CLINICIAN'S INFORMATION GUIDE

Long-Acting Injectable Cabotegravir for HIV PrEP

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ABOUT THIS INFORMATION GUIDE

This information guide from the *National HIV PrEP Curriculum* is intended for health care professionals involved in the care of persons interested in or receiving HIV preexposure prophylaxis (PrEP). The information in this guide emphasizes the dosing of long-acting injectable cabotegravir (CAB-LA) for HIV PrEP. This guide is produced by the University of Washington Infectious Diseases Education and Assessment Program (IDEA) as part of the federally-funded *National HIV PrEP Curriculum* project.

PERMISSION TO USE THIS GUIDE

LAST UPDATED

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GENERAL INFORMATION

What is Cabotegravir

Cabotegravir is a novel integrase strand transfer inhibitor (INSTI) that is available in two preparations: an oral tablet and a long-acting suspension administered as a gluteal intramuscular injection. The oral tablet is an optional lead-in medication to test the tolerability of cabotegravir prior to starting injectable cabotegravir.

Who is it for

Long-acting injectable cabotegravir (CAB-LA) for HIV PrEP is indicated to reduce the risk of sexually-acquired HIV-1 infection in adults and adolescents who weigh at least 35 kg. CAB-LA for HIV PrEP is indicated only for people who do not have HIV.

When not to use

CAB-LA for HIV PrEP should not be administered in any of the following circumstances:

- Absence of a documented negative HIV test result in prior 7 days
- Known hypersensitivity to cabotegravir
- Coadministered medication that significantly decreases cabotegravir concentration

Dosing and Administration

CAB-LA for HIV PrEP must be administered by a health care professional as a gluteal intramuscular injection (preferably at the ventrogluteal site). Each dose of injectable cabotegravir is 600 mg (3 mL). Note each vial of cabotegravir contains 600 mg (3 mL).

Dosing schedule

Optional Oral Lead-In

- Oral cabotegravir can be used to assess the tolerability of cabotegravir. If the oral lead-in is used, the dose is 30 mg taken once daily for approximately 28 days.

Initiation Injections

- If an oral cabotegravir lead-in is used, the first initiation injection should ideally be given on the last day of the oral lead-in. The initiation injection schedule consists of 2 doses of CAB-LA given 1 month apart. Each dose consists of an intramuscular dose of 600 mg (3 mL).
- The second initiation dose can be given up to 7 days prior to or after the scheduled date for the injection (ideally this second dose is never given late).

Continuation Injections

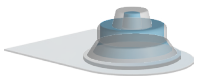
- The first continuation injection is given 2 months after the second initiation injection. The continuation injections are given every 2 months and each dose consists of an intramuscular dose of cabotegravir 600 mg (3 mL).

Manfuacturer's Administration Kit

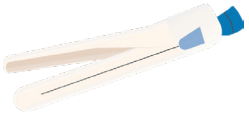
CABOTEGRAVIR VIAL

SYRINGE

VIAL ADAPTER



INJECTION NEEDLE (1.5 INCHES)



EDITOR'S NOTE

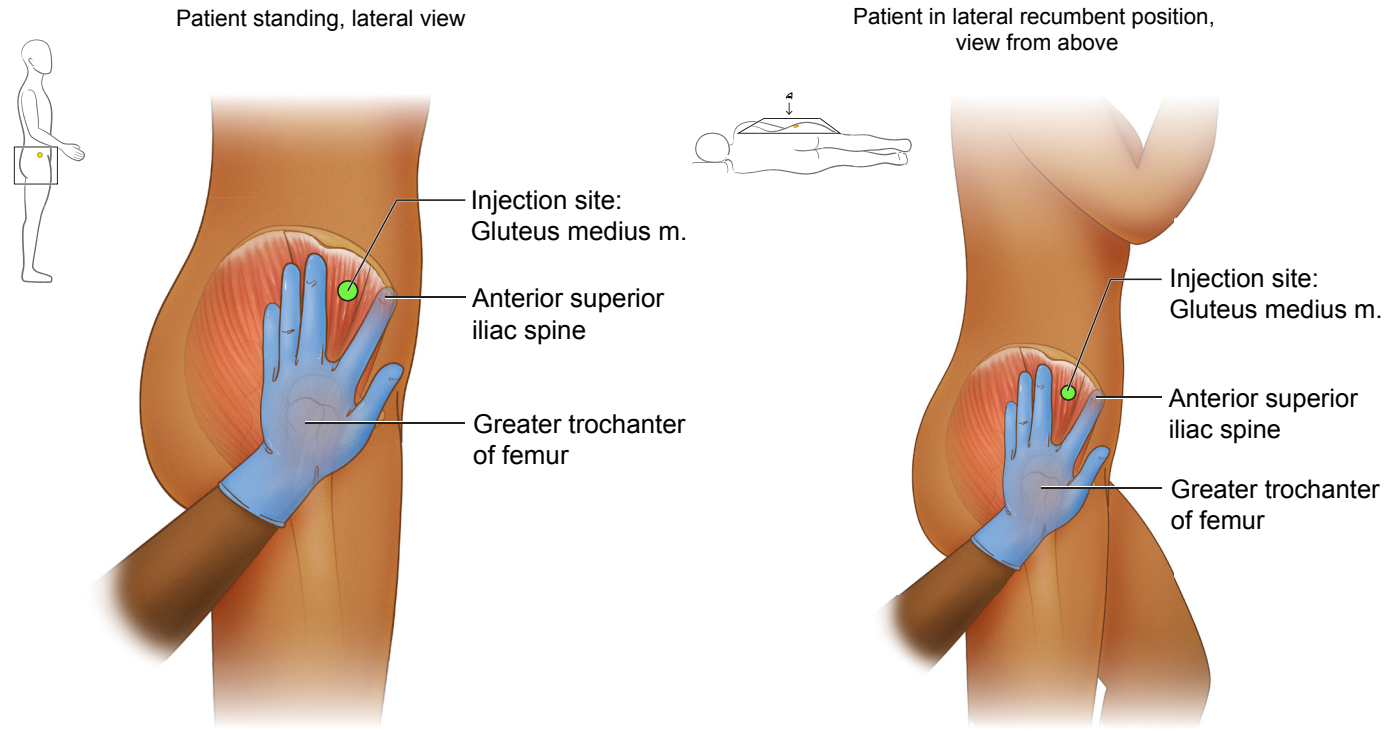
The standard length of the injection needle used for cabotegravir injections is 1.5 inches. For people with a body mass index (BMI) ≥30 kg/m^2, most experts recommend using a 2.0 inch needle. In addition, we recommend planning ahead and keeping 2.0 inch needles in stock.

INSTRUCTIONS FOR CABOTEGRAVIR INJECTIONS

The following illustrations provide basic information on (1) appropriate sites for administering cabotegravir injections, (2) use of the z-track injection technique for this intramuscular injection, and (3) consideration for 1.5" versus 2.0" needle length. For detailed information on instructions for cabotegravir injections, please see the cabotegravir extended-release injectable suspension (*Apretude*) prescribing information section titled Instructions for Use. See the full instructions in the Prescribing information for details on preparing the syringe, cleaning the injection site, drawing up the medication, and administering the medication as an intramuscular injection.

Ventrogluteal Injection Site for CAB-LA

The ventrogluteal injection site is preferred for this intramuscular injection. This site is preferred because it located away from blood vessels and nerves. The CAB-LA injection can be administered with the patient standing or lying on their side. The injection must be given by a health care professional who has been trained in giving intramuscular injections.



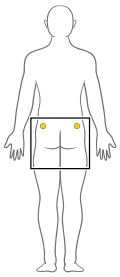
To locate the ventrogluteal region injection point, (1) place the heel of the palm over the greater trochanter of the femur (if the injection is for the right hip use the left hand and if the injection is for the left hip, use the right hand), (2) point the index finger to the anterior iliac crest in the direction of the umbilicus, (3) point the middle finger toward the iliac crest in the direction of the head (the second and third fingers should now be spread apart making a “V” shape, (4) locate and mark a spot in the middle of the ”V” space between the second and third fingers.

