



World Health  
Organization



GUIDELINES ON  
**LONG-ACTING INJECTABLE  
CABOTEGRAVIR FOR HIV  
PREVENTION**

WEB ANNEX G. EVIDENCE-TO-DECISION MAKING TABLE

Guidelines on long-acting injectable cabotegravir for HIV prevention. Web Annex G. Evidence-to-decision making table

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## Summary of judgements

	Judgement						
Problem	No	Probably no	Probably yes	Yes		Varies	Don't know
Desirable effects	Trivial	Small	Moderate	Large		Varies	Don't know
Undesirable effects	Large	Moderate	Small	Trivial		Varies	Uncertain
Certainty of evidence	Very low	Low	Moderate	High			No included studies
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Uncertain
Certainty of evidence of required resources	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Uncertain
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Uncertain
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know
Feasibility	No	Probably no	Probably yes	Yes		Varies	Uncertain

## Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	<b>Conditional recommendation for either the intervention or the comparison</b>	Conditional recommendation for the intervention	Strong recommendation for the intervention
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## Detailed evidence-to-decision making table

Question: Should CAB-LA vs. oral PrEP be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches?	
Population:	All people who could benefit from PrEP
Intervention:	<b>Injectable cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP)</b>
Comparison:	Oral PrEP or non-use of CAB-LA
Main outcomes:	(1) HIV infection, (2) any adverse event (including reported social harms), (3) any stage 3 or 4 adverse event, (4) drug resistance (among those initiating PrEP while acutely infected and among those who seroconvert after PrEP initiation), and (5) sexual and reproductive health outcomes, including 5a) effectiveness of hormonal contraception and gender-affirming hormones, 5b) any adverse pregnancy event, 5c) condom use, 5d) number of sexual partners, 5e) incidence rate of curable STIs
Setting:	Global
Background:	Given the continued high incidence of HIV among populations globally, additional HIV prevention options are needed. CAB-LA could provide an additional option for HIV prevention that is long-acting and allows for discreet use.
Conflict of interests:	V Fonner has received research support from Gilead Sciences (donation of oral PrEP for a research study in which she served as co-investigator) and from Viiv Healthcare (for non-pharmaceutical-related study on implementation science and to study the implementation of home-based CABENUVA among people living with HIV). She has also served as an Advisory Board Member for Viiv Healthcare regarding implementation science.

