Access to long-acting cabotegravir (CAB-LA) for HIV pre-exposure prophylaxis (PrEP)

Q&A

Last updated: November 2023

Summary timeline of MSF's negotiations with ViiV to procure CAB-LA

December 2021: CAB-LA is approved by the US Food and Drug Administration (FDA) for HIV pre-exposure prophylaxis (PrEP).

January 2022: MSF begins negotiations with ViiV to procure CAB-LA for HIV programmes in Mozambique and Eswatini. ViiV's only offer for access is via donation for operational research, provided that ViiV reviews and approves the research protocols. MSF develops operational research proposals for Mozambique and Eswatini.

March 2022: MSF rejects proposed donation in line with MSF's policy not to accept donations from pharmaceutical corporations. MSF requests ViiV CEO to transparently announce its price and allow MSF to procure CAB-LA.

July 2022: MSF places a purchase order for CAB-LA, and ViiV finally agrees to allow procurement, pending signature of a procurement contract between the two parties. Discussions and protocol development advance, in part based on verbal commitment from ViiV to sell MSF the CAB-LA required for these studies by the end of Q2 2023. MSF and ViiV start good faith discussions to finalise the contract. During the contract negotiations, MSF is encouraged by ViiV to seek out further demand. MSF makes efforts to include its projects in several other countries where there is clear demand for the use of CAB-LA for PrEP, including in settings where other partners are not planning implementation studies.

November 2022: Contract expected to be finalised by end of the year, to allow procurement of CAB-LA by end of Q2 2023.

February 2023: After eight months of time and effort invested by MSF's teams to finalise the contract and the implementation research plans, ViiV informs MSF that there are significant supply constraints for CAB-LA and that they cannot guarantee any supply for 2023, pending an FDA approval to increase their manufacturing capacity. MSF therefore makes the pragmatic decision to prioritise implementation in Mozambique, as it is the most advanced in planning, prioritises key populations, and currently has no other implementation studies planned by other actors.

May 2023: ViiV informs MSF that they have secured FDA approval allowing for an increase in production capacity. ViiV commits to supplying only 675 vials to MSF in 2023 and another 675 for 2024. This marks almost one year of discussions with ViiV (since MSF's June 2022 purchase order) for a Purchase Agreement, as required by ViiV before accepting any purchase orders from MSF.

May 2023: ViiV introduces last-minute changes to the Purchase Agreement that are not standard in MSF agreements with manufacturers, including clauses that undermine supply security and make supply contingent on agreeing to confidentiality of the drug's price and other supply terms, akin to signing a non-disclosure agreement (NDA).

August 2023: Faced with ViiV's continued unwillingness to remove the problematic new clauses in the contract, resulting in further delays in access to this critical HIV-prevention drug for the most vulnerable communities, MSF publishes a public letter urging ViiV to reconsider the NDA and supply clauses in the agreement.

October 2023: ViiV withdraws price confidentiality clause and agrees to make the price of CAB-LA public [approximately US$31 per vial in 2023 reducing to $30 in 2024 (excluding distribution costs)]. MSF relaunches negotiations to finalise a contract and procure CAB-LA.

What is the state of the HIV epidemic globally?

According to UNAIDS global HIV and AIDS statistics, 39 million people globally were living with HIV in 2022, and around 1.3 million people were newly infected with HIV in 2022.

Global targets endorsed at the 2022 World Health Assembly aim to reduce new HIV infections to under 370,000 by 2025 and under 335,000 by 2030. In order to meet these targets, it will be essential to urgently and broadly expand access to combination HIV prevention options, including medicines known as pre-exposure prophylaxis (PrEP).

What is long-acting cabotegravir (CAB-LA)?

CAB-LA is a long-acting antiretroviral (ARV) medicine patented and produced by ViiV Healthcare, an offshoot of pharmaceutical corporations Pfizer, GlaxoSmithKline and Shionogi. It is delivered as an injection with the first two injections administered a month apart, followed by an injection every two months.

Clinical trials have shown CAB-LA to currently be the most effective form of PrEP. As CAB-LA is more long-lasting and discreet than oral PrEP, and so may facilitate better adherence, it can help turn the tide against new HIV infections globally.

CAB-LA was approved by the US Food and Drug Administration (FDA) in December 2021 and recommended for HIV prevention by the World Health Organization (WHO) in July 2022. It was also approved by the FDA for treatment of HIV in combination with the long-acting injectable rilpivirine. However, due to the need for cold chain storage for rilpivirine and concerns around drug resistance, this combination (marketed as CABENUVA) has not been prioritised as a treatment option for low- and middle-income countries (LMICs). Further manufacturing capacity of cabotegravir is also required for this treatment combination in countries where it is approved.

Why is access to CAB-LA important?

Adherence to existing PrEP options such as the once-daily oral PrEP pill is frequently influenced and undermined by social factors, including stigmatising associations with pill taking and HIV prevention within relationships, or moralising attitudes within families. Access to the more discreet injectable CAB-LA, which is also the most effective form of PrEP, could allow people at risk of HIV infection to access PrEP without anyone in their family or community knowing and so may enable greater adherence.

Why did MSF refuse to sign an NDA with ViiV?

Confidentiality clauses or non-disclosure agreements (NDAs) prevent one of the parties from disclosing any kind of information provided or shared by the other party. The confidentiality clauses in ViiV's proposed Purchase Agreement would have restricted MSF from disclosing important information on the prices and terms of supply to procure CAB-LA. Such confidentiality clauses hinder our transparency and accountability to people in our care and our donors. Such confidentiality clauses or NDAs would stop us from disclosing the price we pay for medicines, including antiretroviral drugs.

