

# Injectable Cabotegravir: A Breakthrough in HIV PrEP

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## Introduction

A pivotal clinical trial demonstrated that injectable cabotegravir is remarkably effective for preventing HIV in cisgender men and transgender women. This research marked a substantial step forward, establishing its non-inferiority and even superior efficacy when compared to the daily oral regimen of tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) PrEP, thereby introducing a vital new prevention option for populations at elevated risk of HIV acquisition [1].

Building on this, the HPTN 084 trial focused specifically on assessing the effectiveness and safety of injectable cabotegravir for HIV prevention among women in sub-Saharan Africa. The findings from this study were particularly compelling, showing that injectable cabotegravir was not only highly effective but also superior to daily oral TDF-FTC PrEP. This addresses a crucial unmet need for women who often face unique challenges with consistent daily pill adherence, offering a more manageable prevention strategy [2].

From a global implementation standpoint, a comprehensive review has synthesized existing evidence and proposed future directions for rolling out injectable cabotegravir as PrEP worldwide. This analysis underscored both the promising opportunities presented by this highly effective prevention method and the significant challenges that must be overcome. Key areas include developing necessary infrastructure and ensuring equitable access, as the intervention transitions from controlled clinical trials to widespread real-world application [3].

Understanding the pharmacological profile of cabotegravir is essential for its optimal use. This research delved into the pharmacokinetics of cabotegravir within the HPTN 083 study participants. Gaining insight into how the drug behaves in the body of individuals living with HIV and those at risk is vital for refining dosing strategies and maintaining consistent protective drug levels, which is fundamental to the long-acting characteristic of injectable PrEP [4].

Patient preferences play a significant role in the success of prevention strategies. A study explored the preferences of African women participating in the HPTN 084 trial, comparing injectable PrEP to daily oral PrEP. The results clearly indicated a strong preference for the injectable option. This finding is crucial, suggesting that the injectable's benefits, such as discretion and a reduced daily pill burden, could substantially enhance uptake and adherence in populations where these factors significantly impact PrEP effectiveness [5].

Further insights into user experience come from the HPTN 083 study, which evaluated the acceptability of injectable PrEP among cisgender men and transgender women across diverse global settings, including the United States and Thailand. This study reported high levels of acceptability, indicating that the convenience and less frequent dosing associated with injectable PrEP could lead to improved

adherence and broader coverage. This positions it as a highly desirable option for HIV prevention, potentially overcoming adherence barriers associated with daily oral regimens [6].

Specifically focusing on Sub-Saharan Africa, a systematic review identified key challenges and opportunities for the implementation of long-acting injectable PrEP. The review highlighted the critical need for robust health system infrastructure, sustained community engagement, and targeted strategies to address country-specific barriers. These elements are indispensable to ensure the successful and equitable rollout of this promising prevention method in regions with a high burden of HIV [7].

The economic implications of injectable cabotegravir are also important to consider. An analysis provided a crucial perspective on the cost-effectiveness of long-acting injectable cabotegravir for HIV prevention within the United States. It demonstrated that, despite a higher initial acquisition cost, the injectable option can be cost-effective when compared to daily oral PrEP. This is primarily attributed to improved adherence rates and the significant reduction in averted HIV infections, ultimately delivering substantial long-term public health benefits [8].

The preparedness of future healthcare providers is also being evaluated. A study assessed the awareness and willingness to use injectable HIV PrEP among U.S. medical students. The findings showed a moderate level of existing awareness but a notably high willingness to both use and prescribe injectable PrEP once they received appropriate education. This strongly suggests that integrating information about new prevention modalities into medical education is paramount for ensuring future healthcare providers can effectively offer this advanced prevention option to their patients [9].

Finally, extended follow-up data from both the HPTN 083 and HPTN 084 trials have been presented, confirming the sustained long-term efficacy and safety of injectable cabotegravir for HIV prevention. This data strengthens the initial findings, providing more robust evidence for the enduring protection and the overall favorable risk-benefit profile of this innovative PrEP option over an extended period, solidifying its place as a reliable prevention strategy [10].

## Description

Injectable cabotegravir represents a major advancement in HIV prevention, offering a highly effective long-acting option. Initial studies, such as the pivotal trial for cisgender men and transgender women, revealed its superior efficacy compared to daily oral tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) PrEP, providing a much-needed alternative for at-risk groups [1]. Extending this, the HPTN 084 trial specifically demonstrated the compelling efficacy and safety of injectable

cabotegravir for women in sub-Saharan Africa. This was a critical development, as it showed superiority over daily oral PrEP and addressed significant adherence challenges often faced by women in these regions [2]. Long-term follow-up data from both HPTN 083 and HPTN 084 further confirm the sustained efficacy and safety of injectable cabotegravir, reinforcing its durability and positive risk-benefit profile over time as a robust prevention strategy [10].

