Injectable ART Overview

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Objectives

- Discuss cabotegravir and cabotegravir/rilpivirine prescribing and administration parameters
- Explore present and future cabotegravir and cabotegravir/rilpivirine use considerations in clinical practice
- Analyze drug-drug interaction concerns related to cabotegravir and rilpivirine when co-administered with other medications

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Disclosure(s)

- I have nothing to disclose.

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Disclosures

- *This program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1OHA30535 as part of an award totaling $4.2m. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov.*
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AETC Programs and National Centers HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
- **National Clinician Consultation Center –** provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc/ucsf.edu
- **National HIV Curriculum –** provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu

AETC AIDS Education & Training Center Program Southeast

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Diagnosis of HIV infection by patient demographics, 2021 United States | Ending the HIV Epidemic Plan

Ending the HIV Epidemic

Overall Goal: Decrease the estimated number of new HIV infections to 9,300 by 2025 and 3,000 by 2030.

There were **32,100 estimated new HIV infections** in the US in 2021. Of those:

- **70%** (22,400) were among gay, bisexual, and other men who reported male-to-male sexual contact*
- **22%** (7,100) were among people who reported heterosexual contact
- **8%** (2,500) were among people who inject drugs

*Includes infections attributed to male-to-male sexual contact and injection drug use (men who reported both risk factors).

HIV Infections Among Gay, Bisexual, and other Men Who Reported Male-to-Male Sexual Contact[d]

In 2021, gay, bisexual, and other men who reported male-to-male sexual contact accounted for 70% (22,400) of the 32,100 estimated new HIV infections and 86% of estimated infections among all men.

HIV Incidence. Retrieved from https://www.cdc.gov/hiv/statistics/overview/in-us/incidence.html . Accessed on February 23, 2024.

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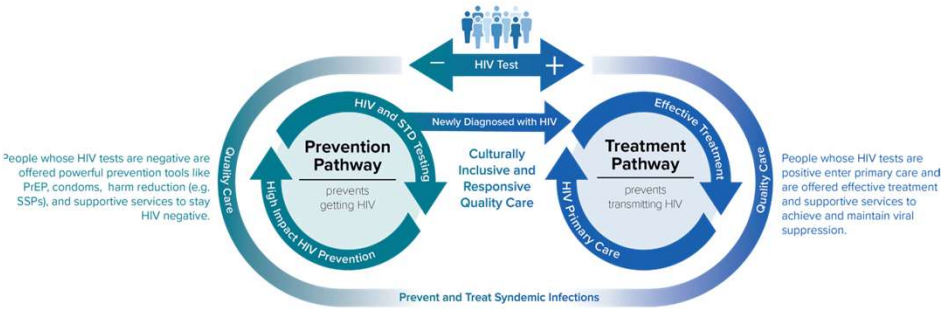
Status Neutral Approach

Status Neutral HIV Prevention and Care



People whose HIV tests are negative are offered powerful prevention tools like PrEP, condoms, harm reduction (e.g. SSPs), and supportive services to stay HIV negative.

People whose HIV tests are positive enter primary care and are offered effective treatment and supportive services to achieve and maintain viral suppression.

Follow CDC guidelines to test people for HIV. Regardless of HIV status, quality care is the foundation of HIV prevention and effective treatment. Both pathways provide people with the tools they need to stay healthy and stop HIV.

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Image credit: https://www.cdc.gov/hiv/images/division-of-hiv-prevention/strategic-plan/graphic-dhp-strategic-plan-supplement-status-neutral-hiv-prevention-and-care-framework.png

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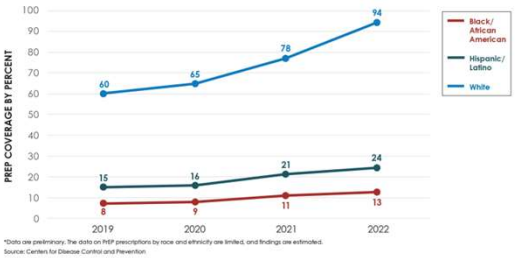
PrEP Use Data

TRENDS IN PREP PRESCRIPTIONS AMONG PEOPLE WHO COULD BENEFIT, BY RACE/ETHNICITY, 2019-2022*



*Data are preliminary. The data on PrEP prescriptions by race and ethnicity are limited, and findings are estimated.
Source: Centers for Disease Control and Prevention

The 2022 preliminary data indicate that more than 40% of males who could benefit from PrEP were prescribed it, compared with 15% of females.