During the COVID pandemic, similar NDAs in purchase agreements that restricted access to the prices and other key terms while procuring vaccines and therapeutics were widely criticised for undermining freedom of information, transparency, and accountability, especially when public money were used. Such clauses further hinder the ability of governments and other procurers to negotiate lower prices with manufacturers.

In October 2023, ViiV made the access price of CAB-LA public.

Why is MSF calling for ViiV, PEPFAR and Global Fund to provide transparency on the current available volume and planned global distribution of CAB-LA?

As highlighted earlier, CAB-LA is approved for use in both treatment (in combination with rilpivirine) and prevention (on its own) of HIV. While cabotegravir/rilpivirine is not more effective than existing ARV combinations for *treatment*, CAB-LA is the most effective agent for *prevention*.

However, there is lack of transparency on the currently available volumes and distribution of CAB-LA across these two indications and across countries. MSF has called for transparency from ViiV, and for distribution to be guided by data demonstrating where available supplies will have the most impact on addressing the HIV epidemic

In addition, knowing that generic manufacturing is essential to allow for an increase in volumes but will not be available for three to five years, MSF also calls for the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and ministries of health that are planning CAB-LA implementation to provide transparency on how people most at risk (i.e. key populations) of HIV infection will be offered CAB-LA in their PrEP choice.

What are the current barriers to accessing CAB-LA?

***Monopoly*:** ViiV applied for the compound patent on CAB-LA in 2006 and this was granted widely, including in key manufacturing countries such as India. As a result, the corporation currently has a monopoly on the supply of the drug. The lack of additional sources of supply carries the risk of shortages**.**

The issue of increasing supply capacity, including through licensing to open up generic competition, has been repeatedly raised by the HIV community during the development of the drug. ViiV has maintained, against all logic, that there would not be significant demand, and they would take responsibility of being the sole supplier globally. ViiV waited 16 years after filing for patents to license this lifesaving medicine. Its current global supply monopoly cannot meet demand, and efforts from the corporation to increase supply through an additional manufacturing plant will likely not have effect until sometime in 2024. In addition, it will take time, with some reports suggesting as long as until 2027, for generic companies to develop, register, and make generic CAB-LA commercially available.

***Pricing*:** ViiV's 2024 access price of approximately $210 per person per year is 10 times higher than what the Clinton Health Access Initiative (CHAI) estimates a generic price could be, namely less than $20 per person per year. The government of South Africa, the country with the highest number of new HIV infections globally, has already announced that this price is unaffordable and will prevent the scale up of CAB-LA. Today's oral HIV PrEP pills are priced at $40 for one year. ViiV and generic manufacturers should work towards a price that reflects the potential generic price and that is comparable to the current price of oral PrEP in LMICs so that governments and treatment providers can accelerate rollout of this lifesaving intervention at the scale needed.

***Registration*:** ViiV has registered CAB-LA in only the EU and seven other countries - the US, Australia, Zimbabwe, South Africa, Malawi, Brazil, and Botswana - and has filed to register in 12 others. Many countries with a high burden of existing and new HIV infections are not included in this list including Mozambique.

How and when will the voluntary license announced by the Medicines Patent Pool (MPP) and ViiV result in an increased global supply of CAB-LA?

In July 2022, ViiV and the Medicines Patent Pool (MPP) announced a voluntary license on CAB-LA. It will allow generic companies that sign the license to supply the generic version of CAB-LA in 90 countries. On 30 March 2023, ViiV and MPP announced the three generic drug manufacturers selected to produce CAB-LA under the voluntary license agreement: Aurobindo, Cipla, and Viatris. However, due to the added complexity of

manufacturing a long-acting agent and the uncertainty of ViiV's willingness to assist in technology transfer, it may take them as long as four to five years to do so.

MSF has concerns about the effectiveness of the voluntary license due to several issues with the terms and conditions offered by ViiV to MPP:

- The geographical scope of the license is limited and does not even match that of the licenses for dolutegravir (2014 and 2020), the other HIV medicine licensed by ViiV to MPP. Further, it excludes 47 out of 54 upper middle-income countries (UMICs).
- Though sublicenses can normally be issued to any qualified manufacturer, in the ViiV/MPP license the number of sublicensees is unreasonably restricted to a maximum of three.
- The license agreement imposes "public market only" restrictions in 10 of the included LMICs. As a result, if the drug is not available in the public market, i.e. with the government, NGOs recognised by the government, UN organisations and other agencies and in the HIV programme in these 10 countries, people will not be able to access more affordable generic versions of CAB-LA on prescription from private medical care providers. This would prevent generic manufacturers from supplying to people who may want to access CAB-LA from private health care providers if it is unavailable in the public market.
- The license contains a clause for "assistance with product development and regulatory approvals," which might help generic sublicensees receive data and sample products needed to conduct bioequivalence studies for developing generic CAB-LA and seeking regulatory approval. However, this assistance would be at the "sole discretion" of ViiV, and be negotiated individually and confidentially with the sublicensees, outside the purview of the ViiV/MPP license.
- Moreover, while ViiV may waive its exclusive rights on regulatory data for a sublicensee, the corporation can revoke its waiver. This clause therefore introduces uncertainty into the development of a generic product.

For more information, please see MSF's recent reports and press release on CAB-LA:

- MSF refuses to sign ViiV's last-minute NDA for access to most-effective HIV prevention drug CAB-LA
- Pharmaceutical corporation ViiV must improve its failing access strategy for lifesaving HIV prevention drug (30 March 2023)
- Agents of change: Long-acting formulations for prevention and treatment of HIV (2 February 2023)
- Cabotegravir: What are we waiting for? (25 July 2022)