will be financed and distributed globally. According to the World Health Organization (WHO, 2025), lenacapavir represents an unprecedented opportunity to accelerate progress toward the global 95-95-95 targets by 2030, but "scientific progress must move in parallel with progress in its access." WHO highlighted that many low-income countries, where more than 60% of new HIV cases occur, face structural constraints, including insufficient funding, limited distribution infrastructure, and a lack of trained health workers to deliver long-acting injections. UNAIDS has been among the strongest voices calling for price reductions and expanded generic production to avoid repeating inequities seen with early antiretrovirals. In its statement of 18 June 2025, the organization emphasized that: "We cannot allow lenacapavir to become a luxury for wealthy countries; it must be a global tool for protection and health justice" (UNAIDS, 2025b). Only a few months earlier, in October 2024, Gilead Sciences had signed voluntary licensing agreements with six generic manufacturers to enable production in low-income countries (UNAIDS, 2024; Sneha, 2024). These agreements were welcomed as a positive step, though nongovernmental organizations cautioned that generic production and distribution could take several years without strong financial support from global partners. Cost is a central challenge. While Gilead has not published an official international price, reporting from NPR News (Lambert, 2025) indicates treatment costs in the United States amount to several thousands of US dollars per person per year, making it unattainable for most developing countries. By contrast, an analysis in *The Guardian* (Lay, 2024) estimates production costs of this drug at roughly USD $40 per patient per year, exposing a large gap between potential and commercial prices. This gap underscores the need for international pricing policies and subsidies. Unitaid and AVAC have also noted that the challenge is not only financial, but logistical and political. Equitable distribution requires collaboration among governments, humanitarian organizations, and the pharmaceutical industry. In a joint statement on 18 June 2025, they called for "urgent action to secure supply, price transparency, and the immediate inclusion of African countries in pilot programs for lenacapavir" (Unitaid, 2025; AVAC, 2025). Gilead Sciences remains central to debates over patent management and distribution. While the company presents lenacapavir (now marketed as Yeztugo) as "the first and only FDA-approved option providing six months of protection with a single injection" (Gilead Sciences, 2025), many experts warn that a de facto monopoly could slow broad access unless licenses are shared widely. At the macroeconomic level, it seems that the benefits extend beyond public health. Preventing new infections is far less costly than lifelong HIV treatment. *Health Affairs* (Killelea & Johnson, 2025) estimates that every dollar invested in prevention

can save up to five dollars in future treatment costs. Investment in lenacapavir is therefore not only a medical decision but also a sustainable economic strategy. Lenacapavir is more than just a pharmaceutical advance in this case. There is well evidenced now that health equity and scientific progress must move together. The challenge now lies not in the drug's effectiveness, but in making this advance accessible to all. If access, licensing, and financing are managed with transparency and accountability, lenacapavir can bridge the gap between scientific promise and global health realities, bringing the world closer to ending the HIV pandemic.

Ethical implications, challenges, and future perspectives

The approval of lenacapavir as a new long-acting form of pre-exposure prophylaxis raises a set of ethical, social, and political questions that extend beyond the laboratory and clinical statistics. The drug represents a major step toward ending the HIV epidemic, but its global success will depend on how the international community addresses core issues such as equitable access, pharmaceutical transparency, stigma, and the ethical responsibilities of patent-holding companies.

A central concern here is justice in terms of distribution of health innovations. As UNAIDS (2025) notes, the history of HIV shows that life-saving drugs have often reached wealthy countries first, while populations across low-income settings waited years to gain access. This precedent is a clear warning: if lenacapavir remains out of reach for the people who need it most, scientific progress loses its human dimension. An international ethical commitment is therefore required to treat this powerful medication as a global public good rather than a commercial luxury. The drug's pricing and patenting raise further ethical questions. Although Gilead has received FDA approval and signed voluntary agreements with generic manufacturers, organizations including Unitaid and amfAR have urged the company to reduce prices substantially to avoid systemic inequities (Unitaid, 2025; amfAR, 2025). Beyond legal considerations, there is a moral dimension: if a drug capable of preventing millions of infections remains inaccessible because of cost, public health becomes a privilege rather than a universal right. Social factors also matter. Stigma and misinformation continue to hinder any new prevention strategy in this area of work. As WHO (2025) and AVAC (2025) emphasize, integrating lenacapavir into national programs requires not only training for health workers, but also public education to counter the perception that use of the drug implies high sexual risk or HIV-positive status. Without this, stigma could limit uptake even where the medication is available. Another practical and ethical challenge is its implementation among vulnerable communities. In some countries, access to HIV care is constrained by gender discrimination, cultural prejudice, and a lack of privacy in health services. Because lenacapavir is administered every six months and is discreet by nature, it may help overcome some barriers, but only