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Cabotegravir (CAB) Overview

- Long-acting injectable for prevention of sexual transmission of HIV-1
- Gluteal intramuscular (IM) administration only
- Integrase inhibitor medication similar to other drugs available on the market within this class

Oral lead-in period may be used for approximately 1 month prior to initiation

Must be administered in healthcare facility

Initiate with single injection given 1 month apart, **then continue Q2 months**

Monotherapy administration for PrEP. It should not be administered with TAF/FTC or TDF/FTC.

Apretude [package insert]. GlaxoSmithKline, Research Triangle Park, NC: 2021

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Cabotegravir route of administration

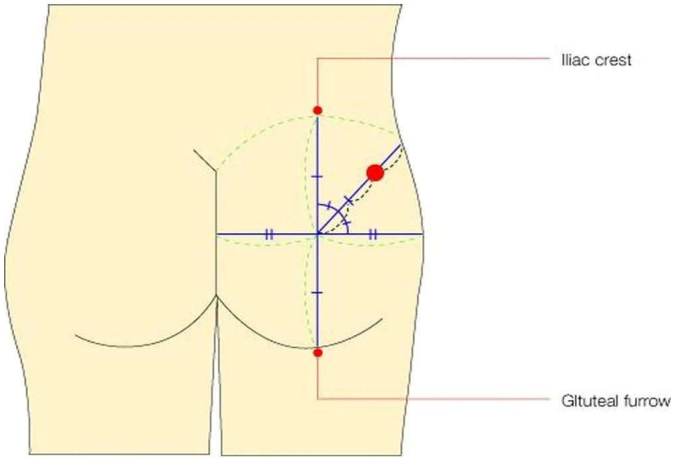

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Image credit: https://www.gtsimulators.com/collections/koken/products/koken-gluteal-intramuscular-injection-model-lm-027

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Cabotegravir administration

- If refrigerated, vial should be brought to room temperature prior to administration
- Cabotegravir can remain in the syringe for up to 2 hours prior to administration
- Injecting 1 ml of air into the vial makes it easier to draw up the medication into the syringe

Apretude [package insert]. GlaxoSmithKline, Research Triangle Park, NC: 2021

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Cabotegravir oral lead-in period (OPTIONAL)

- Oral cabotegravir taken for approximately 28 days
- Utilized to assess tolerability to medication
- Commonly used in complicated allergy histories

Apretude [package insert]. GlaxoSmithKline, Research Triangle Park, NC: 2021

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Anecdotal – Rationales for some entities foregoing oral-lead in period

Product retrieval

Separate company

Delays in medication receipt

Additional step

Added workload among staff

Likely most beneficial in extensive allergy histories

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Audience Response #1

Which statement about cabotegravir injection is correct?

a) Cabotegravir is self-administered as a subcutaneous injection monthly
b) Cabotegravir is the same medication used for oral PrEP but as an injection
c) Cabotegravir should only be used in people with an undetectable viral load
d) Cabotegravir is administered by healthcare personnel as an intramuscular injection once every two months

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Audience Response #1

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b) Cabotegravir is the same medication used for oral PrEP but as an injection
c) Cabotegravir should only be used in people with an undetectable viral load
d) **Cabotegravir is administered by healthcare personnel as an intramuscular injection once every two months**

