AFROCAB

COMMUNITY FORUM

SUPPORTING AFFORDABLE ACCESS TO LONG-ACTING TECHNOLOGIES; THE FUTURE OF HIV PREVENTION AND TREATMENT

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Double Tree by Hilton Hotel

NAIROBI, KENYA

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1. INTRODUCTION

Afrocab is a network that aims to empower community HIV treatment and prevention access advocates in Africa. Its objectives include building leadership and advocacy capacity and creating a platform for engagement with key stakeholders such as drug manufacturers, normative bodies (e.g., WHO), governments, and others. Afrocab facilitates sharing and learning platforms for people living with HIV (PLHIV) leaders and advocates to promote evidence-based advocacy for greater access to safer, better-tolerated, and more effective drugs in Africa.

In July 2022, ViiV Healthcare and the Medicines Patent Pool (MPP) jointly announced a voluntary license agreement for injectable long-acting cabotegravir (CAB-LA), a long-acting antiretroviral (ARV) medication that is patented and produced by ViiV. This agreement enables selected generic companies that sign the license to manufacture and supply the generic version of CAB-LA. During his opening remarks, Afrocab Executive Director Kenly Sikwese provided context on Afrocab's role in promoting access to CAB-LA, along with the roles of its community and civil society advocacy partners. He highlighted the progress made by Afrocab in advocating for access to CAB-LA as well as some of the ongoing barriers to accessing CAB-LA, including the current manufacturer monopoly (ahead of generic availability), lack of transparency in pricing, ViiV's (likely) limited capacity to meet demand, and slow registration at the national level. He stressed the need to avoid similar delays that occurred with previous drugs and ensure that regulatory approval for generic products does not face unnecessary delays. Sikwese also emphasized the importance of improving access to CAB-LA for both prevention and treatment and discussed the benefits of generic manufacturing, which serves to expand production as well as increase access. He acknowledged that the success achieved to date has resulted from the community's collective voice and that the change in ViiV's position to license CAB-LA after initially refusing to do so was driven by shared commitment and efforts. He reminded participants that the meeting would also discuss another long-acting drug – lenacapavir (LEN), a potentially even more important drug that could be

part of some treatment regimens and is currently being investigated for PrEP as a six-monthly injectable.

2. PRESENTATIONS

Presentations during the meeting underscored the critical role of treatment and prevention advocates in improving drug access and emphasized the importance of continued efforts to expand access. Several presentations and activities were conducted to support these objectives. They included:

- ✓ The role of public health-oriented licensing in improving access to medicines
- ✓ Overview of the CAB-LA license
- ✓ CAB-LA updates and the journey to access: progress to date and critical next steps
- ✓ Updates on LEN, Islatravir (ISL), and other long-acting technologies in development
- ✓ Updates on clinical trials - HPTN 083/084 and other studies
- ✓ Overview of the state of long-acting technologies for HIV prevention and treatment: research and development pipeline of long-acting technologies
- ✓ MPP update on long-acting products, early-stage portfolio, and the LA therapeutics patents and licenses database (www.LAPaL.ch)
- ✓ Country preparedness panel: perspectives from Nigeria and Zimbabwe
- ✓ Merck update on ISL, including the journey to access and critical next steps.
- ✓ Overview of Gilead's HIV clinical development program
- ✓ Generic manufacturing readiness, production capacity, timelines for CAB-LA, LEN, and other long-acting technologies access
- ✓ Long-acting products in the context of pediatric and adolescent populations
- ✓ Community preference and acceptability of long-acting products through the lens of HPTN 083/084
- ✓ Advocacy strategies for long-acting treatment and prevention commodities
- ✓ Myths and misconceptions about long-acting products
- ✓ Community mobilization moments and opportunities: defining community position and priority areas for action
- ✓ Steeple chase activity to understand perspectives and preferences for long-acting products, a survey on long-acting pediatric products.
- ✓ Reflections, group work and next steps in advocacy planning.