if distribution programs are designed with cultural sensitivity and respect for patient rights. However, looking ahead, the prospects are highly promising. Many experts view lenacapavir as the start of a new era of pharmacological prophylaxis, in which prevention could last months or even years. Some researchers are already exploring combinations of lenacapavir with other slow-acting molecules to develop even longer-acting regimens or new formulations such as subcutaneous implants (Pao, 2025; Nature, 2024). Unitaid (2025) similarly argues that innovations like lenacapavir should serve as models for building a robust infrastructure for the distribution of long-acting medicines, not only against HIV but also for other infectious and chronic diseases. Investment in logistics, cold-chain storage where needed, and follow-up systems will be essential to long-term success. The ethical and social implications of lenacapavir are as important as its clinical efficacy. This drug should be seen not only as a biotechnology achievement, but as a test of our collective global responsibility to ensure that the benefits of science are shared fairly. If the world implements lenacapavir with equity, transparency, and respect for human dignity, this innovation will be remembered not only as "the drug that stopped HIV," but also as a leading example of science and ethics working together in the service of humanity.

The global impact of Lenacapavir on HIV prevention strategies

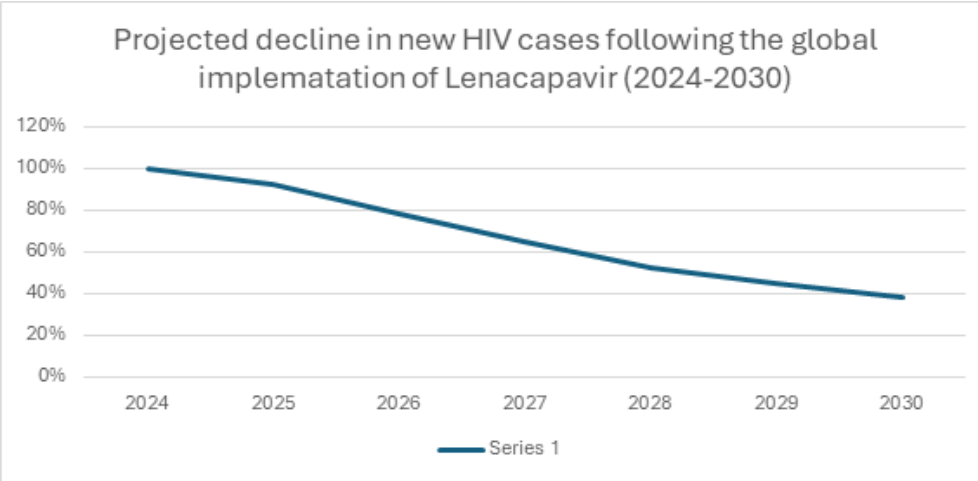
Since the onset of the HIV pandemic in the early 1980s, medical science has made remarkable advances in treatment and management. Yet, the global fight against new infections has remained an ongoing challenge. The development of lenacapavir represents a historic breakthrough, as it is the first pharmacological agent to combine near-complete efficacy, extended duration, and excellent safety in a single, user-friendly preventive option. According to *Bekker et al.* (2024) and *Kelley et al.* (2024), biannual lenacapavir injections would provide complete protection against new HIV infections, clearly surpassing the effectiveness of traditional oral therapies such as F/TDF and F/TAF. This achievement marks a fundamental shift in the paradigm of pre-exposure prophylaxis (PrEP). Until now, the success of oral PrEP has often been limited by poor adherence, treatment fatigue, and social stigma associated with daily pill use. Lenacapavir, administered only twice a year, removes these practical and psychological barriers, making prevention easier, more discreet, and more acceptable for millions of people at risk. This approach can transform how HIV prevention is conceptualized—moving away from individual responsibility and toward a community-based, system-driven model of prevention (WHO, 2025).