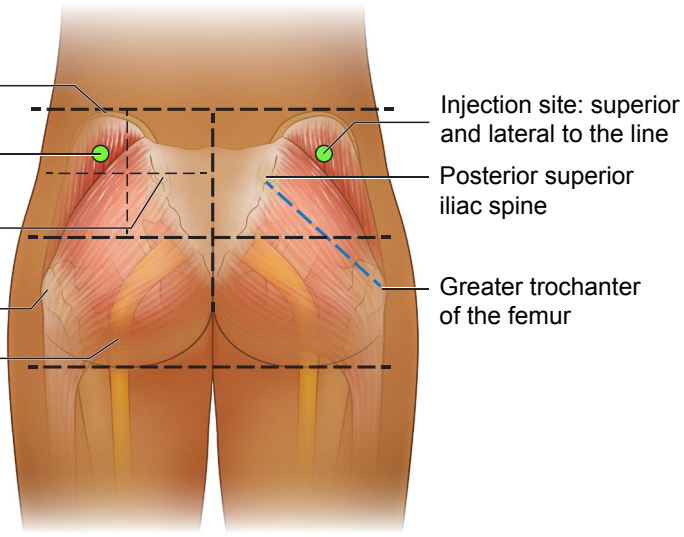
INSTRUCTIONS FOR CABOTEGRAVIR INJECTIONS

Dorsogluteal Injection Site for CAB-LA

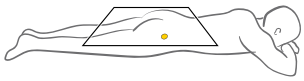
The dorsogluteal injection site is an alternative for this intramuscular injection. The dorsogluteal site is NOT the preferred site because of the proximity to the sciatic nerve and major blood vessels. With the dorsogluuteal injection, it is particularly important to avoid injection into the sciatic nerve, since this may potentially cause iatrogenic nerve injury. The CAB-LA injection can be administered with the patient standing or lying on their stomach. The injection must be given by a health care professional who has been trained in giving intramuscular injections.

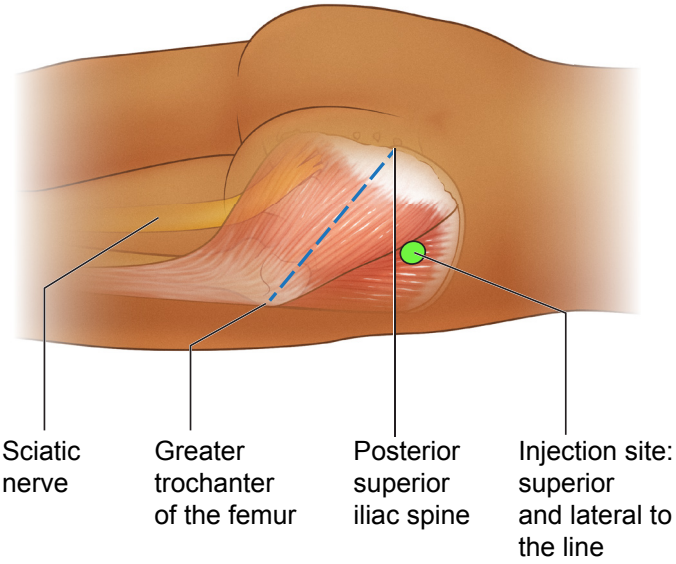
Patient standing, posterior view





Patient prone, view from above angled laterally



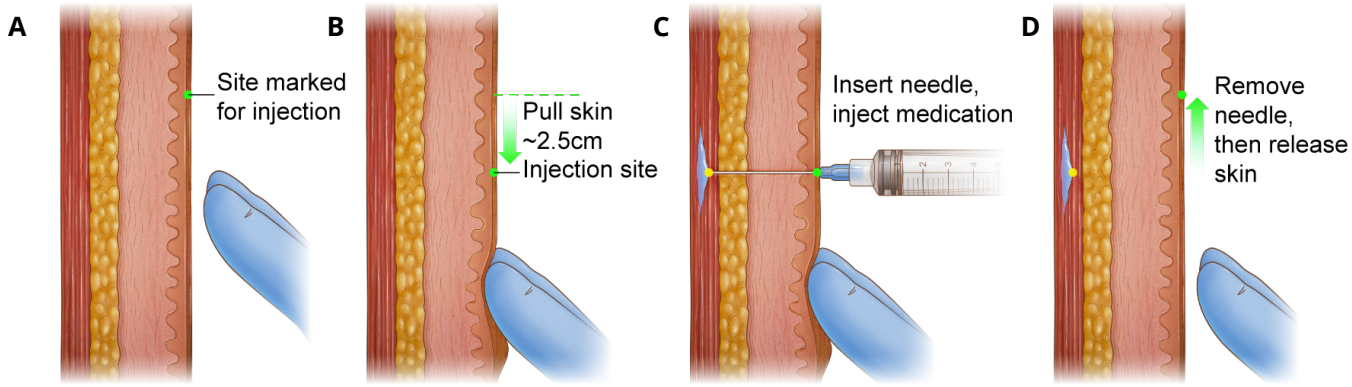


To locate dorsogluteal injection point: (1) Divide the buttock into 4 quadrants; (2) locate the outer upper quadrant; (3) divide this upper outer quadrant into 4 quadrants again and identify the upper outer quadrant of this section (this region corresponds to the upper outer quadrant of the upper outer quadrant); and (4) mark a spot within this region. As an additional safety check, draw a line (shown as dashed blue line) from the posterior superior edge of the iliac spine to the greater trochanter and make sure the injection is given above that line and below the iliac crest.

INSTRUCTIONS FOR CABOTEGRAVIR INJECTIONS

Z-Track Intramuscular Technique for Injection

Cabotegravir injections should be administered as an intramuscular gluteal injection using the z-track injection technique. The main reason for using the z-track technique is to prevent the material that has been injected from leaking out through the skin.

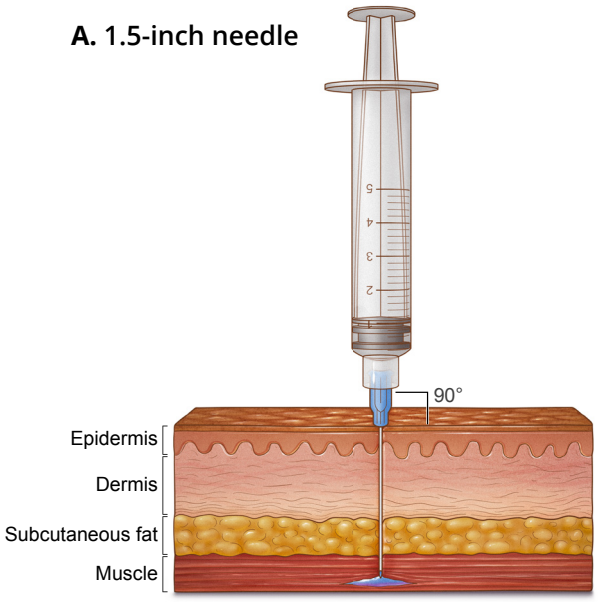


To perform the z-track injection technique, locate the site for injection as outline on the prior page. **A.** Ideally, a marker pen then is used to designate the located injection site (as shown above by the green dot). **B.** Next, pull the skin approximately 2. 5 cm (1 inch); this typically involves pulling the skin down but it also can be done pulling the skin to the side. **C.** Insert the needle at a 90° angle to the skin at the marked site (green dot) and inject the medication into the intramuscular tissue. **D.** Remove the needle and release the skin.

