APRETUDE (cabotegravir)

Dosing and Administration Guide

INDICATION

APRETUDE is indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating APRETUDE (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF APRETUDE FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED HIV-1 INFECTION

Individuals must be tested for HIV-1 infection prior to initiating APRETUDE or oral cabotegravir, and with each subsequent injection of APRETUDE, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of APRETUDE by individuals with undiagnosed HIV-1 infection. Do not initiate APRETUDE for HIV-1 PrEP unless negative infection status is confirmed. Individuals who acquire HIV-1 while receiving APRETUDE for PrEP must transition to a complete HIV-1 treatment regimen.

Please see additional Important Safety Information throughout. Please click on the accompanying full Prescribing Information, including Boxed Warning and Instructions for Use, for APRETUDE.

Apretude
cabotegravir 200 mg/mL
extended-release injectable suspension

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What is APRETUDE?

APRETUDE is an injectable PrEP administered every other month

- APRETUDE (cabotegravir 600 mg [3 mL]) is an HIV-1 integrase strand transfer inhibitor (INSTI) in an extended-release injectable suspension for PrEP
- APRETUDE is for use as PrEP in at-risk individuals, including cisgender men, transgender women, and cisgender women weighing at least 35 kg to reduce the risk of sexually acquired HIV-1 infection
- Patients prescribed APRETUDE must have a negative HIV-1 test immediately prior to initiating APRETUDE (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP
- Before initiation of APRETUDE, carefully select individuals who agree to the required injection dosing and testing schedule, and counsel patients about the importance of adherence to help reduce the risk of HIV-1 infection and development of resistance
- APRETUDE is administered every 2 months after 2 initiation injections administered 1 month apart

This guide will provide information on:

- APRETUDE dosing kit and storage
- The APRETUDE dosing schedule
- Considerations prior to injection
- Managing missed injections
- Preparing and administering injections
- Frequently asked questions

PrEP=pre-exposure prophylaxis.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

- Do not use APRETUDE in individuals:
  - with unknown or positive HIV-1 status
  - with previous hypersensitivity reaction to cabotegravir
  - receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, and rifapentine

WARNINGS AND PRECAUTIONS

Comprehensive Management to Reduce the Risk of HIV-1 Infection:

- Use APRETUDE as part of a comprehensive prevention strategy, including adherence to the administration schedule and safer sex practices, including condoms, to reduce the risk of sexually transmitted infections (STIs). APRETUDE is not always effective in preventing HIV-1 acquisition. Risk for HIV-1 acquisition includes, but is not limited to, condomless sex, past or current STIs, self-identified HIV risk, having sexual partners of unknown HIV-1 viremic status, or sexual activity in a high prevalence area or network. Inform, counsel, and support individuals on the use of other prevention measures (e.g., consistent and correct condom use; knowledge of partner[s] HIV-1 status, including viral suppression status; regular testing for STIs)

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How APRETUDE is supplied, stored, and handled

APRETUDE is supplied in a dosing kit (NDC 49702-264-23), each containing:

- 1 single-dose vial of cabotegravir 600 mg (3 mL) extended-release injectable suspension
- 1 syringe
- 1 vial adapter
- 1 needle for intramuscular injection (23 gauge, 1½ inch)

Note: The vial stopper is not made with natural rubber latex.

Storage and handling

Store at or below 36°F to 77°F (2°C to 25°C) in the original carton until ready to use. Exposure up to 86°F (30°C) permitted. APRETUDE does not require refrigeration.

Do not freeze. APRETUDE does not need further dilution or reconstitution.

APRETUDE does not require refrigeration. If the pack has been stored in the refrigerator, the vial should be brought to room temperature prior to administration (not to exceed 86°F [30°C]).