From an epidemiological perspective, integrating lenacapavir into national prevention programs is projected to have a dramatic effect on reducing new HIV cases. Modelling data published by *UNAIDS* (2025a) suggest that universal implementation of this drug could reduce global HIV incidence by 60–70% by

2030. In regions such as Sub-Saharan Africa, where young women account for over half of new infections, biannual lenacapavir injections could revolutionize protection strategies. *Bekker et al.* (2024) found that including lenacapavir in community-based reproductive health programs significantly increased adherence and acceptance as compared with traditional oral PrEP. In low-income countries with limited healthcare infrastructure, this medication may serve as the simplest logistical solution for a broader population coverage. By eliminating the need for daily pill distribution and constant monitoring, lenacapavir allows public health systems to focus on periodic clinical follow-up, improving efficiency and access (Unitaid, 2025).

Clinically, lenacapavir is the first HIV capsid inhibitor, with a unique mechanism of action that renders the virus unable to replicate at multiple stages of its life cycle. The *PURPOSE-1* trial confirmed that plasma concentrations of lenacapavir remain above protective levels for over 180 days without the need for re-administration (Bekker et al., 2024). Likewise, *PURPOSE-2* validated the same level of protection in men and gender-diverse individuals (Kelley et al., 2024). This extended pharmacokinetic profile provides a major advantage by reducing patients' daily medication burden. Comparisons with other long-acting agents, such as cabotegravir, show that lenacapavir has lower hepatic and renal toxicity and a more consistent bioavailability profile (Jogiraju et al., 2025). Meta-analyses published in *Nature Biotechnology* (2024) and *The Lancet HIV* (Lynch et al., 2025) found a risk ratio (RR) for new infections close to 0.00, with a confidence interval (CI) of 0.00–0.05, indicating near-absolute efficacy. These results position lenacapavir as the most powerful HIV preventive intervention ever developed.

FIG 1. Projected decline in new HIV cases following the global implementation of Lenacapavir (2024- 2030)



Beyond its biological outcomes, lenacapavir carries profound implications for health equity and social justice. Although the drug's initial cost remains high, *UNAIDS* (2025b) and *Unitaid* (2025) report that Gilead has signed voluntary licensing agreements with six generic manufacturers that will make lenacapavir affordable in low-income countries. This initiative could reshape the global landscape of HIV prevention, transforming it from a privilege of wealthy nations into a universal human right. According to the *World Health Organization* (2025), equitable access to lenacapavir is essential for meeting the global target of eliminating HIV as a public health threat by 2030. Economic modelling from *Health Affairs* (Killelea & Johnson, 2025) estimated that widespread lenacapavir use could save up to $5 billion in the next decade by reducing long-term HIV treatment costs. Thus, investing in this medication is not only scientifically justified but also strategically sound and ethically imperative.

An often-overlooked component of HIV prevention is the psychological and cultural dimension. Daily pill use has long been linked to stigma and negative perceptions, especially in communities where HIV remains taboo. Lenacapavir, being discreet and infrequent, can substantially reduce social stigma and enhance the cultural acceptability of preventive treatment. Qualitative studies from *amfAR* (2025) and *AVAC* (2025) show that many participants perceive lenacapavir as "a way to take control without judgment," framing it not as medical treatment but as an act of self-care. This shift in perception may have lasting effects on how societies view HIV and motivate new generations to participate in prevention programs. In summary, lenacapavir's global impact is projected to be multidimensional. Scientifically, it represents a clinical and pharmacological milestone that has redefined HIV prevention; socially and ethically, it stands as a tool for equality and empowerment.

If broadly adopted in public health policies, lenacapavir could serve as the foundation of a new era in HIV prevention, an era where prevention no longer depends on daily effort but on the efficiency of science and collective commitment. This drug is more than a laboratory success; it is a tangible promise for a world without HIV, where technology, ethics, and solidarity unite to end a pandemic that has affected over 85 million people in the past four decades.

Conclusions

The comprehensive body of evidence collected from peer-reviewed scientific literature and global health organizations unmistakably demonstrates that lenacapavir represents one of the most groundbreaking achievements in HIV prevention of the past decade. Unlike earlier prophylactic approaches that relied heavily on daily oral regimens, lenacapavir introduces a new era of long-acting,

biannual HIV prevention that promises both medical and social transformation. Clinical trials published in The New England Journal of Medicine and statements from the World Health Organization (WHO), UNAIDS, and Unitaid confirm that lenacapavir has achieved the highest possible (almost 100%) efficacy in preventing new HIV infections, with an outstanding safety profile and excellent tolerability across diverse populations.