For effective implementation, understanding how the drug behaves in the body is crucial. Research into the pharmacokinetics of cabotegravir within the HPTN 083 study population provides essential insights, helping optimize dosing strategies to ensure consistent protective levels, which is key to its long-acting nature [4]. Beyond the biological aspects, user acceptance plays a vital role in real-world effectiveness. Studies explored preferences for injectable versus daily oral PrEP among African women in the HPTN 084 trial, revealing a strong preference for the injectable option. This highlights its potential to increase uptake and adherence due to factors like discretion and reduced daily pill burden [5]. Similarly, high levels of acceptability of injectable PrEP were observed among cisgender men and transgender women in the HPTN 083 study across diverse settings, suggesting that its convenience and less frequent dosing could significantly improve adherence and coverage [6].

The global rollout of injectable cabotegravir for PrEP involves both significant opportunities and considerable challenges. A comprehensive review synthesizes existing evidence to outline future directions for implementation, pointing to critical needs like robust infrastructure and equitable access as the method moves beyond clinical trials [3]. This is particularly relevant in high-burden regions like Sub-Saharan Africa, where a systematic review identifies crucial challenges and opportunities. It emphasizes the necessity for strong health system infrastructure, active community engagement, and addressing specific country-level barriers to ensure a successful and fair implementation of this promising prevention tool [7].

Economically, injectable cabotegravir presents a compelling case for public health. An analysis in the United States showed that despite its higher acquisition cost, the injectable option can be cost-effective compared to daily oral PrEP. This is primarily due to improved adherence and the resulting prevention of HIV infections, yielding significant long-term public health benefits [8]. Furthermore, the preparedness of the healthcare workforce is an important consideration for widespread adoption. A study among U.S. medical students revealed moderate awareness but a high willingness to use and prescribe injectable PrEP once they receive proper education. This underscores the importance of integrating information about new HIV prevention modalities into medical education to equip future providers to effectively offer this option [9].

In essence, injectable cabotegravir represents a paradigm shift in HIV prevention, offering a highly effective, long-acting method that addresses adherence challenges and meets user preferences across various demographics. While its efficacy and safety are well-established, successful global implementation will require strategic planning to overcome logistical, infrastructural, and equitable access barriers. Its demonstrated cost-effectiveness and growing acceptance among future healthcare providers signify its potential to significantly impact the global fight against HIV.

## Conclusion

Injectable cabotegravir represents a significant breakthrough in HIV prevention, proving highly effective across diverse populations. Studies like HPTN 083 demonstrated its superior efficacy in cisgender men and transgender women compared to daily oral tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) PrEP, offering a crucial alternative for at-risk groups. The HPTN 084 trial further cemented its

value, showing compelling results for women in sub-Saharan Africa, where it outperformed oral PrEP and addressed challenges with daily pill adherence. Understanding the drug's behavior is key. Pharmacokinetic studies on cabotegravir in populations at risk for HIV help optimize dosing, ensuring consistent protective levels for its long-acting nature. Beyond efficacy, patient preferences and acceptability are critical for successful implementation. Research among African women in HPTN 084 revealed a strong preference for the injectable option, recognizing its potential to boost uptake due to discretion and reduced daily pill burden. Similarly, high acceptability was observed among cisgender men and transgender women in HPTN 083 across various settings, indicating convenience and less frequent dosing are highly desirable. The practicalities of global rollout are also under review. Reviews highlight both opportunities and challenges, such as infrastructure needs and equitable access, as injectable PrEP moves from trials to real-world use. In Sub-Saharan Africa, a systematic review underscores the necessity for robust health systems and community engagement to overcome country-specific barriers. Economically, injectable cabotegravir presents a compelling case. Despite higher initial costs, it is deemed cost-effective in the United States due to improved adherence and averted HIV infections, leading to substantial long-term public health benefits. Furthermore, healthcare provider awareness is growing, with U.S. medical students showing a high willingness to use and prescribe injectable PrEP after education, pointing to the importance of integrating this new modality into medical training. Crucially, extended follow-up from HPTN 083 and HPTN 084 confirms the sustained long-term efficacy and safety of injectable cabotegravir, reinforcing its durability and positive risk-benefit profile over time.

## Acknowledgement

None.

## Conflict of Interest

None.

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**How to cite this article:** Ito, Naomi. "Injectable Cabotegravir: A Breakthrough in HIV PrEP." *J AIDS Clin Res* 16 (2025):1092.

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**Received:** 01-Dec-2025, Manuscript No. jar-25-177623; **Editor assigned:** 03-Dec-2025, PreQC No. P-177623; **Reviewed:** 17-Dec-2025, QC No. Q-177623; **Revised:** 22-Dec-2025, Manuscript No. R-177623; **Published:** 29-Dec-2025, DOI: 10.37421/2155-6113.2025.16.1092