IMPORTANT SAFETY INFORMATION (cont'd)

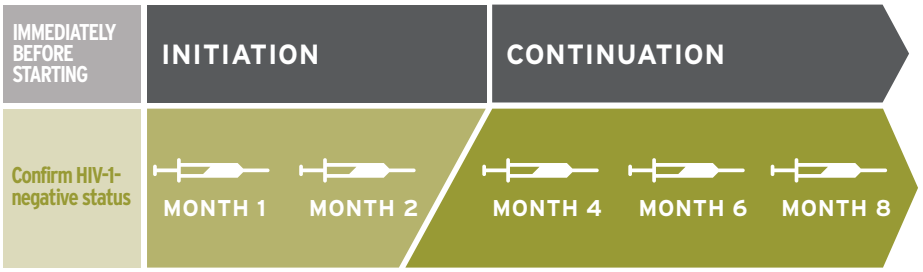
WARNINGS AND PRECAUTIONS (cont'd)

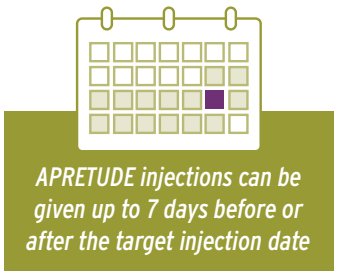
Comprehensive Management to Reduce the Risk of HIV-1 Infection: (cont'd)

- Use APRETUDE only in individuals confirmed to be HIV-1 negative. HIV-1 resistance substitutions may emerge in individuals with undiagnosed HIV-1 infection who are taking only APRETUDE, because APRETUDE alone does not constitute a complete regimen for HIV-1 treatment. Prior to initiating APRETUDE, ask seronegative individuals about recent (in past month) potential exposure events and evaluate for current or recent signs or symptoms consistent with acute HIV-1 infection (e.g., fever, fatigue, myalgia, skin rash). If recent (<1 month) exposures to HIV-1 are suspected or clinical symptoms consistent with acute HIV-1 infection are present, use a test approved or cleared by the FDA as an aid in the diagnosis of acute HIV-1 infection
- When using APRETUDE, HIV-1 testing should be repeated prior to each injection and upon diagnosis of any other STIs
- Additional HIV testing to determine HIV status is needed if an HIV-1 test indicates possible HIV-1 infection or if symptoms consistent with acute HIV-1 infection develop following an exposure event. If HIV-1 infection is confirmed, then transition the individual to a complete HIV-1 treatment
- Counsel individuals without HIV-1 to strictly adhere to the recommended dosing and testing schedule for APRETUDE

Please see additional Important Safety Information throughout. Please click on the accompanying full Prescribing Information, including Boxed Warning and Instructions for Use, for APRETUDE.

Recommended dosing schedule for APRETUDE*





APRETUDE is administered by a healthcare provider as a single 600-mg (3-mL) gluteal intramuscular injection

Healthcare providers should carefully select individuals who agree to the required injection dosing and testing schedule and counsel patients on the importance of adherence to help reduce the risk of HIV-1 infection and development of resistance.

Prior to initiation injections, an optional oral lead-in may be used to assess tolerability of APRETUDE.†

Initiation and continuation injections

- Patients should receive 2 gluteal intramuscular initiation injections administered 1 month apart
- Patients should receive 1 gluteal intramuscular injection every 2 months thereafter for as long as they remain on APRETUDE

Screen all individuals using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 acquisition:

- Before starting APRETUDE
- With each subsequent injection
- Upon diagnosis of any other STI
- When recent exposure to HIV is suspected or clinical symptoms consistent with HIV-1 are present

If an antigen/antibody-specific test is used and provides negative results, then such negative results should be confirmed using an RNA-specific assay. The results of the RNA assay can be available after APRETUDE administration.

- If positive HIV-1 status is confirmed, transition to a complete HIV-1 treatment

*For patients concomitantly receiving rifabutin, please see the full Prescribing Information for the adjusted recommended dosing schedule for APRETUDE.
†The recommended oral lead-in dose is one 30-mg tablet of cabotegravir daily for approximately 1 month (at least 28 days). Initiation injections should be administered on the last day of oral lead-in, if used, or within 3 days thereafter. For more information, please see the full Prescribing Information.
FDA=US Food and Drug Administration; STI=sexually transmitted infection.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Potential Risk of Resistance with APRETUDE:

- There is a potential risk of developing resistance to APRETUDE if an individual acquires HIV-1 either before, while taking, or following discontinuation of APRETUDE. To minimize this risk, it is essential to clinically reassess individuals for risk of HIV-1 acquisition and to test before each injection to confirm HIV-1–negative status. Individuals who are confirmed to have HIV-1 infection must transition to a complete HIV-1 treatment. If individuals at continuing risk of HIV-1 acquisition discontinue APRETUDE, alternative forms of PrEP should be considered and initiated within 2 months of the final injection of APRETUDE