From a biomedical standpoint, lenacapavir fundamentally redefines the concept of pre-exposure prophylaxis (PrEP). As a capsid inhibitor, it targets multiple stages of the viral life cycle entry, replication, and assembly, thereby interrupting HIV propagation in a way that is more comprehensive, stable, and resilient than previous antiretroviral agents. The pharmacokinetic stability of a single subcutaneous injection every six months enhances patient adherence, eliminates the daily burden of pill-taking, and significantly reduces stigma associated with HIV medication use, particularly in vulnerable populations and high-prevalence settings.

Socially and politically, lenacapavir embodies a paradigm of health equity and innovation. Its success is not only a clinical milestone but also a test of the world's commitment to the 95-95-95 global targets set by UNAIDS, which aim to end the HIV epidemic by 2030. However, this amazing potential and progress is threatened by structural barriers, most notably the economic divide between high- and low-income regions. Without affordable pricing, transparent licensing, and coordinated global distribution, lenacapavir risks becoming another example of medical innovation reserved for the privileged few.

Ethically, lenacapavir stands as a measure of collective global conscience, a reminder that scientific breakthroughs must serve humanity, not just its wealthiest parts. Ensuring equitable access, price reductions, and open licensing agreements will determine whether this discovery becomes merely a scientific triumph or a genuine human victory. In conclusion, this overview emphasizes several key points:

1. Lenacapavir is the most advanced and effective HIV prevention drug developed to date, capable of reshaping global health strategies.
2. Its long-acting nature brings profound benefits beyond virological protection, enhancing quality of life, adherence, and dignity for users.
3. The greatest challenge ahead lies in achieving equitable global access and sustainable affordability, to prevent repeating the historic injustices that once limited access to life-saving HIV treatments.

Ultimately, lenacapavir represents not just a scientific innovation, but a moral and public health imperative, and a chance for the global community to prove that progress in science can be matched by progress in justice.

References

1. Bekker et al. (2024). Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. N Engl J Med. 2024 Oct 3;391(13):1179-1192. doi: 10.1056/NEJMoa2407001. Epub 2024 Jul 24. PMID: 39046157.
2. Kelley CF, Acevedo-Quiñones M, Agwu AL, et al. (2025). Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons. N Engl J Med. 2025 Apr 3;392(13):1261-1276. doi: 10.1056/NEJMoa2411858
3. World Health Organization (WHO) (2025). FDA approval of injectable lenacapavir marks progress for HIV prevention. (cited 2025 Jun 25). Available from: https://www.who.int/news/item/19-06-2025-fda-approval-of-injectable-lenacapavir-marks-progress-for-hiv-prevention
4. UNAIDS. Accelerating access to long-acting HIV prevention: the case of lenacapavir [Internet]. [cited 2025 Jun 25]. Available from: https://www.unaids.org/en/speeches/2025/20250516_WHA-statement_lenacapavir_en.pdf
5. UNAIDS. UNAIDS response to Gilead's announcement on signing voluntary licensing agreements on lenacapavir with six generic manufacturers [Internet]. [cited 2025 Jun 25]. Available from: https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2024/october/20241002_gilead-lenacapavir
6. UNAIDS. UNAIDS urges Gilead to drop price of new HIV prevention shot (2025) [cited 2025 Jun 25]. Available from: https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2025/june/20250618_lenacapavir
7. Gilead Sciences. Yeztugo (lenacapavir) is now the first and only FDA-approved HIV prevention option offering 6 months of protection [press release]. [cited 2025 Jun 25]. Available from: https://www.gilead.com/news/news-details/2025/yeztugo-lenacapavir-is-now-the-first-and-only-fda-approved-hiv-prevention-option-offering-6-months-of-protection
8. Unitaid. Unitaid welcomes U.S. FDA approval of lenacapavir and calls for urgent action on affordability and access [press release]. [cited 2025 Jun 25]. Available from: https://unitaid.org/news-blog/unitaid-welcomes-u-s-fda-approval-of-lenacapavir-and-calls-for-urgent-action-on-affordability-and-access
9. amfAR. Statement from amfAR on FDA approval of lenacapavir for HIV pre-exposure prophylaxis [Internet]. 2025 Jun 18 [cited 2025 Jun 25]. Available from: https://www.amfar.org/press-releases/statement-from-amfar-on-fda-approval-of-lenacapavir-for-hiv-pre-exposure-prophylaxis
10. AVAC. FDA approves injectable lenacapavir for PrEP: A historic milestone must now be matched by urgent action [press release]. 2025 Jun 18 [cited 2025 Jun 25]. Available from: https://avac.org/press-release/fda-approves-injectable-lenacapavir-for-prep
11. International AIDS Society. New data on twice-yearly lenacapavir for HIV prevention announced at HIVR4P 2024 [press release]. 2024 Oct 7 [cited 2025 Jun 25]. Available from: https://www.iasociety.org/news-release/new-data-twice-yearly-lenacapavir-hiv-prevention-announced-hivr4p-2024
12. Beasley D, Steenhuysen J. US FDA approves Gilead's twice-yearly injection for HIV prevention. *Reuters* [Internet]. 2025 Jun 18 [cited 2025 Jun 25]. Available from: https://www.reuters.com/business/healthcare-pharmaceuticals/us-fda-approves-gileads-twice-yearly-injection-hiv-prevention-2025-06-18/