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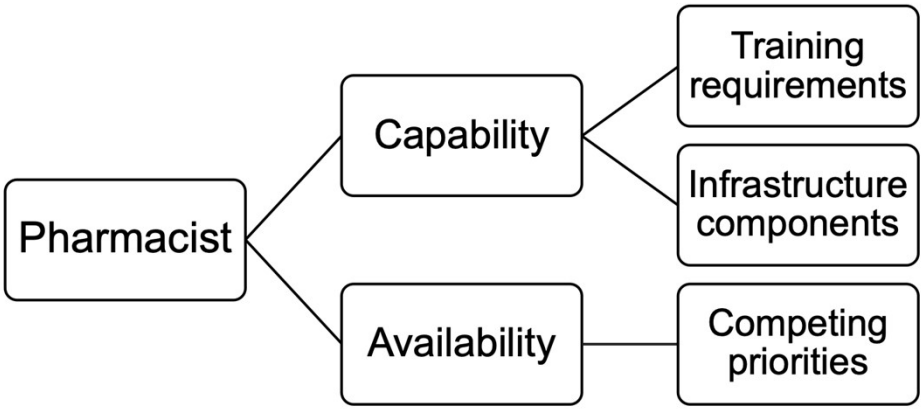
Should pharmacists be able to administer cabotegravir in pharmacies?



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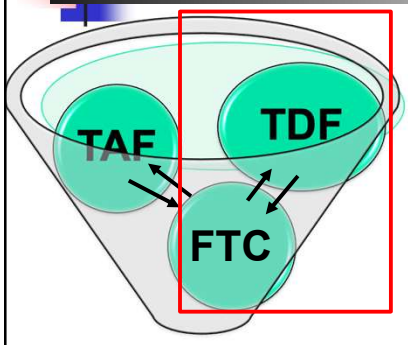
Comparison of FDA Approved Options for PrEP



CAB

Cabotegravir (CAB)

Integrase Strand Transfer Inhibitor

Nucleoside Reverse Transcriptase Inhibitors

http://clipart-library.com/injection-cliparts.html

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Efficacy of TDF/FTC vs Cabotegravir – HIV-1 prevention (HPTN 083)

Cabotegravir	TDF/FTC
n = 2278	n = 2281
HIV-1 infections = 12	HIV-1 infections = 39

Hazard Ratio: 12 /39 = 0.31

Interpretation:
Risk of HIV infection **reduced by 69%** with cabotegravir as compared to TDF/FTC

Application:
Cabotegravir was superior to TDF/FTC for HIV-1 prevention

APRETUDE PI. APRETUDE (cabotegravir extended-release injectable suspension) prescribing information. 2021.

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Top 5 reasons for study participants preferring cabotegravir as opposed to TDF/FTC (descending order) (n = 770)

- Prefers injections and rather avoid pills
- Cabotegravir demonstrated superiority to TDF/FTC
- Cabotegravir's convenience and easier adherence
- Concern about potential side effects from TDF/FTC
- Opportunity to participate in research

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Clement ME, CROI 2023: PS V6: #994

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Top 5 reasons for study participants preferring TDF/FTC as opposed to cabotegravir (descending order) (n = 33)

- Prefers pills and rather avoid injections
- Side effects of TDF/FTC are more known/reasonable
- Resistance concerns if cabotegravir does not work
- Challenging to coordinate recurring clinical visits
- Overall uncertainty about cabotegravir

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Clement ME, CROI 2023: PS V6: #994

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Identifying a cabotegravir administration date

Example target injection date of 15th

Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	**15**	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

- Preferable that same injection date is utilized every 2 months
- +/- **7 day** dosing window around the identified injection date

ViiV. Cabotegravir extended release injectable suspension [Apretude] for Pre-exposure Prophylaxis (PrEP). April 2023.

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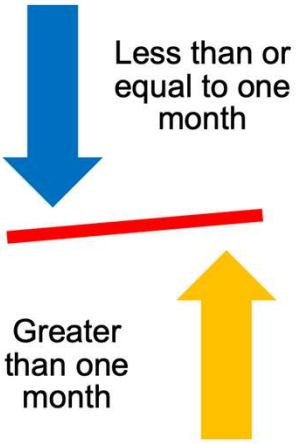
What happens if a cabotegravir injection dose is missed?

- If the time since the missed injection date is less than or equal to one month
  - Continue with injections on the last day of oral cabotegravir or within a 3-day period
  - Resume every 2-month dosing schedule
- If the time since the missed injection date is greater than one month
  - Restart initial injection series (2 injections separated by one month) on the last day of oral cabotegravir or within a 3-day period
  - Resume every 2-month dosing schedule



Confirmation of HIV-negative status required in above scenarios

Cabotegravir LA USPI. December 2021.