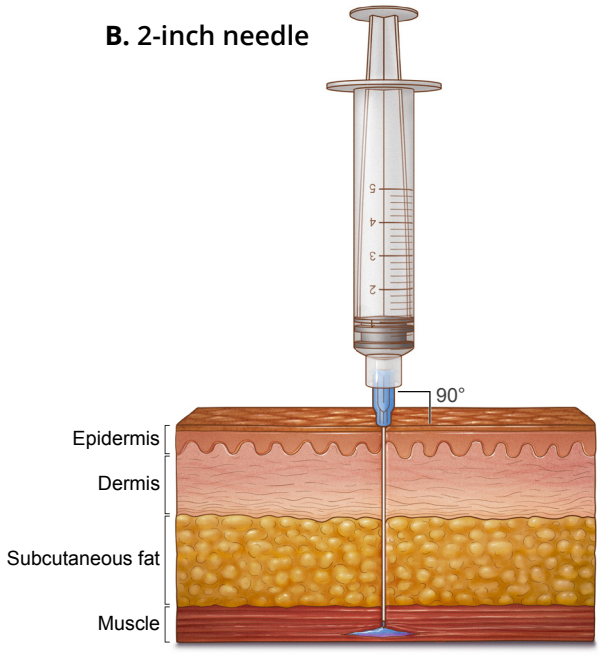
Needle Length for Injection Based on Adipose Tissue Thickness

The manufacturers administration kit contains a standard 1.5" needle. **A.** For most people, the 1.5" needle is usually adequate in length to reach the muscle tissue. **B.** The 2" needle may be required to reach the muscle tissue in anyone with a larger gluteal subcutaneous fat pad; the need for the 2" needle is more likely in a person with a higher BMI (e.g., >30 kg/m^2).

A. 1.5-inch needle

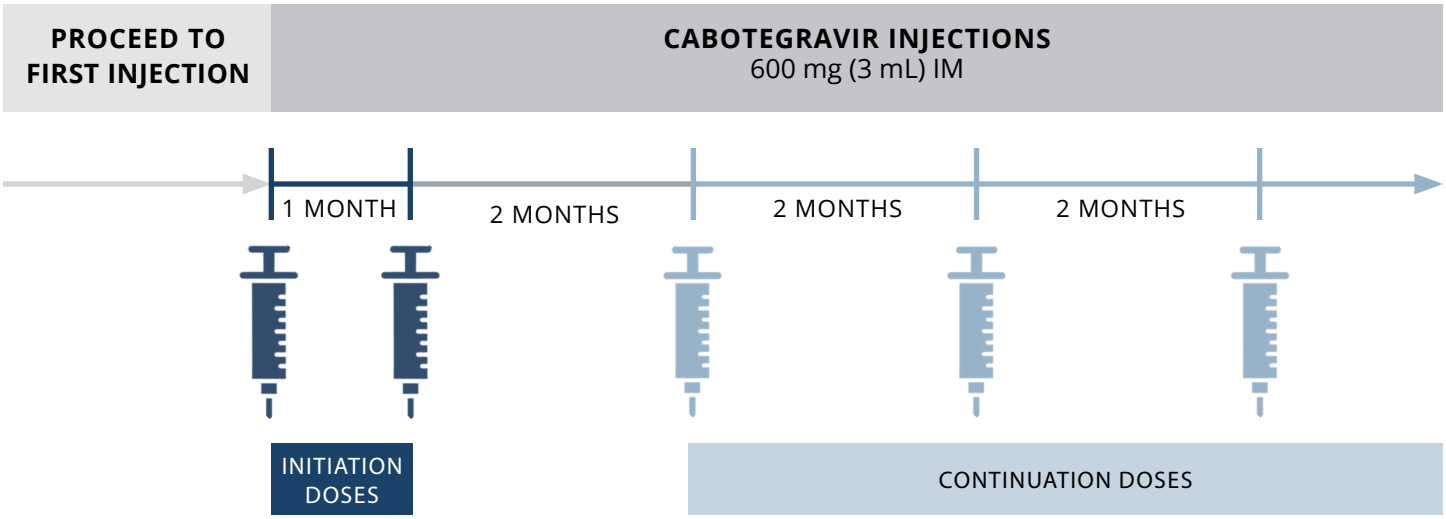


B. 2-inch needle

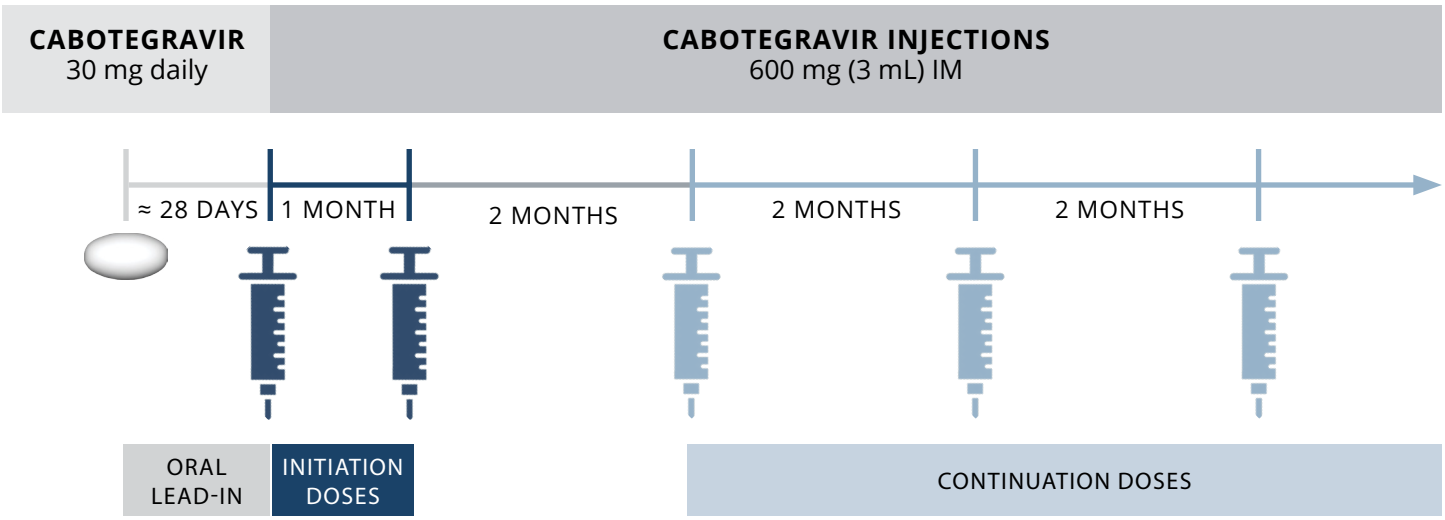


DOSING SCHEDULES: DIRECT TO INJECT & OPTIONAL ORAL LEAD-IN

Dosing schedule: direct-to-inject (without optional oral lead in)



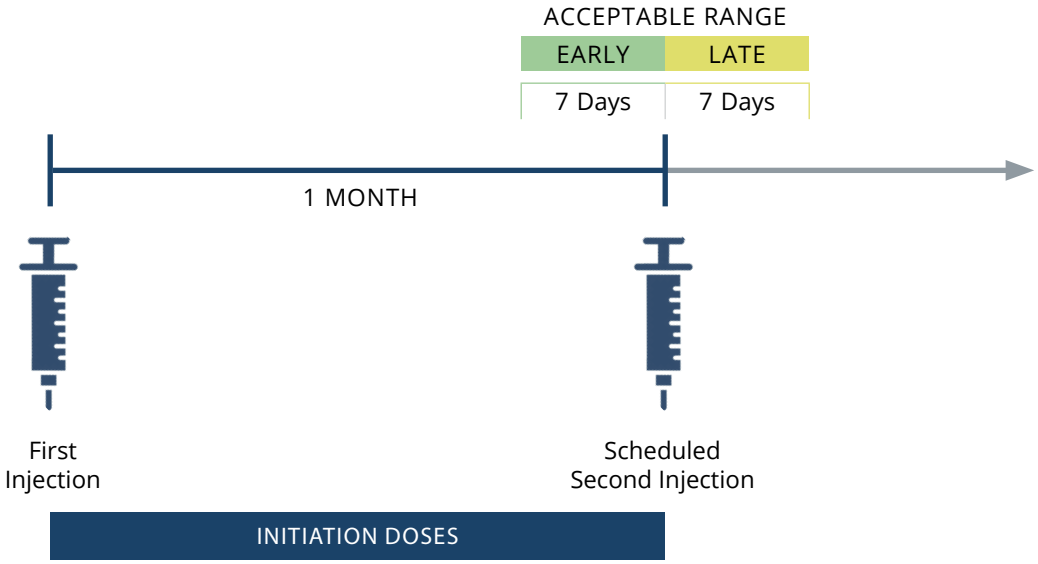
Dosing schedule: with optional oral lead-in



ACCEPTABLE RANGE FOR DOSING

Acceptable dosing range for second initiation injection

After the first CAB-LA initiation dose has been administered, the acceptable range for administering the second initiation dose is 7 days before OR after a date of one month from the prior injection.

