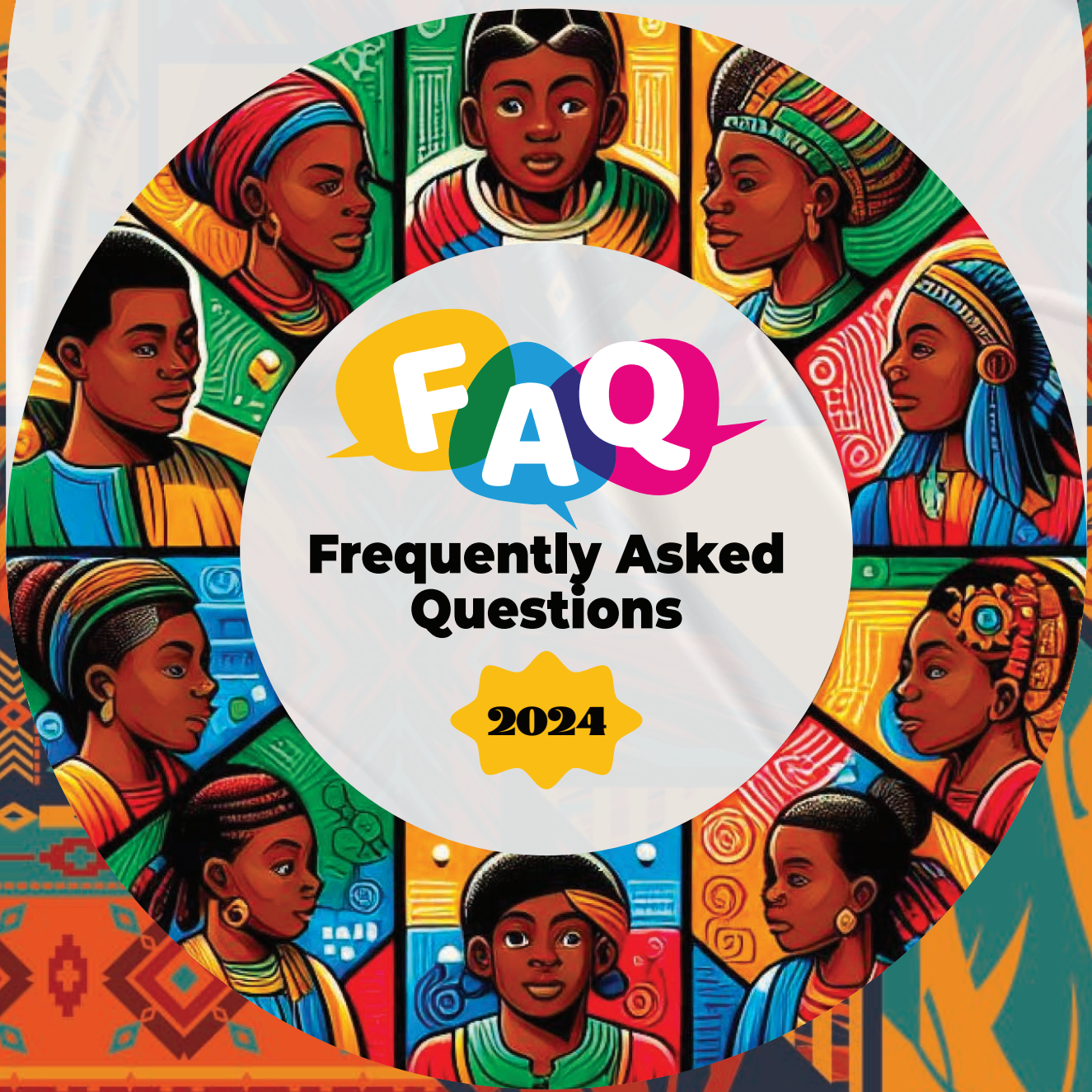
Cabotegravir Long-Acting Injectable (CAB-LA) for HIV PrEP



FAQ

Frequently Asked Questions

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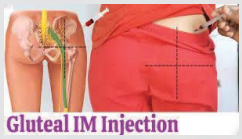
Product Profile