## Assessment

Problem – Is the problem a priority?		
Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>No</li> <li>Probably no</li> <li>Probably yes</li> <li>Yes</li> <li>Varies</li> <li>Don't know</li> </ul>	<ul style="list-style-type: none"> <li>Globally approximately <b>37.7 million people are currently living with HIV</b>, and an <b>additional 1.5 million people newly acquired HIV</b> in 2020 [1], despite the increasing availability of biomedical prevention options, such as oral PrEP.</li> <li>Studies on the implementation of oral PrEP programs have demonstrated that oral PrEP uptake can be low, and among those using PrEP, maintaining effective use can be challenging [2].</li> <li>Overall, this evidence demonstrates that additional HIV prevention options are needed for populations who could benefit from PrEP.</li> </ul>	
Desirable Effects – How substantial are the desirable anticipated effects?		
Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>Trivial</li> <li>Small</li> <li>Moderate</li> <li>Large</li> <li>Varies</li> <li>Don't know</li> </ul>	<ul style="list-style-type: none"> <li>Pooled results from two phase III randomized controlled trials, <a href="#">HPTN 083</a> and <a href="#">HPTN 084</a> (see Annex 1 for study summaries), <b>demonstrated a significant reduction in HIV incidence (Relative risk: 0.21, 95% CI: 0.07–0.61) comparing people randomized to receive CAB-LA vs. those randomized to receive daily oral PrEP, which translates to a 79% relative reduction in risk of HIV infection.</b></li> <li><b>HPTN 083</b>, the study among men who have sex with men and transgender women who have sex with men, demonstrated a <b>66% relative reduction in risk of HIV infection</b> (hazard ratio: 0.34, 95% CI: 0.18–0.62), comparing people randomized to receive CAB-LA vs. oral PrEP [3].</li> <li><b>HPTN 084</b>, the study among cisgender women, <b>demonstrated an 88% relative reduction in risk of HIV infection</b> (hazard ratio: 0.12, 95% CI: 0.05–0.31), comparing those randomized to receive CAB-LA vs. oral PrEP [4].</li> <li><b>15 incident HIV Infections were identified among the 3857 individuals randomized to CAB-LA across the blinded portion of the phase III trials. Of these, 5 were classified as “breakthrough infections”</b> (i.e., infections that occurred following recent exposure to CAB).</li> <li><b>Recent data from HPTN 083 identified an additional 13 infections in the CAB-LA arm, 2 of which occurred during the blinded phase of the study and were classified as “breakthrough infections” and 11 of which occurred after unblinding of study participants.</b></li> </ul>	<p><b>Modelled population-level impact of CAB-LA on HIV transmission</b></p> <ul style="list-style-type: none"> <li>Preliminary results on the impact, effectiveness, and cost–effectiveness of two mathematical models for MSM in high-income settings (Atlanta and Montreal) and two models for South Africa compared scenarios of scale-up of PrEP that included CAB-LA with scenarios restricted to oral PrEP.             <ul style="list-style-type: none"> <li>Results suggest impact of CAB-LA varies considerably across populations.</li> <li>In MSM models, switching from oral PrEP to CAB-LA has a small effect on HIV infections averted over 20 years (up to 3% of additional HIV infections averted). <b>Increasing overall PrEP coverage (oral or CAB-LA) has markedly stronger impact.</b></li> <li>One model for South Africa suggests that an additional 4% of HIV infections could be prevented when switching from oral PrEP to CAB-LA, while another model for South Africa suggests ~double effect if PrEP use is highly targeted among those at substantial risk. transmission. <b>Both South Africa models suggest that increasing overall PrEP coverage has a stronger impact than switching from oral PrEP to CAB-LA.</b></li> </ul> </li> <li>A mathematical model of introduction of CAB-LA in sub-Saharan Africa with rapid scale-up of PrEP and near complete switch to CAB-LA suggests a reduction in HIV incidence from about 0.4 to 0.3 per 100 person-years by 2032.</li> </ul>