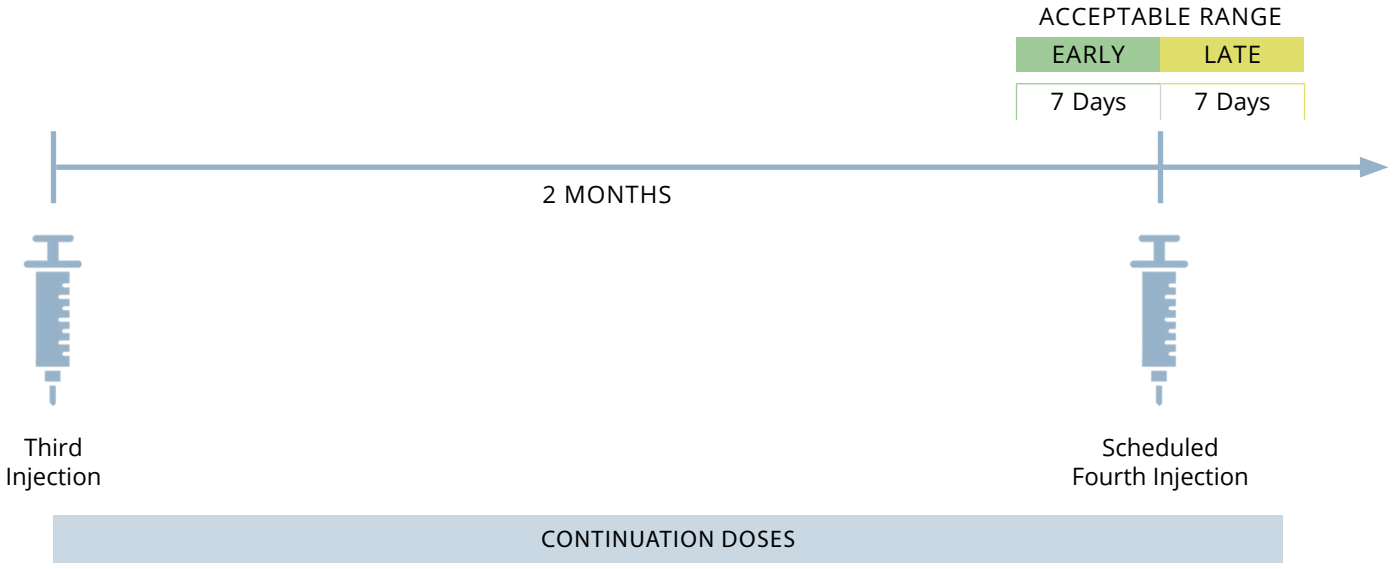


EDITOR'S NOTE

For the second initiation dose of CAB-LA we strongly recommend NOT giving this dose late. This recommendation is based on observed low trough concentrations that occur between the first and second injection in some people. It is ideal to give the second injection 21-28 days after the first injection.

Acceptable dosing range for continuation injections

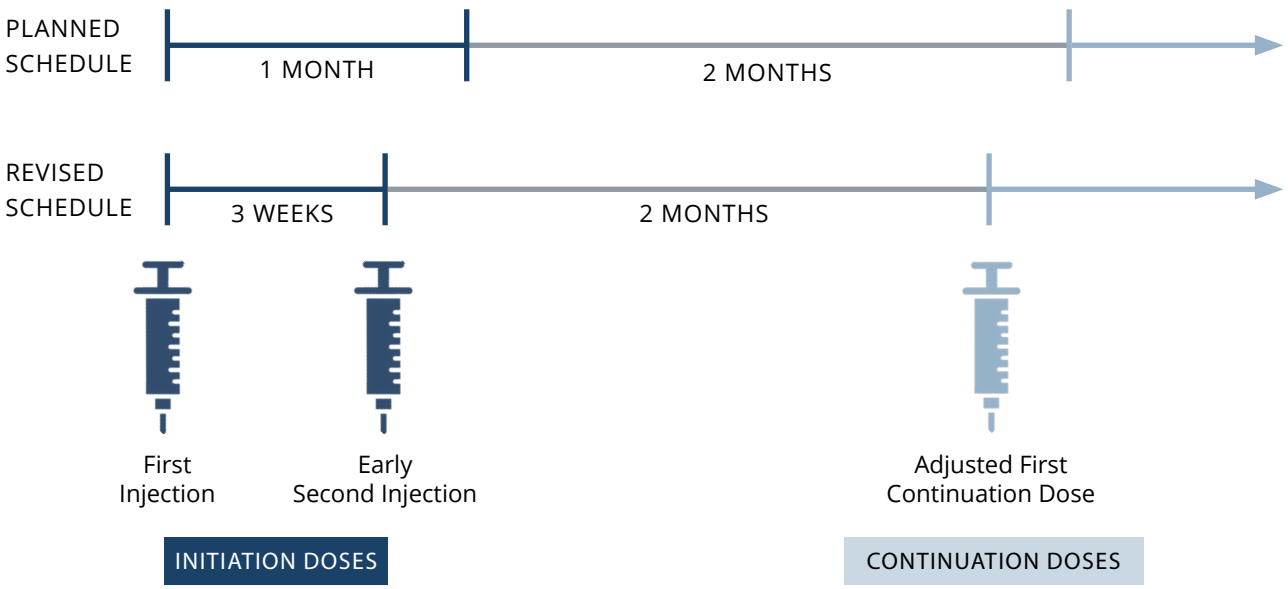
For all continuation injections, the acceptable range for administering CAB-LA is 7 days before or after a date of 2 months from the prior injection.



ACCEPTABLE RANGE FOR DOSING — EXAMPLES

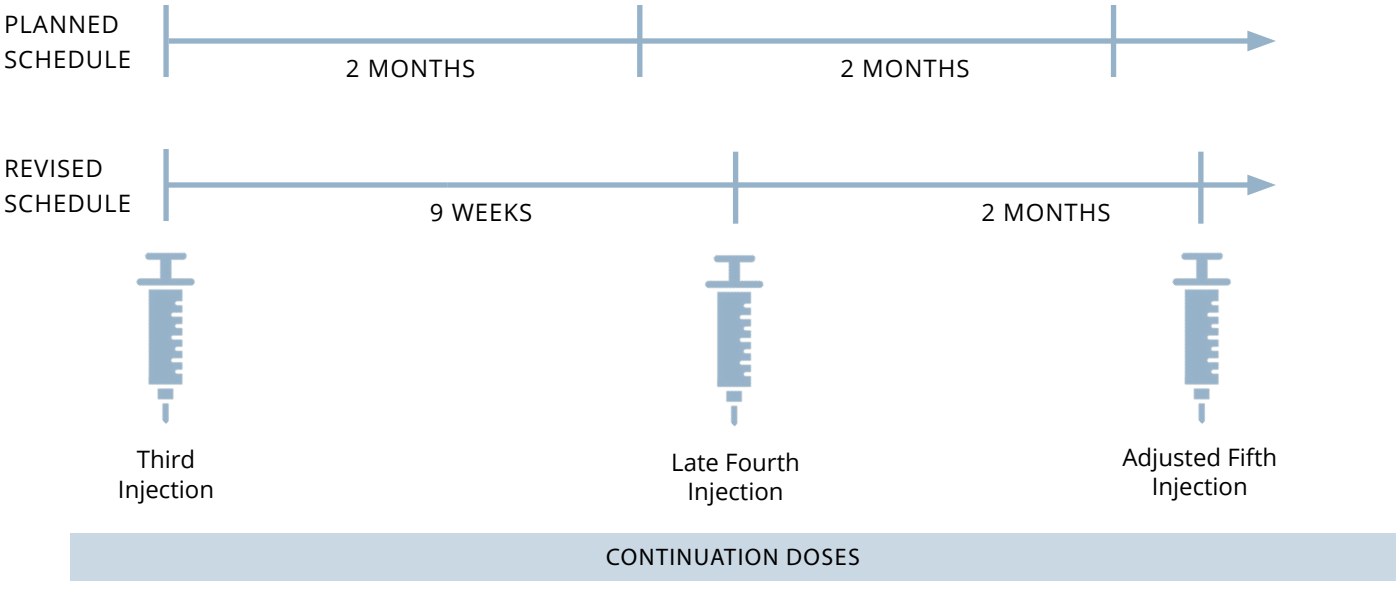
Example: Subsequent dosing after EARLY injection

If a dose of injectable cabotegravir is given EARLY, the timing of the next dose should be based on the date when the early dose was given and not on the date of the original planned schedule.