13. Neergaard L. The world's only twice-a-year shot to prevent HIV could stop transmission — if people can get it. *Associated Press* [Internet]. 2025 Jun 18 [cited 2025 Jun 25]. Available from: https://apnews.com/article/hiv-prevention-shot-lenacapavir-gilead-80fb37e2c5ac9b452488d7b86a10d568
14. Mandavilli A. Regulators approve a twice-yearly shot to prevent H.I.V. infection. *New York Times* [Internet]. 2025 Jun 18 [cited 2025 Jun 25]. Available from: https://www.nytimes.com/2025/06/18/health/hiv-lenacapavir-fda.html
15. Rice A. FDA approves "breakthrough" twice-yearly injection to prevent HIV. *Healthline* [Internet]. 2025 Jun 23 [cited 2025 Jun 25]. Available from: https://www.healthline.com/health-news/fda-approves-twice-yearly-injection-hiv-prevention
16. Pao W. The decades-long journey to Gilead's twice-a-year HIV prevention drug lenacapavir. *STAT News* [Internet]. 2025 Jun 23 [cited 2025 Jun 25]. Available from: https://www.statnews.com/2025/06/23/fda-approval-lenacapavir-yeztugo-gilead-history-development-breakthrough-william-pao/
17. Nature. Stunning trial shows twice-yearly shots can prevent HIV infection. *Nature*. 2024;632(233). Available from: https://doi.org/10.1038/d41586-024-02493-4
18. Nature Biotechnology. HIV drug 100% protective. *Nat Biotechnol*. 2024;42(8):1164. Available from: https://doi.org/10.1038/s41587-024-02369-y
19. Killelea A, Johnson J. A perfect storm: "Gamechanger" HIV prevention medicine launches in the midst of health system and public health cuts. *Health Affairs* [Internet]. 2025 Jun 17 [cited 2025 Jun 25]. Available from: https://www.healthaffairs.org/content/forefront/perfect-storm-gamechanger-hiv-prevention-medicine-launches-midst-health-system-and
20. Lambert J. FDA approves HIV medication lenacapavir, but it's costly. *NPR News* [Internet]. 2025 Jun 24 [cited 2025 Jun 25]. Available from: https://www.wvia.org/2025-06-24/fda-approves-hiv-medication-lenacapavir-but-its-costly?utm_source=chatgpt.com
21. Sneha SK. Gilead signs deal with 6 generic drugmakers to sell HIV drug in low-income countries. *Reuters*. 2024 Oct 2 [cited 2025 Jun 25]. Available from: https://www.reuters.com/business/healthcare-pharmaceuticals/gilead-signs-deals-with-6-generic-drugmakers-sell-hiv-drug-low-income-countries-2024-10-02/
22. Cairns G. No HIV infections seen in groundbreaking trial of twice-yearly injectable PrEP. *aidsmap*. 2024 Jun 22 [cited 2025 Jun 25]. Available from: https://www.aidsmap.com/news/jun-2024/no-hiv-infections-seen-groundbreaking-trial-twice-yearly-injectable-prep
23. Idoko, J., & Chinedu, E. (2025). *Long- acting lenacapavir is a breakthrough for preventing HIV infection, but HIV vaccine research must continue. Frontiers in Medicine, 19*(3), 543–547. https://doi.org/10.1007/s11684-025-1137-3