## Undesirable – Effects How substantial are the undesirable anticipated effects?

Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>• Large</li> <li>• Moderate</li> <li>• Small</li> <li>• Trivial</li> <li>• Varies</li> <li>• Don't know</li> </ul>	<p><b>Adverse events</b></p> <ul style="list-style-type: none"> <li>• The pooled effect estimate yielded <b>no significant difference in any adverse event (grade 2 or higher)</b> comparing those randomized to CAB-LA vs. oral PrEP (RR= 1.0, 95% CI: 0.98–1.01). Similar results were found within the safety studies. However, <b>injection site reaction (ISR) rates were higher across trials among participants randomized to CAB-LA vs. oral PrEP.</b> ISRs were most commonly reported as pain at the injection site. ISR rates diminished over time.</li> <li>• <b>The pooled effect estimate for serious adverse events also demonstrated no significant difference</b> comparing participants randomized to CAB-LA vs. oral PrEP (RR=0.99, 95% CI:0.79–1.23). Similarly, no significant differences were found across CAB-LA and placebo arms among the two included safety studies.</li> <li>• There is some evidence that CAB-LA could lead to weight gain, although this finding was not confirmed across all included studies.             <ul style="list-style-type: none"> <li>◦ In HPTN 083, a weight gain of 1.23 kg per year was observed in the CAB-LA arm vs. an increase of 0.37 kg in the TDF-FTC group [3]. However, differences occurred primarily in the first 40 weeks and were similar thereafter.</li> <li>◦ In HPTN 084, investigators noted an initial, immediate weight gain among participants randomized to CAB (mean weight increase= 0.4kg)[4], after which time investigators found weight gains across both study arms. The annualized weight increase in the CAB arm was 2.4kg and 2.2 kg/year in the TDF-FTC arm (p=0.041) [4]</li> <li>◦ HPTN 077, a phase 2a, found no difference in distributions of weight changes across arms or by sex at birth [5].</li> </ul> </li> </ul> <p><b>Drug resistance</b></p> <ul style="list-style-type: none"> <li>• There is evidence that CAB-LA is associated with integrase inhibitor (INSTI) drug resistance among those who begin using CAB-LA as PrEP when acutely infected or acquire HIV during CAB-LA use. <b>Seven of the 20 cases of HIV infection (including baseline infections) identified among the groups randomized to CAB had INSTI drug resistance.</b> Notably, no resistant infections were identified during the tail phase.</li> <li>• When comparing rates of INSTI resistance among participants randomized to CAB-LA vs. oral PrEP, <b>the relative risk of having an INSTI resistant infection was 20.9 (95% CI: 2.19–199.74).</b> The estimate is imprecise due to the small number of infections overall.</li> </ul>	<p><b>Drug resistance</b></p> <ul style="list-style-type: none"> <li>• Modelling of sub-Saharan Africa suggest that rapid scale-up of PrEP and near complete switch to CAB-LA would lead to an increase in INSTI resistance.             <ul style="list-style-type: none"> <li>◦ By 2032, the model suggests that 7% of all people who initiate ART have INSTI resistance in scenarios with CAB-LA introduction compared to 0.5% in the absence of CAB-LA.</li> <li>◦ About 66% of these additional INSTI cases due to CAB arise while on CAB and 34% during the tail.</li> <li>◦ Using more sensitive RNA HIV testing technology instead of 3rd generation HIV tests had only marginal effects on mortality estimates.</li> </ul> </li> </ul>

	<p><b>Delay in diagnosing HIV infection</b></p> <ul style="list-style-type: none"> <li>Both efficacy studies reported a delay in HIV diagnosis found across the CAB-LA and oral PrEP arms, often in conjunction with low levels of viremia.</li> <li>In HPTN 083, a delay in HIV detection was observed in 21 of 58 infections (36.8%), including in 11 of 16 infections among participants randomized to CAB-LA (68.8%) [6].</li> <li>In HPTN 084, there was a delay in detection in one case randomized to CAB and eight cases randomized to oral PrEP, all of which were acute infections [7].</li> </ul> <p><b>Contraceptive effectiveness, adverse pregnancy-related events, and gender-affirming hormone therapy</b></p> <ul style="list-style-type: none"> <li>There were relatively few pregnancies identified (n=49 in HPTN 084 and n=3 in <a href="#">HPTN 077</a>, a phase 2a study that also included women) as all cisgender women enrolled had to agree to be on an effective form of contraception during the trials. Of pregnancies identified, no congenital abnormalities were identified.</li> <li>There was no reported difference in pregnancy incidence comparing CAB-LA and oral PrEP arms in HPTN 084, suggesting CAB-LA probably does not influence contraceptive effectiveness.</li> <li>In HPTN 084, participants who became pregnant and were randomized to CAB-LA did report more pregnancy-related AEs than those randomized to oral PrEP (n=6), but none of these AEs were considered to be product-related.</li> <li>Data comparing pregnant cisgender women in HPTN 084 to non-pregnant cisgender women in HPTN 077 found no significant differences in the terminal half-life of CAB-LA [8].</li> <li>No data were presented on potential interactions of CAB-LA and gender-affirming hormone therapy.</li> </ul> <p><b>Sexual behavioural outcomes</b></p> <ul style="list-style-type: none"> <li>No outcomes related to sexual behaviour were reported.</li> <li>There were no reported significant differences in incidence of sexually transmitted infections (STI) comparing CAB-LA to oral PrEP arms for HPTN 083 and HPTN 084.</li> </ul>	<p><b>Adverse pregnancy-related events</b></p> <p>Studies are ongoing to better understand adverse events and pharmacokinetics related to CAB use during pregnancy. For example, the <a href="#">HPTN 084 open-label extension study</a> is not requiring participating women to use contraception, and participants who become pregnant can continue using CAB during pregnancy and breastfeeding under close monitoring. HPTN 084 participants who become pregnant can also co-enrol in the <a href="#">IMPAACT 2026 study</a>, which is assessing the pharmacokinetics and pharmacodynamics of ARVs in women during and after pregnancy.</p>
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### Certainty of evidence – What is the overall certainty of the evidence of effects?

Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>• Very low</li> <li>• Low</li> <li>• Moderate</li> <li>• High</li> <li>• No included studies</li> </ul>	<p><b>Summary</b></p> <p>Data available from 4 studies, including 2 phase 2b/3 multi-site, randomized controlled trials and 2 phase 2 RCTs. Phase 2b/3 trials had low risk of bias and phase 2a trials mostly had low risk of bias. Approximately 8120 individuals were enrolled across the four trials, with 4114 individuals randomized to receive CAB-LA. Data only available for cisgender women, cisgender men, and transgender men who have sex with men aged <math>\geq 18</math> years.</p> <p><b>Certainty of evidence</b></p> <ul style="list-style-type: none"> <li>• High certainty of evidence for HIV infection, adverse event outcomes, and contraceptive effectiveness.</li> <li>• Moderate certainty of evidence for drug resistance.</li> <li>• Low certainty of evidence for adverse pregnancy-related outcomes.</li> </ul> <p><b>Gaps in knowledge</b></p> <ul style="list-style-type: none"> <li>• Data are lacking for people who inject drugs, adolescents aged <math>&lt; 18</math> years, sex workers, and transgender men.</li> <li>• No evidence for impact of CAB-LA on gender-affirming hormone therapy.</li> <li>• Few absolute events for drug resistance and reproductive health outcomes (women taken off study product once pregnancy was known).</li> </ul>	

Values & preferences – Is there important uncertainty about or variability in how much people value the intervention?		
Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>• Important uncertainty or variability</li> <li>• Possibly important uncertainty or variability</li> <li>• Probably no important uncertainty or variability</li> <li>• No important uncertainty or variability</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Results from the values and preferences review suggest there is overall interest in and preference for CAB-LA across a variety of populations and geographies. However, there is also notable variation in preferences both within populations and geographies.</b> <ul style="list-style-type: none"> <li>◦ Among MSM, there was mixed preference for injectable PrEP. Relative to other regions, injectables are often favoured in Europe and Central Asia, Latin America, and U.S., though some US-based MSM still preferred/felt more comfortable with oral PrEP.</li> <li>◦ Women in sub-Saharan Africa often reported greater interest in injectables than women in other regions.</li> <li>◦ Mixed preference for injectables among trans men and women.</li> <li>◦ General preference for injectables among adolescents.</li> <li>◦ PWID in the US expressed interest in/preference for injectables.</li> <li>◦ Preference for injectables is dependent on lifestyle fit and may be preferred by those valuing discretion, those who are familiar and comfortable with needles (e.g., PWID, women accustomed to contraceptive injectables, or those experienced with gender-affirming hormones) or those who would have trouble storing daily pills (e.g., adolescent or the homeless/marginally-housed).</li> </ul> </li> <li>• <b>Key advantages of injectable PrEP identified in the values and preferences review</b> <ul style="list-style-type: none"> <li>◦ Injectable PrEP helps reduce adherence-related burden associated with daily pill-taking.</li> <li>◦ Infrequent dosing makes it more convenient, easier to use.</li> <li>◦ Injectable PrEP provides longer-lasting coverage and fits with a busy lifestyle.</li> <li>◦ Familiar method for medication administration (e.g. in LMICs), e.g. DMPA, gender-affirming Rx, vaccines.</li> <li>◦ Discretion/invisibility &amp; low potential for stigma.</li> <li>◦ Simplify integration with existing health services already obtained (e.g. FP, drug dependency care, etc.)</li> <li>◦ Value of long-acting PrEP could increase if proven most effective or if low cost.</li> </ul> </li> </ul>	