Example: Subsequent dosing after LATE injection

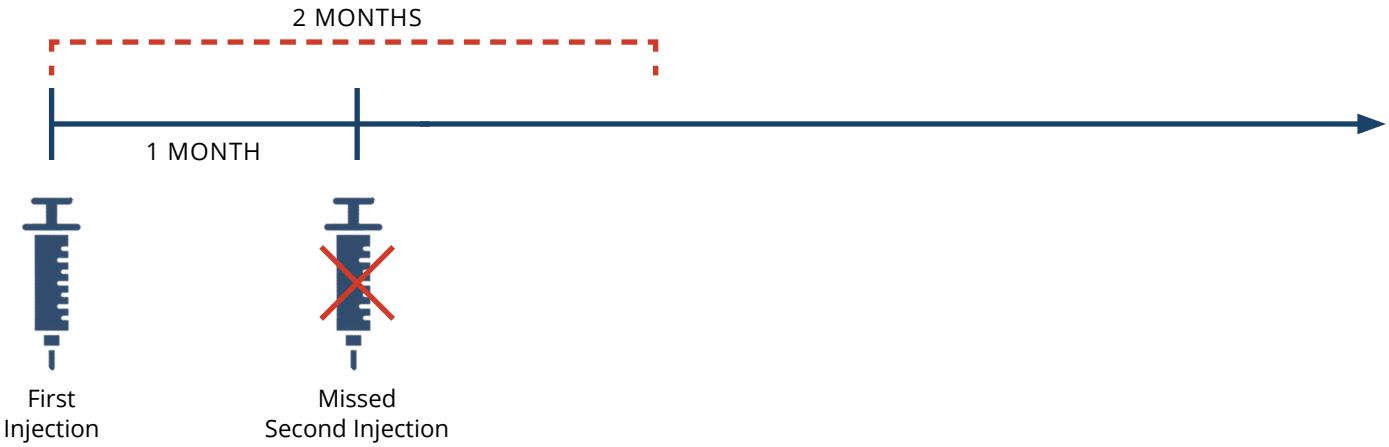
If a dose of injectable cabotegravir is given LATE, the timing of the next dose should be based on the date when the late dose was given and not on the date of the original planned schedule.



UNPLANNED MISSED DOSES

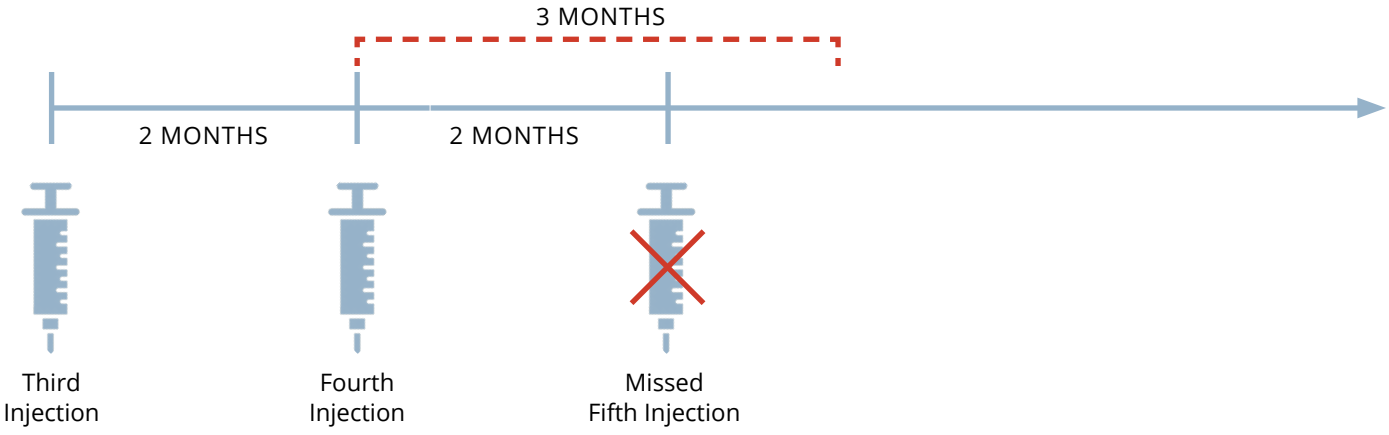
If second initiation injection is MISSED, recommendation based on time since first injection:

≤2 MONTHS	>2 MONTHS
Administer 600 mg (3 mL) cabotegravir injection as soon as possible, then continue to follow the every 2-month injection dosing schedule.	Restart with 600 mg (3 mL) cabotegravir injection, followed by a second 600 mg (3 mL) initiation injection dose 1 month later. Then continue with every 2-month injection dosing schedule thereafter.



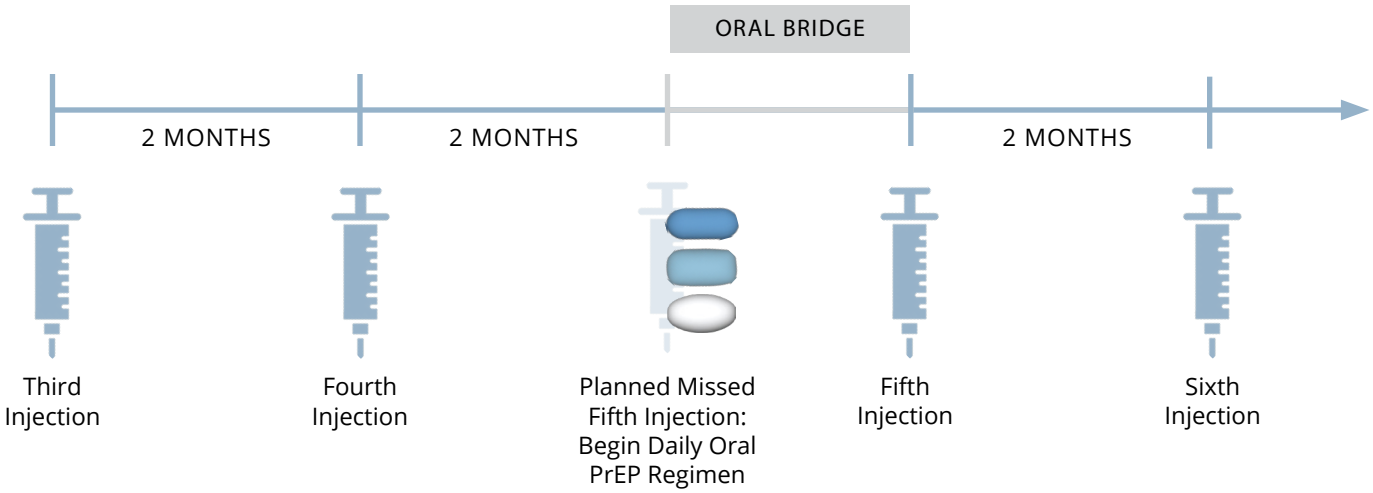
If third or later injection is MISSED, recommendation based on time since prior injection:

≤3 MONTHS	>3 MONTHS
Administer 600 mg (3 mL) cabotegravir injection as soon as possible, then continue to follow the every 2-month injection dosing schedule.	Restart with 600 mg (3 mL) cabotegravir injection, followed by a second 600 mg (3 mL) initiation injection dose 1 month later. Then continue with every 2-month injection dosing schedule thereafter.



PLANNED MISSED DOSES

If an individual plans to be more than 7 days delayed in receiving a scheduled every-2-month injection visit, take oral cabotegravir (30 mg tablet) OR a recommended oral daily HIV PrEP regimen (tenofovir DF-emtricitabine [TDF-FTC] or tenofovir alafenamide-emtricitabine [TAF-FTC]). The first dose of the oral PrEP bridge should be taken approximately 2 months after the last injection of CAB-LA. Restart the CAB-LA injections as soon as possible. If oral bridge dosing is needed for longer than 2 months, oral cabotegravir should not be used.