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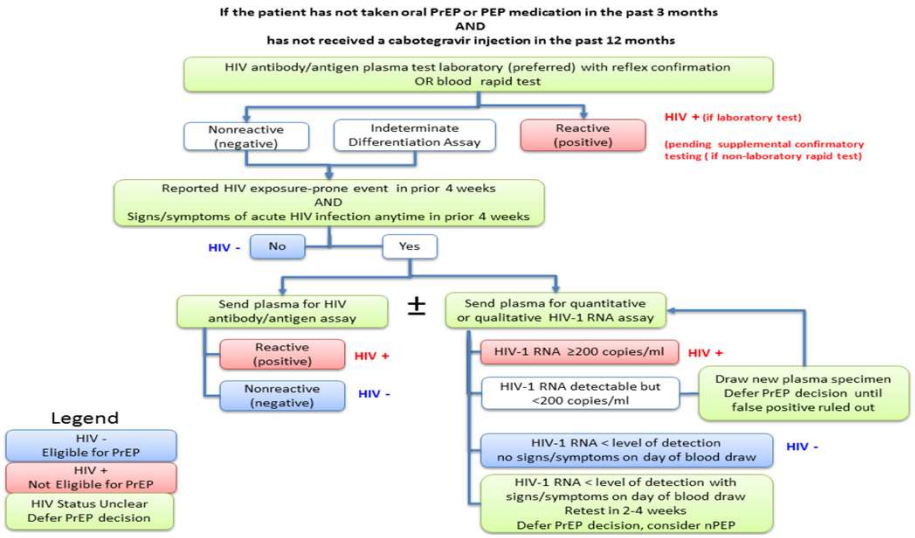
Figure 4a Clinician Determination of HIV Status for PrEP Provision to Persons without Recent Antiretroviral Prophylaxis Use



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CDC Clinical Practice Guideline: PrEP for the Prevention of HIV Infection in the United States . https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf Accessed September 24, 2023

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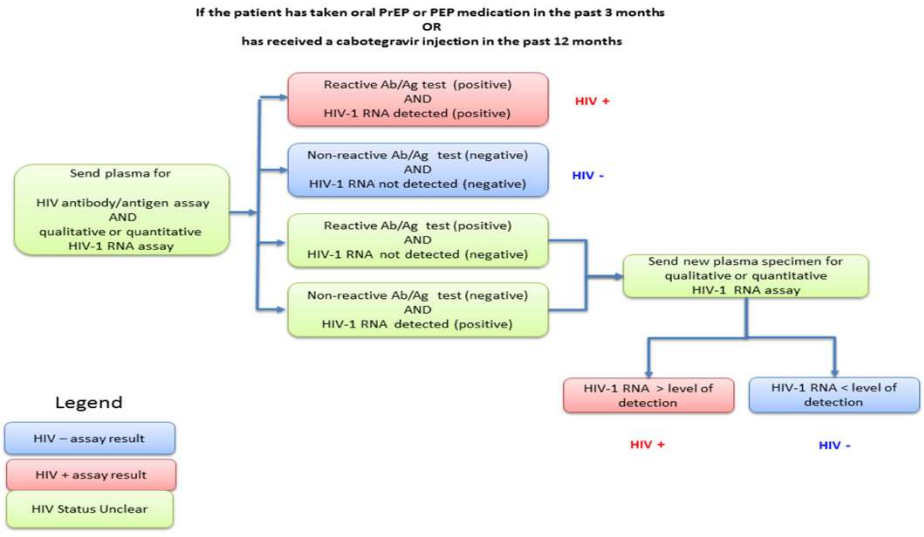
Figure 4b Clinician Determination of HIV Status for PrEP Provision to Persons with Recent or Ongoing Antiretroviral Prophylaxis Use



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CDC Clinical Practice Guideline: PrEP for the Prevention of HIV Infection in the United States . https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf Accessed September 24, 2023

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Audience Response #2

- A patient presents to a local community pharmacy with a request for the pharmacist on duty to administer cabotegravir to her to decrease her risk of HIV acquisition. What is a CORRECT pharmacist response?
  a) Yes, I will administer cabotegravir to you irrespective of your HIV status
  b) No, I will not administer cabotegravir to you as it is not approved for use in people identifying as female
  c) Yes, I will administer cabotegravir to you, provided that you are undetectable
  d) No, I will not administer cabotegravir to you as the current recommendations stipulate administration in a healthcare facility