Indication	HIV Prevention (pre-exposure prophylaxis or "PrEP")	**Dosing**	Every 8 weeks after initial dose (first two injections are 4 weeks apart)
Drug class	Integrase strand transfer inhibitor (INSTI)	**Storage**	No refrigeration required, ~36-month shelf-life
Developer	ViiV Healthcare	**Regulatory Status**	First approved by the US FDA in December 2021. As of January 2024, non-generic CAB-LA is also approved in these countries Note: select "cabotegravir" under compound to see list of countries that have approved CAB-LA
Delivery Form	 See injection training video here	**Normative Guidance**	 WHO recommended CAB-LA as an additional HIV prevention option for people at substantial risk of HIV infection in guidelines released July 2022
Safety	Clinical trials (HPTN 083 and 084, see further details below) have demonstrated CAB-LA is a fairly safe HIV prevention method. Further studies are needed to better characterize CAB-LA safety in pregnant and breastfeeding individuals as well as in populations not highly represented in the studies	**Efficacy**	Both oral PrEP and CAB-LA are highly effective at preventing HIV when taken as directed (~99%). In clinical trials, CAB-LA was shown to have superior efficacy than oral PrEP because adherence was higher in the CAB-LA arm

Frequently Asked Questions

What is pre-exposure prophylaxis or "PrEP"?

•Pre-exposure prophylaxis or "PrEP" prevents HIV acquisition and is only taken by those who are HIV-negative who may be at risk of HIV infection. We can include the statement only taken by those who are HIV-negative who may be at risk of HIV infection. We can then remove the wording below: However, PrEP should only be taken by those who are HIV-negative.

•Daily oral PrEP is the most widely used form of PrEP, but other dosing patterns (e.g., "2-1-1" or "event-driven PrEP") and product forms of PrEP have been recently approved or are under review (such as the dapivirine vaginal ring and long-acting cabotegravir (CAB-LA)). Other forms (such as implants and longer-acting injections) are in development. While significant progress has been made to achieve high rates of treatment coverage, with 1.3 million new HIV infections in 2022 alone, more prevention options and PrEP products are urgently needed to help people protect themselves from HIV. See https://www.prepwatch.org/ for up-to-date PrEP information.

What is CAB-LA?

•CAB-LA, or long-acting [LA] injectable cabotegravir [CAB], is an injectable HIV prevention product that was recently shown to be highly effective at preventing HIV in two large-scale efficacy trials conducted across 13 countries (including 7 countries in sub-Saharan Africa). These clinical trials (research) are conducted to determine if drugs indeed achieve their desired outcome – in this case, the prevention of new HIV infection.

•Cabotegravir belongs to a class of antiretroviral drugs (ARVs) called integrase inhibitors. CAB-LA may also be known as 'CAB for PrEP'. It is administered in the buttocks by a trained health care provider every 8 weeks (after the first two doses, which are delivered 4 weeks apart to help the drug reach protective levels in the body as soon as possible).

What are the advantages of CAB-LA for prevention?

• While oral PrEP is highly effective at preventing HIV when taken as directed, many people struggle with taking a daily pill or may prefer other product forms. When someone misses oral PrEP doses, either because they forget to take the pills or choose not to, they will not be protected from HIV. In clinical trials, CAB-LA was shown to be more effective than daily oral PrEP because adherence was higher among participants in the CAB-LA arm (fewer missed doses). Similarly, in real life, CAB-LA may be a better option for people who prefer bimonthly injections over daily pills for HIV prevention.

"CAB-LA will give me the power to have the freedom of choice" -**Community Advocate**

• Long-acting injections may also provide a more private or discreet option because users do not have to carry around a pill bottle that rattles or worry about hiding their pills. While CAB-LA may not be the best option for everyone (such as those who dislike injections), it provides a highly effective, long-acting option, expanding choice for those at risk of HIV.

Are there any known disadvantages or limitations, such as drug-drug interactions, for CAB-LA?

• For CAB-LA to be effective, injections must be taken on time and cannot be interrupted. This may be challenging for clients who cannot attend follow-up visits every 2 months.

• Drug-drug interactions can bring a change in a drug's effect on the body when the drug is taken together with a second drug. CAB-LA can be used safely with contraception – data shows that there are no drug-drug interactions between CAB LA and hormonal contraceptives. However, two drugs used in the treatment of tuberculosis, rifampicin and rifapentine, cannot be used at the same time as CAB-LA.