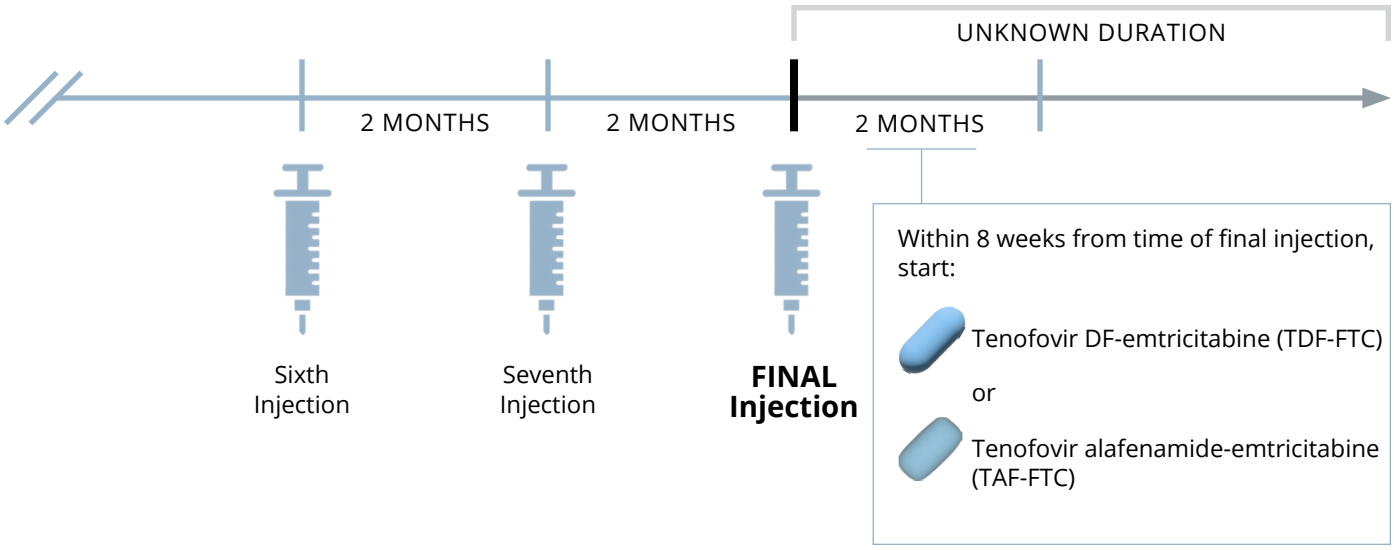


EDITOR'S NOTE

Accessing oral cabotegravir for oral bridge dosing has been difficult. Thus, instead of using oral cabotegravir as the oral bridge, we recommend using daily oral tenofovir DF-emtricitabine (TDF-FTC) or tenofovir alafenamide-emtricitabine (TAF-FTC) as the oral bridge, unless there is a contraindication. Note that TAF-FTC is not recommended as HIV PrEP with receptive vaginal sex. If TDF-FTC or TAF-FTC is used for an oral bridge, it is important to check a serum creatinine level (to estimate creatinine clearance) and hepatitis B status (since these agents have activity against hepatitis B virus). Hepatitis B virus and may cause a hepatic flare if abruptly stopped.

WHEN STOPPING LONG-ACTING INJECTABLE CABOTEGRAVIR (CAB-LA)

CABOTEGRAVIR INJECTIONS 600 mg (3 mL) IM	TAIL PHASE
	For persons with ongoing risk for HIV acquisition, all available HIV prevention strategies should be leveraged including the use of oral HIV PrEP (and within 8 weeks of stopping CAB-LA). Continue follow-up visits quarterly for 12 months.



EDITOR'S NOTE

The choice for the oral HIV PrEP medication should be chosen based on appropriate indications and recommendations. The duration of the oral HIV PrEP medications will depend on the ongoing risk for HIV acquisition and the need for HIV PrEP. Note that tenofovir alafenamide-emtricitabine (TAF-FTC) is not recommended as HIV PrEP with receptive vaginal sex.

ESTABLISHED AND POTENTIALLY SIGNIFICANT DRUG INTERACTIONS

Drug Interactions with Long-Acting Injectable Cabotegravir (CAB-LA) for HIV PrEP*		
Concomitant Drug Class: Drug Name	**Effect on Concentration**	**Clinical Comment**
Anticonvulsants: Carbamazepine Oxcarbazepine Phenobarbital Phenytoin	↓ Cabotegravir	Coadministration is contraindicated with injectable cabotegravir due to potential for significant decreases in plasma concentration of injectable cabotegravir.
Antimycobacterials: Rifampin Rifapentine	↓ Cabotegravir	
Antimycobacterial: Rifabutin	↓ Cabotegravir	When rifabutin is started before or concomitantly with the first initiation injection of cabotegravir, the recommended dosing of cabotegravir is one 600-mg (3-mL) injection, followed 2 weeks later by a second 600-mg (3-mL) initiation injection and monthly thereafter while on rifabutin. When rifabutin is started at the time of the second initiation injection or later, the recommended dosing schedule of cabotegravir is 600 mg (3 mL) monthly while on rifabutin. After stopping rifabutin, the recommended dosing schedule of cabotegravir is 600 mg (3 mL) every 2 months.
Based on drug interaction study results, the following drugs can be coadministered with cabotegravir or given after discontinuation of cabotegravir (antiretrovirals and non-antiretrovirals) without a dose adjustment: midazolam, antidepressants, oral contraceptives containing levonorgestrel and ethinyl estradiol.		

*This table is based on information in this cabotegravir (*Apretude*) prescribing information.

EDITOR'S NOTE
For more detailed information about potential drug interactions with cabotegravir, see the University of Liverpool: HIV Drug Interaction Tracker

Table based on 2021 CDC Clinical Practice Guidelines for HIV PrEP

Laboratory Evaluation in Persons Receiving Injectable Cabotegravir (CAB-LA) for HIV PrEP

TEST	Initial visit	1 month	Q2 months	Q4 months	Q6 months	Q12 months	When stopping
 HIV-1 RNA	ALL*	ALL	ALL				ALL
 HIV Antigen/ Antibody	ALL*¶	ALL¶	ALL¶				ALL¶
 Syphilis	ALL			MSM/TGW	MSW/WSM		MSM/TGW
 Gonorrhea	ALL			MSM/TGW	MSW/WSM		MSM/TGW
 Chlamydia	ALL			MSM/TGW	MSW/WSM		MSM/TGW
 Hepatitis B Serology	ALL#						
 Hepatitis C Serology	ALL#					MSM/TGW	
 Pregnancy Test	ALL^			ALL^			

LEGEND:

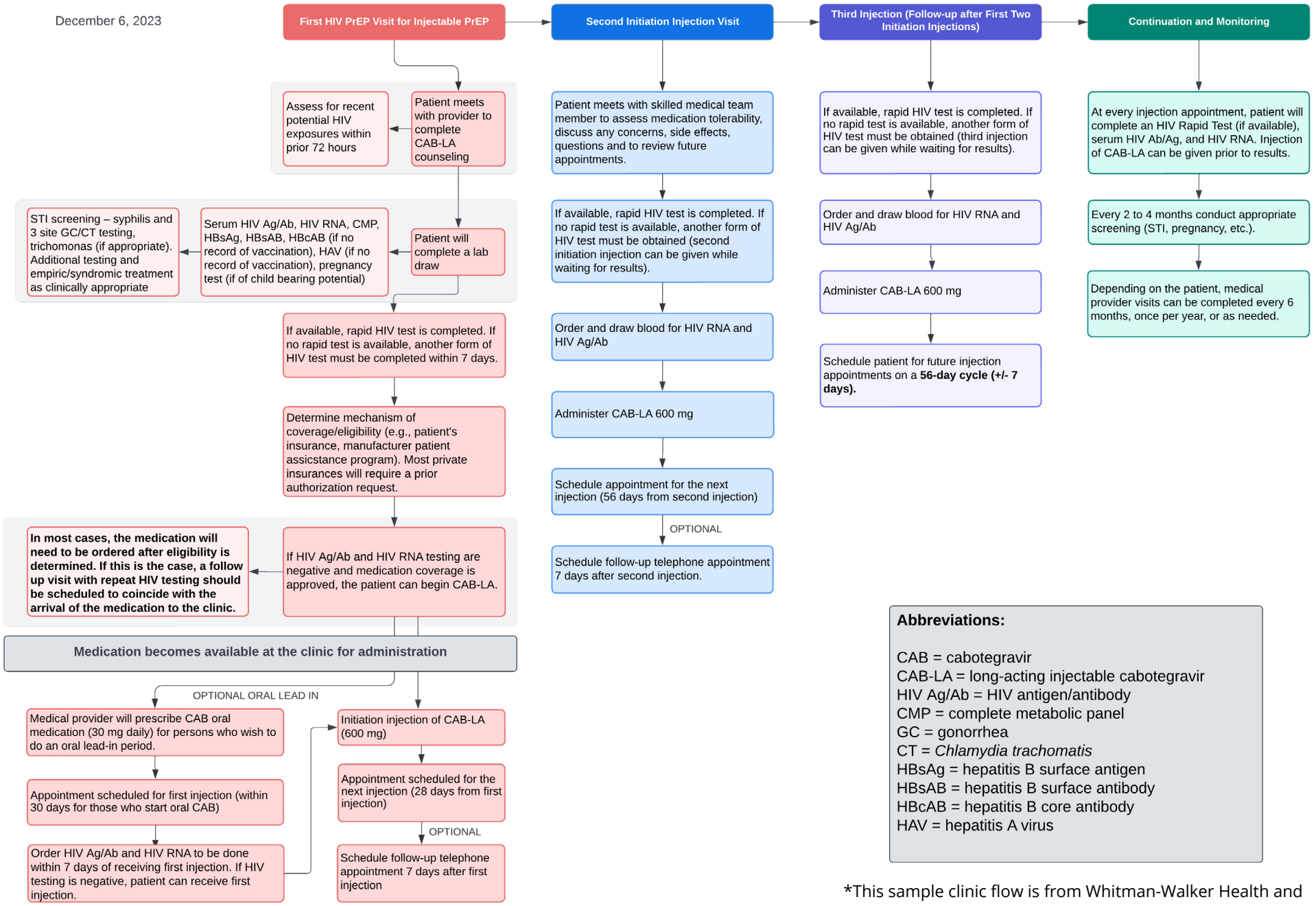
- * Perform within 7 days of starting HIV PrEP. If an oral cabotegravir lead-in is used, the initial HIV testing should be done within 7 days of starting the oral lead-in and repeated within 7 days of the first initiation dose.
- ¶ Laboratory-based preferred. Point of care blood acceptable but oral fluid testing not recommended.
- # One-time screening recommended for all adults in the United States
- ^ For persons with childbearing potential; advised for counseling purposes

ABBREVIATIONS:
MSM = men who have sex with men; TGW = transgender woman; MSW = men who have sex with women; WSM = women who have sex with men

EDITOR'S NOTES

1. Results for the HIV RNA and Ag/Ab should be available prior to administering the first cabotegravir initiation injection. For all subsequent injections, the laboratory studies can be drawn on the same day the injection is given.
2. Individuals who develop symptoms consistent with an STI should undergo prompt STI testing and receive appropriate treatment as clinically indicated; this evaluation should occur regardless of when the next routine STI screening is due.

SAMPLE CLINIC FLOW FOR INITIATING CABOTEGRAVIR FOR HIV PREP*



Abbreviations:

CAB = cabotegravir
CAB-LA = long-acting injectable cabotegravir
HIV Ag/Ab = HIV antigen/antibody
CMP = complete metabolic panel
GC = gonorrhea
CT = *Chlamydia trachomatis*
HBsAg = hepatitis B surface antigen
HBsAB = hepatitis B surface antibody
HBcAB = hepatitis B core antibody
HAV = hepatitis A virus

*This sample clinic flow is from Whitman-Walker Health and was adapted and modified for this guide with permission.

NATIONAL CLINICIAN CONSULTATION CENTER
Translating science into care

The National Clinician Consultation Center (NCCC) provides free expert consultation and guidance for clinicians on providing HIV PrEP, including:

- Medication initiation
- Long-acting injectable cabotegravir for HIV PrEP
- Ongoing follow-up in persons receiving HIV PrEP
- Diagnosing HIV in persons receiving HIV PrEP
- Initiation of antiretroviral therapy for persons receiving HIV PrEP who are diagnosed with HIV

Call for a PHONE CONSULTATION
(855) 448-7737 or (855) HIV-PrEP
Monday – Friday, 9 a.m. – 8 p.m. ET

To Submit Your Case Online
Go to the NCCC Web Site (https://nccc.ucsf.edu/clinician-consultation/prep-pre-exposure-prophylaxis/) or scan the QR code above

Note: The *National HIV PrEP Curriculum* does not provide clinical consultation or medical advice.

HPTN 083

Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women

Summary

Long-acting injectable cabotegravir (CAB-LA) was superior to daily oral tenofovir DF-emtricitabine (TDF–FTC) in preventing HIV infection among cisgender men who have sex with men (MSM) and transgender women (TGW) who have sex with men

Study Design

Randomized, double-blind, double-dummy, noninferiority trial

Participants

Overall

4,566
HIV-seronegative adults

Subgroups

3,992
Cisgender MSM

570
TGW who have sex with men

Interventions

Cabotegravir
Oral cabotegravir lead-in followed by CAB-LA

n = 2,282

TDF-FTC
Daily oral tenofovir DF-emtricitabine

n = 2,284

Results

	Cabotegravir		TDF-FTC	
New HIV Infections	13		39	
Incident HIV Infection (per 100 person-years)	0.41 Overall	0.39 0.54	1.22 Overall	1.14 1.80

Results were readjudicated, demonstrating 58 observed infections overall: 16 with CAB and 42 with TDF-FTC, resulting in HIV incidence of 0.37 in CAB group (95% CI 0.19 to 0.65)

Source: Landovitz RJ, Donnell D, Clement ME, et al. Cabotegravir for HIV Prevention in cisgender men and transgender women. N Engl J Med. 2021;385:595-608. [PMID: 34379922]

HPTN 084

Cabotegravir for HIV Prevention in Cisgender Women

Summary

Long-acting injectable cabotegravir (CAB-LA) was superior to daily oral tenofovir DF-emtricitabine (TDF-FTC) for preventing HIV infection among cisgender women

Study Design

Randomized, double-blind, double-dummy, superiority trial

Participants

3,224
HIV-seronegative cisgender women

18 - 45
Years of age

20
Sites in Sub-Saharan Africa

Interventions

Cabotegravir
Oral cabotegravir lead-in followed by CAB-LA

n = 1,614

TDF-FTC
Daily oral tenofovir DF-emtricitabine

n = 1,610

Results

	Cabotegravir	TDF-FTC
New HIV Infections	4	36
Incident HIV Infection (per 100 person-years)	0.20 (95% CI 0.06-0.52)	1.85 (95% CI 1.3-2.57)
HIV Risk Reduction	88% lower risk of new HIV infections in CAB-LA arm; superiority of CAB-LA driven by adherence advantage over TDF-FTC	

Source: Delany-Moretlwe S, Hughes JP, Bock P, et al. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. Lancet. 2022;399:1779–89. [PMID: 35378077]

FREQUENTLY ASKED QUESTIONS

1. **Do we recommend using an oral cabotegravir lead in?**

   For most persons interested in taking injectable cabotegravir (CAB-LA), we do not believe the 28-day oral cabotegravir lead-in is needed. The downside of using an oral cabotegravir lead-in is that it requires adherence with oral medication, which may be problematic in a person who has already self-selected their preference to receive CAB-LA over oral HIV PrEP. For persons with a history of multiple drug allergies or very poor tolerance to medications, it is reasonable to use an oral cabotegravir lead in.