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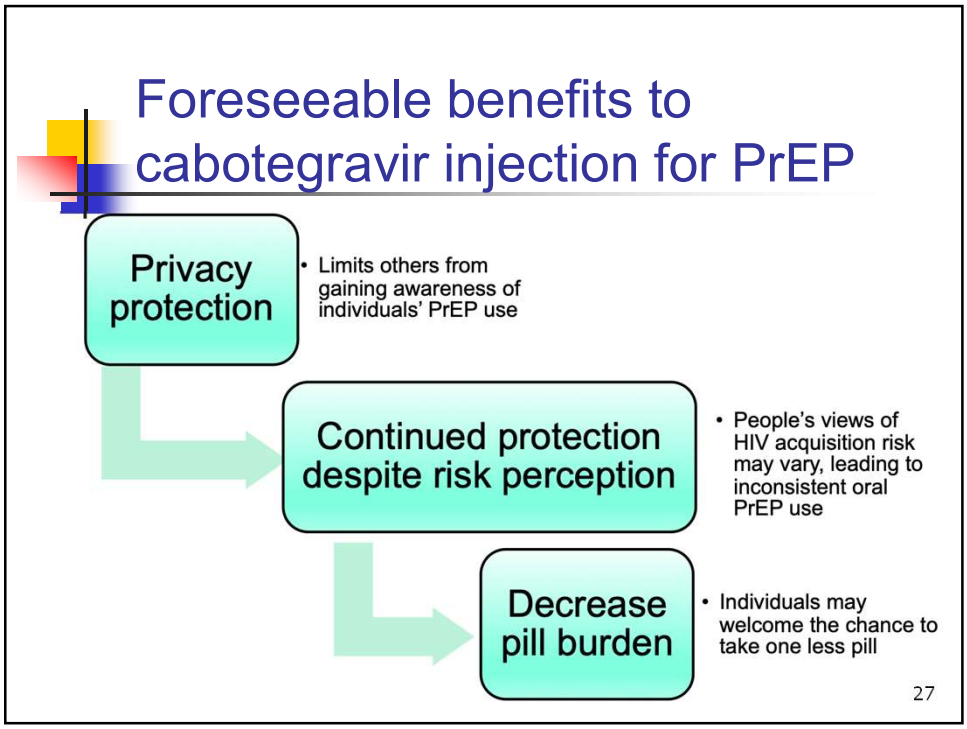
Foreseeable benefits to cabotegravir injection for PrEP
Privacy protection
• Limits others from gaining awareness of individuals' PrEP use
Continued protection despite risk perception
• People's views of HIV acquisition risk may vary, leading to inconsistent oral PrEP use
Decrease pill burden
• Individuals may welcome the chance to take one less pill
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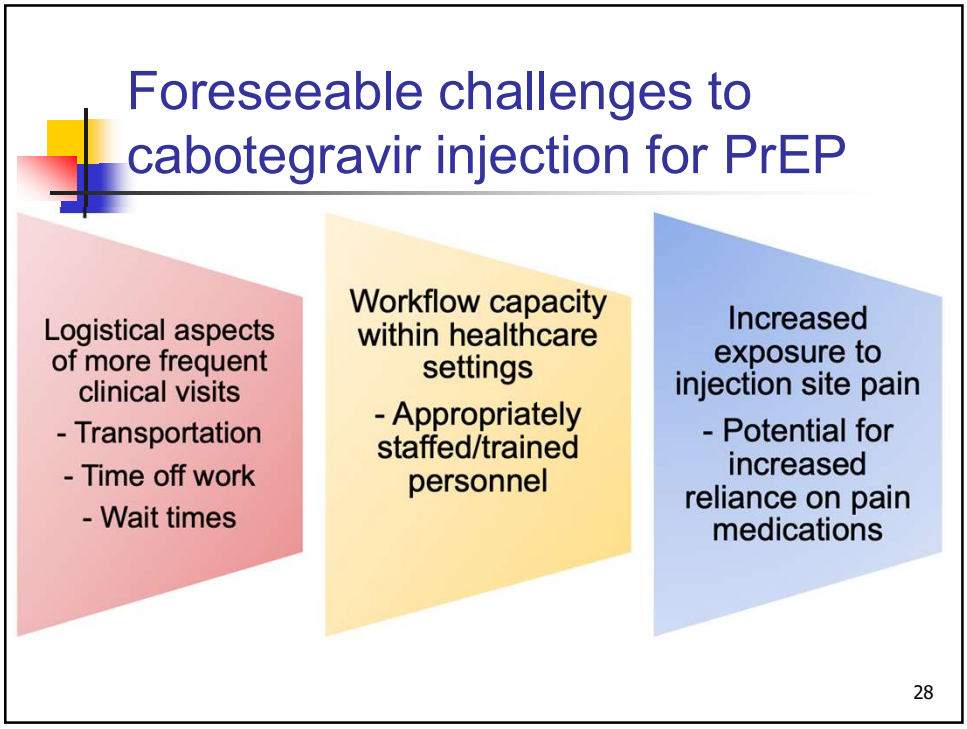
Foreseeable challenges to cabotegravir injection for PrEP
Logistical aspects of more frequent clinical visits
- Transportation
- Time off work
- Wait times
Workflow capacity within healthcare settings
- Appropriately staffed/trained personnel
Increased exposure to injection site pain
- Potential for increased reliance on pain medications
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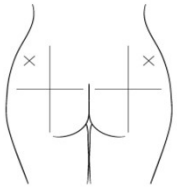
Examples of injections that may also be administered via intragluteal route