3. KEY POINTS FROM PRESENTATIONS

Licenses: The presentation explained how patents work and the role that licensing can play in facilitating the early entry of generic manufacturers in low- and middle-income countries (LMICs) before the patents expire. Without licenses, market entry of generic manufacturers would typically have to wait until patent expiry. Competition from generic manufacturers generally contributes to reducing the prices of products, thereby facilitating affordable access in LMICs and ensuring that enough supply is available in LMICs to meet demand. The presentation also explained how public-health-oriented voluntary licences work, and some of the key features of those negotiated by the MPP, including their transparency and public health focus. It also recognized that licensing is only a first step in facilitating access and that many other important steps are needed to ensure that new medicines reach those who need them, and highlighted the critical role that can be played by communities.

CAB-LA updates and the journey to access: The presentation focused on long-acting cabotegravir (CAB-LA), an ARV currently approved in several countries for both HIV treatment (in combination with rilpivirine) and as a standalone injection for pre-exposure prophylaxis (PrEP). While a cabotegravir/rilpivirine formulation has been approved for treatment in the US, Canada, and several other countries, there are concerns about NNRTI cross-resistance and cold chain requirements of rilpivirine, limiting its use in LMICs. On the prevention side, to ensure access to CAB-LA, ViiV Healthcare needs to take several steps, including registering it widely, announcing its not-for-profit price, and ensuring sufficient manufacturing capacity. Ongoing studies are evaluating its use for adolescents, children, and postnatal prophylaxis for exposed infants. However, the high cost of production and complexity of the manufacturing process poses challenges in making CAB-LA widely available.

In July 2022, ViiV Healthcare and MPP signed a new voluntary licensing agreement for patents relating to CAB-LA for PrEP to help enable affordable access in 90 countries, with the presentation highlighting some of the key features of the agreement. It is expected that this agreement will help to enable at-scale access to generic CAB-LA for PrEP.

In March 2023, MPP signed sublicensing agreements with Aurobindo Pharma, Cipla, and Viatris (Mylan) to manufacture generic versions of CAB-LA for PrEP for supply in 90 countries. While Aurobindo and Viatris will be manufacturing in India, Cipla also has plans to manufacture in South Africa.

This announcement came just seven months after the first regulatory approval of CAB-LA for PrEP in the world, by the US Food and Drug Administration (US FDA). Through this agreement, the selected generic manufacturers now have the opportunity to develop, manufacture and supply generic versions of CAB-LA for PrEP, the first long-acting HIV prevention medicine, in these countries, subject to required regulatory approvals being obtained. It will be critical for ViiV Healthcare and other technical partners to support these companies with technical expertise as the manufacturing process for CAB-LA is complex.

Unitaid, WHO, UNAIDS, the Global Fund and PEPFAR (with AVAC as Secretariat) have established a coalition to accelerate access to this medication. While some progress has been made by these organizations (including PEPFAR purchasing CAB-LA for introduction in 2023 in select countries), nearly 18 months after CAB-LA was first approved by the US FDA, the product has still not reached any users outside of clinical trials. Moreover, critical technical partnerships and incentives that will be needed to accelerate generic development have not been established.

Long-acting technologies for HIV prevention and treatment: This presentation discussed long-acting technologies for HIV prevention and treatment, including currently registered formulations like CAB-LA dosed every two months, cabotegravir with rilpivirine for treatment given via intramuscular injections, and LEN subcutaneous six-monthly for treatment (in combination with a background regimen, for treatment-experienced PLHIV) and a six-monthly injection being investigated for PrEP. Several of the Islatravir (ISL) investigational programs were put on hold in December 2022 due to the observation of significant lymphocyte count drops in participants receiving ISL across the treatment and PrEP programs in which ISL was used. Currently, ISL is no longer being investigated by Merck for use as PrEP. As of the date of this meeting, only two clinical programs have resumed for treatment, and only one of them is investigating a long-acting regimen: a once-weekly oral dosing of ISL together with LEN.