	<ul style="list-style-type: none"> <li>• <b>Key main disadvantages of LAI for PrEP</b> <ul style="list-style-type: none"> <li>◦ Dislike/fear of needles and injection site pain.</li> <li>◦ Side effects and not having control over side effects; misconceptions about side effects, including interference with pregnancy.</li> <li>◦ Invasiveness of injection site location (adolescents and MSM).</li> <li>◦ Logistical challenges, including needing to return for appointments on a regular basis.</li> <li>◦ Lack of control, concerns about reversibility.</li> <li>◦ Most reports of preference for injectables are based on stated preference based on hypotheticals rather than enacted preference based on experience.</li> </ul> </li> <li>• <b>Quality of care by providers important for</b> <ul style="list-style-type: none"> <li>◦ Uptake and persistence with injections.</li> <li>◦ Understanding the intervention and assuaging fears with rumours and misperceptions.</li> <li>◦ Normalizing/de-stigmatizing preventive behaviour.</li> </ul> </li> </ul>	
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#### Balance of effects – Does the balance between desirable and undesirable effects favor the intervention or the comparison?

Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>• Favours the comparison</li> <li>• Probably favours the comparison</li> <li>• Does not favour either the intervention or the comparison</li> <li>• Probably favours the intervention</li> <li>• Favours the intervention</li> <li>• Varies</li> <li>• Don't know</li> </ul>	<ul style="list-style-type: none"> <li>• Results from the systematic review and meta-analysis show that CAB-LA has promising benefits regarding HIV prevention among cisgender men who have sex with men, transgender women who have sex with men, and cisgender women.</li> <li>• Results identified no significant difference in any adverse event (grade 2 or higher) or any serious adverse event among those randomized to CAB-LA vs. oral PrEP; however, injection site reactions were more common among participants randomized to CAB-LA, and CAB-LA could possibly be related to weight gain, although this finding was not confirmed across all included studies.</li> <li>• There is evidence that CAB-LA is associated with INSTI drug resistance as seven of the 20 cases of HIV infection (including baseline infections) identified among the groups randomized to CAB had INSTI drug resistance. Notably, no resistant infections were identified during the tail phase.</li> </ul>	

	<p><b>Research gaps</b></p> <ul style="list-style-type: none"> <li>• More research is needed to understand the effects of CAB-LA among pregnant and lactating women as CAB-LA use within the reviewed studies was discontinued immediately following pregnancy detection.</li> <li>• More research is also needed among populations not included in the trials, such as people who inject drugs, adolescents aged &lt;18 years, sex workers, and transgender men.</li> <li>• Most data from the review occurred within controlled trial settings, although some data from the open-label extension portion of HPTN 083 was also included. More research is needed regarding the implementation of CAB-LA in non-research settings.</li> </ul>	
<b>Resources required – How large are the resource requirements (costs)?</b>		
<b>Judgement</b>	<b>Research evidence</b>	<b>Additional considerations</b>
<ul style="list-style-type: none"> <li>• Large costs</li> <li>• Moderate costs</li> <li>• Negligible costs and savings</li> <li>• Moderate savings</li> <li>• Large savings</li> <li>• Varies</li> <li>• Don't know</li> </ul>	<p>Confidential cost information will be shared at the meeting.</p> <p>LIC settings</p> <ul style="list-style-type: none"> <li>• oral PrEP ≈ US\$ 50 per annum</li> <li>• CAB-LA ≈ US\$ xxx per annum (plus \$22 x7 = \$154 if NAT testing required)</li> </ul> <p>HIC settings</p> <ul style="list-style-type: none"> <li>• Oral PrEP ≈ US\$ 1000 per annum</li> <li>• CAB-LA ≈ US\$ 22 000 per annum + &gt;US\$ 500 for NAT testing</li> </ul> <p>30 in-depth interviews with diverse PrEP providers from all WHO regions were conducted on perspectives regarding CAB-LA.</p> <ul style="list-style-type: none"> <li>• Providers raised concerns regarding resources necessary for CAB-LA implementation. Particularly, costs related to HIV testing if tests other than 3rd generation antibody tests are needed.</li> </ul> <p>Providers were concerned about additional human resources necessary to provide CAB-LA, particularly if injections have to be provided by physicians.</p>	<p>Increased frequency of facility visits.</p> <p>Viral load testing costs?</p> <p>Human resources requirements</p> <p>Service delivery costs (testing, syringes, etc.)</p>