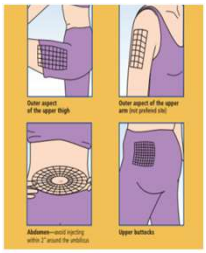
Testosterone
(typically self-administered)

- May also be given at alternate sites
- Other available formulations



Vitamin B_{12}
(typically self-administered)

- May also be given at alternate sites
- Other available formulations



Individuals using one or both of the above products may be less likely to initiate cabotegravir-based injections

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https://www.unimed.co.uk/wp-content/uploads/2020/05/B12-self-injecting.pdf https://www.med.umich.edu/1libr/SpinalCordInjuryProgram/IMselfInjectionTesto.pdf

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Clinically significant drug interactions with cabotegravir

Table 8. Drug Interactions with APRETUDE

Concomitant Drug Class: Drug Name	Effect on Concentration	Clinical Comment
Anticonvulsants: Carbamazepine Oxcarbazepine Phenobarbital Phenytoin	↓Cabotegravir	Coadministration is contraindicated with APRETUDE due to potential for significant decreases in plasma concentration of APRETUDE.
Antimycobacterials: Rifampin Rifapentine	↓Cabotegravir	
Antimycobacterial: Rifabutin	↓Cabotegravir	When rifabutin is started before or concomitantly with the first initiation injection of APRETUDE, the recommended dosing of APRETUDE 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 APRETUDE is 600 mg (3 mL) monthly while on rifabutin. After stopping rifabutin, the recommended dosing schedule of APRETUDE is 600 mg (3 mL) every 2 months.

↑ = Increase, ↓ = Decrease, ↔ = No change.

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Apretude [package insert]. GlaxoSmithKline, Research Triangle Park, NC: 2021

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Cabenuva

- Cabenuva is a long-acting (LA) HIV therapy which is the first approved by the FDA
- Approval of Cabenuva was announced **January 2021**
- Cabenuva is a drug indicated for administration via IM route in the buttocks **once a month** in a healthcare setting
  - One injection of **each** of the two drugs in Cabenuva (Cabotegravir and Rilpivirine)

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Cabenuva optional oral lead-in

Will the patient start with the optional oral lead-in?

- ○ No
- ◉ Yes

Prescribe 2 tablets (1x30-mg cabotegravir and 1x25-mg rilpivirine) to be taken once daily with a meal for approximately 1 month (at least 28 days) to assess tolerability.