Lenacapavir (LEN) is a potent HIV capsid inhibitor with a long duration of action and a new mechanism of action interfering with virus replication. It is being investigated as

part of combination therapy for treatment and as a monotherapy for HIV prevention. It has been approved for use in 31 countries including the European Union, UK, Canada, and the US, for the treatment of HIV infection, together with a background regimen, in PLHIV who are treatment experienced. It is designed to disrupt HIV at multiple stages of its viral lifecycle and has no known cross-resistance to other existing drug classes. LEN is the only HIV treatment option that allows for the possibility of a twice-yearly administration. In clinical trial settings, LEN was generally well tolerated, with no study drug-related serious adverse events (AEs). The most common AEs observed were injection site reactions (ISRs), which were generally mild or moderate in severity. LEN cannot be used for treatment as a single agent and needs to be administered with companion drugs. No other companion drug with a similar frequency of administration has been approved so far to constitute a full six-monthly regimen for HIV treatment based on LEN. LEN is also being studied as a potential PrEP product, with one key difference from injectable CAB-LA for PrEP, which is that injectable LEN is being studied as a subcutaneous injection, making it potentially eligible for self-injection. Ongoing studies evaluate the use of LEN as an injectable PrEP option administered every six months. LEN is not approved by any regulatory authority outside of the United States, United Kingdom, Canada, or the European Union for any use.

Innovators: **Gilead Sciences and Merck** have a partnership to develop a long-acting treatment regimen for HIV, using Gilead's LEN and Merck's ISL as a once-weekly oral dosing of each of the drugs, to provide a new treatment option for PLHIV. Both Gilead and Merck gave no clear commitments on licensing to generic manufacturers for access to the products investigated in these programs in LMICs. The forum discussed the need for demanding transparency from the manufacturers on accessibility plans (licenses, costs, filing plans) to communities as early as possible in the drug development process**.**

Generic Manufacturer: **Viatris,** the largest ARV supplier globally, presented the company's efforts to meet international needs for ARVs, support HIV programs, and enhance affordability for tenofovir, lamivudine, efavirenz (TLE). The discussion highlighted the demand for long-acting medicines (both for PrEP and treatment), particularly among vulnerable populations in LMICs, as they could address some of the barriers related to daily oral pills by reducing stigma, supporting higher adherence, and reducing pill fatigue. Community engagement and support are crucial for initiating negotiations for licenses covering as many LMICs as possible and accelerating the development of long-acting medicines. Other agencies' and stakeholders' support is

necessary to ensure the uptake of licensed products in countries. No clear timelines were given for when generic versions of CAB-LA would be available for use in LMICs. This was attributed to the uncertainties linked to the development of the active pharmaceutical ingredient (API) and process complexity. Viatris agreed to be contacted periodically to check for updates on the development of their generic version of CAB-LA, including reconvening with community advocates virtually or in-person at the International AIDS Society Conference (IAS) in July 2023.

Country Preparedness: The Country Preparedness Panel discussed the implementation of CAB-LA in Nigeria and Zimbabwe, as well as addressed any steps needed to ensure preparedness for rapid introduction and uptake. Nigeria needs to address several barriers to ensure a smooth rollout, including regulatory control, supply chain management, staffing, and demand creation. In contrast, Zimbabwe has established a Technical Working Group to discuss the latest developments in HIV prevention, treatment, and care, and is addressing supply chain management and pharmacovigilance challenges. Both countries have established task forces and working groups to oversee CAB-LA's implementation and ensure that all key stakeholders are involved. Lessons learned from Nigeria and Zimbabwe include disseminating guidelines to service providers and considering high-risk groups' needs. The importance of partnerships and involving all stakeholders from the start was emphasized, and these insights can be useful in implementing CAB-LA in other sub-Saharan countries.

Long-acting products in the context of paediatric and adolescent populations: The presenter explored the use of long-acting antiretroviral (LA-ART) medication in pediatric and adolescent populations, including its potential benefits for youth living with HIV and LA PrEP for adolescents. LA injectable formulations of CAB and RPV have been approved for virologically suppressed HIV-infected patients ≥12 years of age with a weight of >35 kg. The presenter also discussed the practical and pharmacokinetic considerations for the use of LA-ART in pediatric and adolescent populations, as well as the limited experience with the use of LA agents for other medical conditions during childhood. PLHIV on treatment struggling with adherence challenges may be at risk for developing resistance, leading to limited long-term treatment options. More research and operational planning are needed to develop effective LA PrEP delivery systems for adolescents and appropriate LA treatment regimens for children and adolescents. The presenter highlighted the importance of community feedback and real-world data

collection in developing future LA prevention and treatment products for these populations.

