Expanding access to long-acting HIV therapy in low-income and middle-income countries

The global HIV response stands on the threshold of a defining moment. Scientific breakthroughs have ushered in long-acting antiretroviral therapy (ART), which has redefined how HIV can be managed. Injectable formulations, such as cabotegravir–rilpivirine administered every 2 months, have shown high efficacy, safety, and preference across diverse populations and age groups.[1–4] Encouragingly, independent studies IMPALA (NCT05546242), CARES (Pan African Clinical Trials Registry 202104874490818), and MOCHA (NCT03497676) have shown that long-acting ART is efficacious, acceptable, and highly preferred in African settings.[5]

Promising long-acting ARTs are emerging that include oral and injectable formulations of lenacapavir. A once-weekly oral combination of lenacapavir–islatravir has shown encouraging efficacy, with 94% of participants maintaining viral suppression at 48 weeks. A 2024 US case series of 34 people with adherence challenges and documented resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) found that 94% of participants reached virological suppression when given injectable lenacapavir administered biannually plus cabotegravir every 4 or 8 weeks.[6] Recent data suggest that lenacapavir can be administered annually, and a new investigational long-acting formulation of cabotegravir can be given every 16 weeks. These results underscore the potential of this NNRTI-sparing combination, which eliminates the need for cold-chain storage and supports extended dosing intervals. To establish the broader efficacy and programmatic relevance of lenacapavir–cabotegravir, larger and well-designed clinical trials are urgently warranted.

Despite substantial scientific progress, there is growing concern that low-income and middle-income countries (LMICs)—with populations that include more than two-thirds of people living with HIV—risk being excluded from the benefits of long-acting ART, echoing inequities seen with earlier innovations. Landmark studies conducted within LMIC settings have provided key evidence to support the integration of long-acting ART regimens into global treatment guidelines, laying the groundwork for future innovations. Access to long-acting ART remains non-existant in LMICs, including Africa.[7]

The rationale for prioritising long-acting ART in LMICs is compelling. Daily oral adherence is hindered by stigma, pill fatigue, and several structural barriers. Long-acting ART directly addresses these issues by reducing the frequency of dosing and lowering the visibility of treatment, offering a promising path towards sustained viral suppression, avoidance of HIV-related illness and deaths, reduced HIV transmission, and enhanced overall quality of life.

Despite the evidence available for long-acting ART, issues persist, including limited registration and availability in LMICs, an absence of generic suppliers, cold chain logistics, and health system capacity to support injectable delivery at scale in LMICs.

Addressing these access gaps requires a multipronged strategy. First, the inclusion of long-acting ART in WHO treatment guideline sets a crucial precedent and precede future long-acting HIV regimens, including next-generation injectables. However, such inclusion needs to be accompanied by coordinated investment and interventions to address implementation barriers.[8]

Second, public-health-oriented voluntary licensing approaches could be applied to long-acting ART, enabling generic production and affordability. For example, the July 2025 expansion of the Medicines Patent Pool licence with ViiV Healthcare for cabotegravir allows generic manufacturers to produce long-acting cabotegravir for HIV treatment, creating a path to access in 133 countries.[9] The rapid development of new long-acting regimens will also require collaboration between innovators, funders, researchers, and people with HIV to generate the needed evidence.

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Third, expedited regulatory and registration pathways need to be supported, alongside real-world implementation research that reflects the diverse contexts of LMICs. Cost-effectiveness data will also be essential to support evidence-based policy decisions. Implementation barriers need to be addressed, such as recall mechanisms to support adherence to injection schedules, management of injection site reactions, screening for chronic hepatitis B, and ensuring that

people transitioning to long-acting ART have received hepatitis B vaccination. The acceptability of injectable therapy across diverse populations should also be considered to target people who have the highest need initially.[10] National readiness planning will be key, including infrastructure, workforce training, procurement, and scale-up feasibility.

National governments, donors, and civil society need to also begin deliberate readiness planning by investing in delivery systems, health worker training, pharmacovigilance systems, and community education. Integrating long-acting ART with differentiated service delivery models and ensuring gender-responsive approaches will further drive equitable uptake.

We need to learn from the early ART scale-up era and prioritise equity in the delivery of next-generation HIV care. Without urgent and coordinated action across global health agencies, funders, originator companies, generic manufacturers, access mechanisms (eg, Medicines Patent Pool), policy makers, national governments, implementation partners, and civil society, LMICs might face the inequities of the early ART era. Global health stakeholders need to act now to ensure timely and equitable access to the next frontier of HIV treatment. The global health community needs to act swiftly and cohesively to ensure that long-acting ART does not become an innovation that widens inequities, but instead, becomes a means to close them.

FV receives support from the Gates Foundation, SA Medical Research Council, National Institutes for Health, Unitaid, Foundation for Innovative New Diagnostics, Children's Investment Fund Foundation, United States Agency for International Development, Gilead, ViiV Healthcare, Merck, J&J and Merck; recieves honoraria from Gilead, ViiV Healthcare, Mylan and Viatris, Merck, Adcock-Ingram, Aspen, Abbott, Roche, J&J, Sanofi, Virology Education, and US National Institutes of Health Data Safety and Monitoring Board. FVC receives grants from Wellcome, Janssen, and ViiV Healthcare. CO receives grants, payments, or honoraria from MSD, ViiV Healthcare, Gilead Sciences, and Bavarian Nordic; and is member of the International AIDS Society Governing Council and the WHO Global Preparedness Monitoring Board for mpox. MP and LG are employees of Medicines Patent Pool, which is funded by Unitaid, the Swiss Agency for Development and Cooperation, the French Ministry for Europe and Foreign Affairs, the German Agency for International Cooperation, and the Ministry of Foreign Affairs of Japan. All other authors declare no competing interests.

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