2. **In people with high body mass index (BMI), should a longer injection needle be used?**

   The most important aspect of drug delivery with injectable cabotegravir (CAB-LA) is to ensure the drug makes it into the muscle. For most people who have a body mass index (BMI) less than 30 kg/m^2, the standard 1.5-inch needle that is included in the packet is adequate. For some individuals with a higher BMI, particularly if 30 kg/m^2 or greater, a longer (2 inch) needle may be required; the 2-inch needles are not included in the packets. There are no strict rules on the size of needles related to BMI since individuals distribute fat differently. For clinics administering CAB-LA, we strongly recommend planning ahead and obtaining a stock of 2-inch needles in the event they are needed. In addition, there have been some stock-outs of 2" needles of smaller gauge (e.g., 25 or 23 gauge), but note there is no requirement for use of needle of a certain gauge, except that the viscosity of the product may make it take longer to accomplish the injection with larger gauge (smaller bore size) needles.

3. **Can long acting injectable cabotegravir (CAB-LA) be used in someone who has gluteal/buttock implants (fillers)?**

   The answer to this question is not straightforward. First, it is important to note that the preferred and recommended site for CAB-LA administration is the ventrogluteal region; the alternative and acceptable site is the dorsogluteal (upper outer quadrant) region. Second, it is important to ask what cosmetic procedures were performed (e.g., gluteal implants, fillers, injections with materials such as silicone or fat) and to have a clear idea of all anatomic locations where the procedures were performed. (e.g., posterior buttock, lateral thigh, or inner thigh). We also recommend asking about any other surgical procedures that may have involved any gluteal region. If a person has previously received gluteal implants and/or fillers that are not overlapping with the ventrogluteal region, then it may be possible to administer CAB-LA. In general, however, gluteal injections are not recommended in the same anatomic area where an implant or filler has been placed for two reasons: (1) the injection needle may not reach the intramuscular space for proper administration of the medication and (2) the needle and medication may potentially damage or disrupt the implant or filler. At this time, needles longer than 2 inches for the administration of cabotegravir have not been recommended for CAB-LA injections. Given the complexity of this issue, expert consultation and/or radiographic evaluation of the location of the gluteal implant may be required to determine the adequate needle size that can reach the intramuscular space and if injections are possible in the ventrogluteal area. At this time, there is no evidence or FDA approval to administer intramuscular CAB-LA in a site other than ventrogluteal or dorsogluteal regions. In addition, CAB-LA injections should not be administered subcutaneously or intradermally at any body site.

4. **Is it OK to use long acting injectable cabotegravir (CAB-LA) when someone is taking oral hormonal contraceptives or gender-affirming hormone therapy?**

   Yes. Oral contraceptives and hormones use for gender-affirming care do not impact cabotegravir levels. Similarly, CAB-LA does not impact the effectiveness or safety of oral hormonal contraceptives or gender-affirming hormone therapy.

5. **Can you use an FDA-approved oral HIV PrEP regimen (tenofovir DF-emtricitabine [TDF-FTC] or tenofovir alafenamide-emtricitabine [TAF-FTC]) instead of oral cabotegravir as the oral bridge for planned missed doses?**

   The FDA recommended approach is to use oral cabotegravir 30 mg once daily for all oral bridging doses up to 2 months of bridging. We prefer the use of TDF-FTC or TAF-FTC as the oral bridge for several reasons. First oral cabotegravir can be very difficult to obtain in settings other that starting an oral lead-in. Second, if non-adherence occurs during the oral bridge, the impact of development of drug resistance with cabotegravir has more profound implications than resistance to TDF-FTC or TAF-FTC. Further, little is known about the efficacy of oral cabotegravir as HIV PrEP. The choice of TDF-FTC or TAF-FTC in this bridge setting should be based on recommended use for HIV PrEP. For example, TAF-FTC should not be used as an oral bridge in cisgender women who are taking HIV PrEP to prevent vaginal acquisition of HIV.

6. **How can the health care team proactively address the likely scenario that some patients taking long-acting injectable cabotegravir (CAB-LA) will be late for or miss their scheduled CAB-LA injection?**

   The CAB-LA prescribing information addresses both planned and unplanned missed injections. This categorization may confuse clinic staff. To simplify the work flow, some experts have not rigidly followed this distinction of planned or unplanned missed injections, and instead, attempt to proactively anticipate late or missed cabotegravir injections with all persons who are receiving CAB-LA, especially when serving communities where significant challenges may exist with frequent and regular clinic visits. To this end, during the same visit for discussing HIV PrEP injections and initiation, some clinics will proactively provide a prescription for a recommended daily oral HIV PrEP regimen—tenofovir DF-emtricitabine [TDF-FTC] or tenofovir alafenamide-emtricitabine [TAF-FTC]—along with instructions about when to initiate the oral HIV PrEP with late or missed doses. In this situation a 30-day supply with a maximum of 1 refill is typically given. This focus moves away from patient planned or unplanned missed doses and instead utilizes clinic and medical provider planning for any missed or late dose, regardless of the cause. With this strategy, it is important that TAF-FTC not be used for prevention of HIV acquisition through receptive vaginal sex. In addition, if TDF-FTC or TAF-FTC is prescribed, a baseline serum creatinine level should be checked (to estimate creatinine clearance and ensure it is safe to administer these medications) and hepatitis B status should be evaluated (since these agents have activity against hepatitis B virus and stopping and starting TDF-FTC or TAF-FTC in a person with hepatitis B could potentially cause a flare of hepatitis B). For persons maintaining TDF-FTC or TAF-FTC as a standby medication, it is important to track expiration dates if these medications are not used soon after a prescription is filled. Persons without HBV infection or immunity should receive hepatitis B immunization.

7. **If someone stops taking long-acting injectable cabotegravir (CAB-LA) and they have continued need for HIV PrEP, when do you need to start oral PrEP in relation to the last injection?**

   If someone is discontinuing long-acting injectable cabotegravir (CAB-LA) permanently, and they have ongoing risk for HIV acquisition, oral HIV PrEP with either tenofovir DF-emtricitabine (TDF-FTC) or tenofovir alafenamide-emtricitabine (TAF-FTC), as appropriate for the population, should be initiated no later than 8 weeks after the final cabotegravir injection. We recommend beginning the oral HIV PrEP regimen in the 7-to-8-week time frame after the final injection.

8. **If someone is taking oral HIV PrEP with tenofovir DF-emtricitabine (TDF-FTC) or tenofovir alafenamide-emtricitabine (TAF-FTC) (or completing the oral cabotegravir lead-in), is there expert guidance on transitioning to long-acting injectable cabotegravir (CAB-LA)?**

   First, if transitioning from an oral HIV PrEP regimen (TDF-FTC or TAF-FTC) to CAB-LA, it is important to exclude HIV infection by retesting with HIV-1/2 antigen-antibody and HIV-1 RNA, within 7 days prior to the first injection of CAB-LA. To provide continuity of HIV PrEP, we recommend avoiding any gap between stopping the oral medication and the first injection of CAB-LA. Further, in this situation, to provide maximal protection, we recommend ideally overlapping and extending the oral HIV PrEP medication for 7 days after the first injection of CAB-LA; the rationale for this recommendation is to provide additional protection while the cabotegravir levels may not yet have reached adequate levels for HIV prevention. For analogous reasons, some experts have used a similar overlap strategy when transitioning from the oral cabotegravir lead-in to the first injection of CAB-LA.

9. **If someone acquires HIV while receiving long-acting injectable cabotegravir (CAB-LA), what initial antiretroviral regimen is recommended?**

   In this situation, we strongly recommend immediately obtaining an HIV drug resistance genotype, which should include a standard and an integrase genotype. If the HIV RNA level is too low to perform a standard genotype, then some experts would consider attempting an archived (proviral) HIV DNA genotype, but there is sparse experience with this approach. While waiting for results, we recommend starting empiric antiretroviral treatment with 2 nucleoside reverse transcriptase inhibitors (tenofovir alafenamide-emtricitabine [TAF-FTC] or tenofovir DF-emtricitabine [TDF-FTC]) in combination with a boosted protease inhibitor (e.g., darunavir-cobicistat if the person is not pregnant). Most experts would not favor empirically starting treatment with bictegravir-tenofovir alafenamide-emtricitabine or dolutegravir plus 2 nucleoside reverse transcriptase inhibitors. In this situation, expert consultation should be obtained if the clinician does not have significant experience in managing drug-resistant HIV.

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