Community preferences and acceptability of long-acting regimens for PrEP and treatment: The presenter discussed a study conducted in several African countries to compare the acceptability of injectable and oral PrEP for HIV prevention. The study found that injectable PrEP was preferred over oral methods, with convenience and adherence advantages being key factors. Adolescent participants also found the treatment acceptable, and acceptability was associated with high adherence and continuation. Healthcare providers were found to influence product choice, with several factors being important, such as population, discretion, pregnancy intention concerns, and social networks. Strategies to support choice included decision support tools, improved client knowledge, and risk perception. The presentation also addressed questions related to using LA-ART for newborns, the potential for a cure, and the real-world implications of high acceptability. The study concluded that community engagement and advocacy are crucial to address barriers to access and uptake of long-acting HIV prevention methods.

Steeplechase activities

4. AGREED ACTION POINTS

- ✓ Advocate for the inclusion of long-acting PrEP and treatment in Global Fund funding by engaging with PEPFAR and the Global Fund well in advance of COP 24/25 to establish a consensus on funding for long-acting products.
- ✓ Initiate Twitter campaigns directed towards pharmaceutical companies and the WHO, conveying the community's stance on long-acting PrEP and stressing the urgency of expediting product development by generics. Furthermore, arrange a press conference to underscore the community's position on long-acting products and share statements with embassies and public figures to amplify our voice in demand generation.
- ✓ Establish connections with other global Community Advisory Boards to amplify our voice in demand generation within community spaces, and collaborate to

enhance advocacy efforts, particularly at major events such as the International Conference on AIDS and STIs in Africa (ICASA) and IAS 2023.

- ✓ Utilize international conferences such as e.g., IAS, ICASA, CROI, etc. to strengthen advocacy efforts for CAB-LA at the national level and engage with relevant stakeholders to garner more support for long-acting PrEP.

Group discussion activities

- ✓ Identify potential allies with funders in PEPFAR, UNAIDS, and the Global Fund who could support our advocacy efforts. (This could include contacting individuals such as Ambassador John Nkengasong and Winnie Byanyima).
- ✓ Improve regional coordination of civil society organization (CSO) engagement to ensure that advocacy efforts are aligned and impactful.
- ✓ Increase demands for better coordination efforts between WHO and generics to fast-track regulatory processes. This could involve advocating for streamlined approval processes for generic products.
- ✓ Task and follow up with ViiV on rapid technology transfer to generic manufacturers to ensure timely production of affordable and accessible HIV medication.
- ✓ Continue to hold donors (Bill and Melinda Gates Foundation, CIFF, Unitaid, USAID, PEPFAR) accountable for ensuring critical investments are in place to ensure rapid impact with CAB-LA, including funding for incentives and technical partnerships to drive accelerated generic development and country-level introduction planning.

- ✓ Advocate for the simplification of product approval processes for the US FDA and the WHO to reduce barriers and accelerate entry for generic manufacturers as well as at the national level.
- ✓ Task generics manufacturers to ensure that their products meet high-quality standards to guarantee efficacy and safety for patients. This could involve partnering with relevant regulatory bodies to develop and enforce quality standards for generic products.
- ✓ Conduct health care worker trainings and ensure health system preparedness to deliver long-acting products once available.
- ✓ Develop and implement an advocacy strategy, beginning with the community statement to be released, to ensure and accelerate access to generic Lenacapavir in LMICs. Drawing upon the success of previous licensing experiences for other products, e.g., the recent CAB-LA licence, the advocacy strategy will target Gilead and involve other global stakeholders to ensure Lenacapavir is affordable and available through a transparent public-health driven/access-oriented licence through MPP.
- ✓ Determine the community's involvement and impact in developing new products, access strategies for LMICs, rapid registrations, and uptake in countries.

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