• Injection site reactions and soreness at the injection site were common during clinical trials (most often occurring at the first injection) but did not result in discontinuations among any participants in the trial conducted in sub-Saharan Africa.

• It is also important to consider that injections may not be a preferred form of prevention for all users, especially if they do not like needles or are satisfied with another form of HIV prevention (such as oral PrEP, condoms, or the ring).

• As CAB-LA is currently required to be delivered by a trained healthcare provider (rather than self-administered), this may present challenges for people who are not able to travel to, or be visited by, trained healthcare workers at the required regular CAB-LA dosage intervals.

• Although there have been rare instances of breakthrough infections and some risk of resistance if testing missed acute HIV infection, CAB-LA was safe and well-tolerated in clinical trials. The most common side effect was injection site reactions – participants receiving CAB-LA were more likely to experience pain or tenderness at the injection site (buttocks). A small percentage (2.2%) of men who have sex with men and transgender women in HPTN 083 clinical trial discontinued CAB-LA due to an injection-related adverse event. In HPTN 084, the study conducted among women in sub-Saharan Africa, there were no discontinuations due to injection site reactions.

•Because CAB-LA is an antiretroviral drug (ARV), users may experience other similar side effects like diarrhea, headache, fever, and tiredness as happens with oral PrEP.

Injection site reactions in HPTN 084

Injection number	CAB-LA group (1519 participants)
1	25
2	8
3	6
4	1
5	1
6	1
7	8
8	0
Total	**32%**

Most injection site reactions occurred at the first injection

No participants in the CAB-LA group discontinued due to injection site reactions!

What happens if you are late for an injection?

•Like oral PrEP, missed or late dosing decreases the effectiveness of CAB-LA and users may not be protected from HIV. In clinical trials, participants were given a "target visit window," of approximately one week during which the participant should return for their next injection. If the participant received their injection at any time during that week, it is considered "on-time" dosing and CAB-LA can be expected to be at its highest protection levels.

Specific guidance on late visits will likely vary by country. In countries more experienced with the use of CAB-LA, like the US, if a user knows they will miss their injection visit by more than 7 days, they are recommended to take daily oral PrEP until they can return for an injection.

See training module.

What is the evidence behind the safety and efficacy of CAB-LA?

• CAB-LA has been evaluated for safety and efficacy in two global randomized, controlled, double-blind studies.

These trials enrolled nearly 8,000 participants in total from 13 countries. Randomized controlled trials, or "RCTs" represent the gold standard for evaluating drug effectiveness. These trials compared CAB-LA to daily oral PrEP – half of the participants were given oral PrEP and the other half were given CAB-LA and then researchers compared the number of HIV infections in each group.

• Both CAB-LA and oral PrEP were shown to be safe and highly effective at preventing HIV. However, there were fewer new HIV infections in the CAB-LA arm compared to the oral PrEP, reflecting a higher "risk reduction" for CAB-LA. Because we know that oral PrEP is highly effective when taken as directed, researchers hypothesized that the higher effectiveness for CAB-LA was likely due to better adherence in the CAB-LA arm.

Study	Population and Countries	Results
HPTN 083 an HIV prevention clinical trial	4,570 men & transgender women who have sex with men in Argentina, Brazil, Peru, US, South Africa, Thailand, Vietnam	CAB-LA prevented more HIV infections than oral PrEP resulting in a **66% reduction in new HIV infections compared to oral PrEP**
HPTN 084 Long-acting Injectable For the Epidemic	3,224 women in Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, Zimbabwe	CAB-LA prevented more HIV infections than oral PrEP resulting in **an 89% reduction in new HIV infections compared to oral PrEP**

Will CAB-LA increase rates of HIV resistance?

• Resistance testing in both trials is ongoing, but data is limited because CAB-LA is highly effective at preventing HIV so very few trial participants seroconverted while on CAB-LA.

• Recently published data from HPTN 084 showed no instances of resistance among those who acquired HIV. In the participants who acquired HIV in the CAB-LA arm, two participants had not yet received any injections and one participant had delayed injections – she was found to be HIV-positive 16 weeks (4 months) after her last CAB injection.