### Certainty of evidence of required resources – What is the certainty of the evidence of resource requirements (costs)?

Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>• Very low</li> <li>• Low</li> <li>• Moderate</li> <li>• High</li> <li>• No included studies</li> </ul>	<ul style="list-style-type: none"> <li>• Cost of resource requirements would vary by setting.</li> <li>• Low certainty of evidence given the disparate findings of cost and cost-effectiveness studies identified in the systematic review.</li> </ul>	

### Cost-effectiveness – Does the cost-effectiveness of the intervention favor the intervention or the comparison?

Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>• Favours the comparison</li> <li>• Probably favours the comparison</li> <li>• Does not favour either the intervention or the comparison</li> <li>• Probably favours the intervention</li> <li>• Favours the intervention</li> <li>• Varies</li> <li>• No included studies</li> </ul>	<ul style="list-style-type: none"> <li>• Seven studies were identified in the systematic review that were related to cost and/or cost-effectiveness:             <ul style="list-style-type: none"> <li>◦ Of these, six modelled data and scenarios specific to South Africa [9-14]</li> <li>◦ One study assessed costs for men who have sex with men and transgender women in the United States [15]</li> </ul> </li> <li>• Studies varied widely in terms of populations, comparisons, assumptions, and thresholds.</li> <li>• In some studies, CAB-LA (or injectable PrEP more generally) was determined to be cost-effective or cost-saving in certain scenarios; in other studies, CAB-LA was not cost-effective nor cost-saving.</li> <li>• Notably, CAB-LA was seen as cost-effective in several scenarios involving high-risk women in South Africa, and in circumstances where injectable PrEP could be leveraged with complementary products (e.g., contraceptives and multipurpose prevention products).</li> <li>• Only one study included data from the CAB-LA studies in the cost models [15].</li> <li>• An unpublished mathematical model of CAB-LA introduction among MSM in Atlanta found that CAB-LA is not cost-effective compared to generic oral PrEP (due to low costs of generic oral PrEP and assumed high effectiveness of oral PrEP in this population), although it may be cost-effective compared to branded oral PrEP. A related mathematical model on CAB-LA introduction among MSM in Montreal found that CAB-LA is unlikely to be cost-effective due to low HIV incidence in this population, even if the price of CAB-LA is similar to oral PrEP.</li> </ul>	