Initiation injections should be administered on the last day of oral lead-in.

https://cabenuvahcp.com/dosing-and-administration/dosing/#drug-drug-interactions

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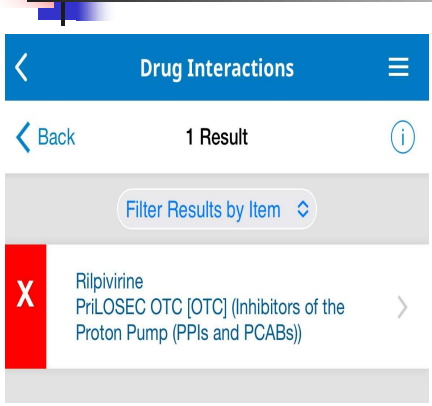
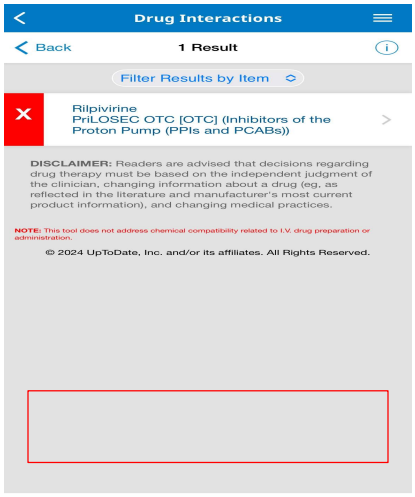
Oral rilpivirine DDI potential





DDI: Drug-Drug Interaction

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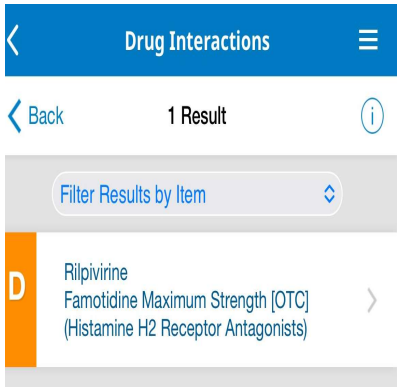
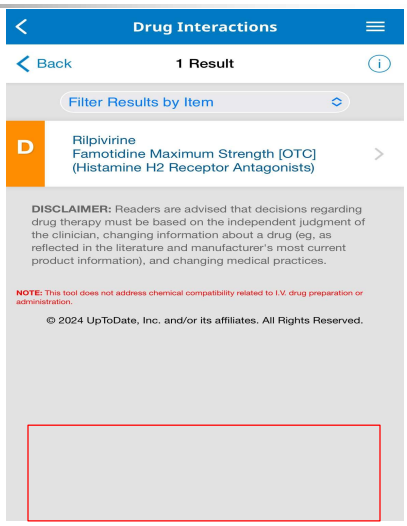
Oral rilpivirine DDI potential





DDI: Drug-Drug Interaction

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Who can take Cabenuva??

- Individuals who have been on 6 months of uninterrupted antiretroviral therapy (ART)
- Individuals with viral load less than 50 copies/ml
- Individuals who are 18 years old and above
- No history of treatment failure or known/suspected resistance to cabotegravir or rilpivirine

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Anecdotal feedback about Cabenuva's use in people with "detectable" viral loads

- Increasingly more common in clinical practice
  - Consistent theme that some providers rather initiate Cabenuva upon diagnosis than wait for undetectable status to be reached with oral ARV medications
  - Cabenuva's use in consumers with detectable viral load is considered an off-label approach
    - Strategy is not currently FDA-approved but likely in the future
- Noted limitation
  - Insurance companies less likely to cover therapeutic approaches that are inconsistent with product labeling

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Audience Response #3

- A provider is planning to initiate Cabenuva in a person newly with diagnosed HIV that does not have an undetectable viral load. Among these options, which is the provider MOST likely to initiate Cabenuva in a person with a detectable viral load?
  a) 300 copies/mL
  b) 3,000 copies/mL
  c) 30,000 copies/mL
  d) 300,000 copies/mL

Note: Cabenuva is indicated in persons living with HIV who have an undetectable viral load. Currently, use of Cabenuva in populations with detectable viral loads has not been FDA-approved.

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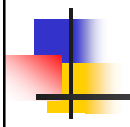

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