• In HPTN 083, resistance associated with CAB-LA has been seen in 7 cases (CROI 2022 Presentation). However, modelling which informed the WHO guideline found that the benefits of CAB-LA introduction are likely to outweigh the risk of resistance – in other words, even if CAB-LA leads to increased rates of resistance, CAB-LA introduction is still expected to reduce HIV-related deaths overall because it is so effective at preventing new infections.

For further reading on resistance associated with CAB-LA, please read Fonner et al's 2023 meta-analysis of CAB-LA safety and efficacy

What populations has CAB-LA been tested in? Is there data on pregnant and breastfeeding people?

• HPTN 083 enrolled men and transgender women who have sex with men and HPTN 084 enrolled women aged 18-45 years. Research to determine safety, tolerability and acceptability among adolescents under the age of 18 is ongoing through HPTN 083-01 and HPTN 084-01.

• When HPTN 084 started, women were required to use long-acting reversible contraception, so there were very few pregnancies. In the small number of pregnancies that occurred, women were transitioned to oral PrEP and monitored, and no safety issues were observed. HPTN 084 is now in its "open-label extension" phase, meaning participants are given a choice between oral PrEP and CAB-LA, regardless of which arm they were randomized to at the start of the trial.

• Based on positive safety data so far and to gain more evidence and support access to CAB-LA among pregnant and breastfeeding women, women are no longer required to use long-acting reversible contraception so more data on safety during pregnancy and breastfeeding will be available soon.

When will CAB-LA be available for HIV PrEP in low- and middle-income countries (LMICs)? What is the process for regulatory approval?

• Timelines for CAB-LA availability in LMICs depend on several different factors. Some countries have approved the use of CAB-LA while other regulatory authorities are reviewing the product data, but review and approval times may vary by country. See link to check registration status by country and filter for "cabotegravir" under "compound."

• Currently, CAB-LA is only available as an originator product from ViiV Healthcare and is not yet available as a generic. ViiV's "non-profit price" for CAB-LA is ~USD 30 per injection, which is not affordable for most low and middle-income countries.

(see also: GHSC-PSM e-catalog reference price)

• Similarly to other HIV drugs, availability of generic versions of CAB LA and competition among generic manufacturers will be essential for affordable and at-scale access in LMICs. A key first step for enabling the development of generic CAB-LA was a voluntary license, signed by ViiV Healthcare and Medicines Patent Pool (MPP) in July 2022. MPP-licensed generic manufacturers have benefited from the transfer of technical knowhow from ViiV. They also already started developing the product. However, CAB-LA is a more challenging product to develop than oral pills and development will approximately take until 2026-2027. Until then, ViiV will remain the sole supplier, possibly meaning that CAB-LA will be available in limited volumes until generic products are developed and approved

See full license: https://medicinespatentpool.org/licence-post/cabotegravir-long-acting-la-for-hiv-pre-exposure-prophylaxis-prep

• Several donors, including Unitaid, USAID, and others are supporting operational research which will support CAB-LA access in the near term. During this time, it will be important for stakeholders in countries to gain experience and understand how to effectively deliver CAB-LA, i.e. to prepare the ground for market entry of generic CAB LA , so that countries are fully ready to scale up once generics are available. Once MPP-licensed generic companies will have developed CAB-LA , they will submit dossiers for WHO prequalification and/or US FDA Tentative Approval to ensure the quality of the products and as necessary steps prior to filing for registration by national regulatory authorities.

Community Perspectives on Long-Acting Injections for HIV Prevention and Treatment:

"I would choose injections because I like knowing I'm protected, and protection is more important than anything. With CAB-LA, I would know I'm protected for 2-months. Some days you just do not feel like taking a daily pill."

– Community Advocate

"With oral PrEP every time you move, you hear the pill bottle rattle. I would prefer a long-acting injection because no one can see it"

– Community Advocate

"I don't have to be connected to a pill bottle, and I no longer have any anxiety within myself about taking my pill. When I think about what it means for adherence to go from 365 pills to 6 shots, its revolutionary. We need to do everything we can to make sure everyone has access to that."

– Long-Acting Injectable HIV Treatment User

"An injection is easier for women – you don't have to worry about it every day."

– Young woman from South Africa