	<ul style="list-style-type: none"> <li>• An unpublished mathematical modelling of rapid scale-up of PrEP and near complete switch to CAB-LA in sub-Saharan Africa suggests that CAB-LA can be cost-effective if the price is up to 2x the price of oral PrEP in populations where HIV incidence is &gt;0.5 per 100 person-years.</li> <li>• Two unpublished models for South Africa evaluated the cost-effectiveness of CAB-LA. One model found that CAB-LA could be as cost-effective as oral PrEP if priced at \$19/injection (<math>\leq 2x</math> of oral PrEP price). Another model found that CAB-LA could be cost-effective if the costs of the drug and delivery are less than current PrEP delivery costs + US\$ 75–375 per year.</li> </ul>	
<b>Equity – What would be the impact on health equity?</b>		
<b>Judgement</b>	<b>Research evidence</b>	<b>Additional considerations</b>
<ul style="list-style-type: none"> <li>• Reduced</li> <li>• Probably reduced</li> <li>• Probably no impact</li> <li>• Probably increased</li> <li>• Increased</li> <li>• Varies</li> <li>• Don't know</li> </ul>	<ul style="list-style-type: none"> <li>• CAB-LA offers an additional biomedical HIV prevention option.</li> <li>• Expanding PrEP options through offering CAB-LA in addition to oral PrEP and the dapivirine vaginal ring could help meet the diverse needs and preferences of people who could benefit from PrEP.</li> <li>• Cost of CAB-LA and the routine clinic visits required to administer CAB-LA could prevent some people from gaining access.</li> <li>• Access to CAB-LA for people could also provide additional opportunities for sexual and reproductive health services.</li> <li>• Preventing HIV infection among populations through offering CAB-LA could help sustain their health and that of their sexual partners.</li> <li>• Costs for CAB-LA would potentially require diversion of funds away from other prevention interventions/HIV services given the static nature of HIV funding.</li> </ul>	

## Acceptability – Is the intervention acceptable to key stakeholders?

Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"> <li>• No</li> <li>• Probably no</li> <li>• Probably yes</li> <li>• Yes</li> <li>• Varies</li> <li>• Don't know</li> </ul>	<ul style="list-style-type: none"> <li>• Results of systematic review on values and preferences found:               <ul style="list-style-type: none"> <li>◦ Attitudes: Some healthcare providers from Kenya prefer oral PrEP, although attitudes are divided [16].</li> <li>◦ Burden: Some healthcare providers from the southern US felt long-acting injectable (LAI) PrEP could reduce barriers to adherence seen with oral PrEP but raised concerns that the frequency of visits required for LAI PrEP might be a barrier to adherence [17]. Other providers for people who inject drugs felt LAI PrEP would reduce barriers to adherence faced with oral PrEP and could help facilitate PrEP use [18].</li> <li>◦ Opportunity costs: Some providers worry that drug resistance could emerge if access to clinics to receive LAI PrEP is limited/irregular [18].</li> </ul> </li> <li>• A survey among 1353 PrEP providers and in-depth interviews with 30 providers from all WHO regions were conducted on values and preferences regarding CAB-LA.               <ul style="list-style-type: none"> <li>◦ PrEP providers generally expressed acceptability of the intervention and 71% of survey respondents noted that they would consider providing CAB-LA if/when there is regulatory approval in their country.</li> <li>◦ The main benefits reported by providers were the reduced adherence burden on clients, which would improve impact of PrEP, and perceived enthusiasm for this method by clients, which was expected to increase uptake of PrEP.</li> <li>◦ Providers raised a range of concerns, including regarding potential costs, HIV testing requirements, adherence by clients to a 2-monthly injection schedule, drug resistance, the “re-medicalization” of PrEP, and additional burden on healthcare providers. Additional concerns included uncertainty around efficacy, side effects, and drug-drug interactions in certain populations (including people who use drugs and transgender populations).</li> </ul> </li> </ul>	

Feasibility – Is the intervention feasible to implement?		
Judgement	Research evidence	Additional considerations
<ul style="list-style-type: none"><li>• No</li><li>• Probably no</li><li>• Probably yes</li><li>• Yes</li><li>• Varies</li><li>• Don't know</li></ul>	<ul style="list-style-type: none"><li>• Two studies of CAB-LA have been conducted, thus proving its feasibility across a variety of trial sites.</li><li>• Very limited implementation outside well supported and controlled trial sites.</li><li>• Issues relating to stopping CAB-LA and switching need to be considered.</li><li>• Testing requirements.</li><li>• For people who seroconvert potential costs and complexities of drug resistance testing and 2nd line ART with costs and supply chain issues.</li></ul>	

**MSM:** men who have sex with men; **ISR:** injection site reaction; **TDF-FTC:** tenofovir disoproxil fumarate/emtricitabine; **INSTI:** integrase inhibitor; **STI:** sexually transmitted infection; **LAI:** long-acting injectable

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