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extended-release injectable suspension

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Considerations prior to injection

Prepare

- Since injections should be administered in a discreet setting, establish a private administration area where patients will be comfortable
- Ensure staff is properly trained for administration

Communicate

- Let patients know what to expect with the injection
- Allow enough time to address patient questions

Empower

- Include patients in decision-making, timing, and choice of location for injection

Encourage relaxation

- Give patients time to relax prior to injection
- Deep breathing, music, or distractions can help

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Long-Acting Properties and Potential Associated Risks with APRETUDE:

- Residual concentrations of cabotegravir may remain in the systemic circulation of individuals for prolonged periods (up to 12 months or longer). Take the prolonged-release characteristics of cabotegravir into consideration and carefully select individuals who agree to the required every-2-month injection dosing schedule because non-adherence or missed doses could lead to HIV-1 acquisition and development of resistance

Hypersensitivity Reactions:

- Serious or severe hypersensitivity reactions have been reported with APRETUDE, including Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)
- Discontinue APRETUDE immediately if signs or symptoms of hypersensitivity reactions develop. Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated

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Pre-injection overview

Preparation

- A complete dose of APRETUDE requires 1 injection: 600 mg (3 mL) of cabotegravir
- APRETUDE does not need further dilution or reconstitution
- APRETUDE must be administered by a healthcare provider by gluteal intramuscular injection

Note: The ventrogluteal site is recommended.

Prior to administration

- Once APRETUDE has been drawn into the syringe, it can remain in the syringe for up to 2 hours before injecting. The filled syringe should not be placed in the refrigerator. If 2 hours are exceeded, the filled syringe and needle must be discarded

Consider the patient's build and use medical judgment to select an appropriate injection needle length.

Consider the body mass index (BMI) of the individual to ensure that the needle length is sufficient to reach the gluteus muscle. Longer needle lengths may be required for individuals with higher BMI (ie, >30 kg/m^2) to ensure that the injection is administered intramuscularly as opposed to subcutaneously.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hepatotoxicity:

- Hepatotoxicity has been reported in a limited number of individuals receiving cabotegravir with or without known pre-existing hepatic disease or identifiable risk factors
- Clinical and laboratory monitoring should be considered and APRETUDE should be discontinued if hepatotoxicity is suspected and individuals managed as clinically indicated

Depressive Disorders:

- Depressive disorders (including depression, depressed mood, major depression, persistent depressive disorder, suicidal ideation or attempt) have been reported with APRETUDE
- Promptly evaluate patients with depressive symptoms

Risk of Reduced Drug Concentration of APRETUDE Due to Drug Interactions:

- The concomitant use of APRETUDE and other drugs may result in reduced drug concentration of APRETUDE
- Refer to the full Prescribing Information for steps to prevent or manage these possible and known significant drug interactions, including dosing recommendations. Consider the potential for drug interactions prior to and during use of, and after discontinuation of APRETUDE; review concomitant medications during use of APRETUDE

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Missed injections

Time since missed target injection date

≤ 1 MONTH

Resume continuation injections as soon as possible

> 1 MONTH

Restart with initiation injections

Oral Bridging

Oral cabotegravir can be prescribed for up to 2 months to replace a missed injection. The first dose should be taken 2 months after the last APRETUDE injection. Restart APRETUDE within 3 days of last oral dose

Adherence to the injection dosing schedule is strongly recommended. Individuals who miss their Target Injection Date should be clinically reassessed to ensure resumption of APRETUDE remains appropriate.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥1%, all grades) with APRETUDE were injection site reactions, diarrhea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, abdominal pain, vomiting, myalgia, rash, decreased appetite, somnolence, back pain, and upper respiratory tract infection.

DRUG INTERACTIONS

- Refer to the full Prescribing Information for important drug interactions with APRETUDE
- Drugs that induce UGT1A1 may significantly decrease the plasma concentrations of cabotegravir

USE IN SPECIFIC POPULATIONS

- **Lactation:** Assess the benefit-risk of using APRETUDE to the infant while breastfeeding due to the potential for adverse reactions and residual concentrations in the systemic circulation for up to 12 months or longer after discontinuation
- **Pediatrics:** Not recommended in individuals weighing less than 35 kg

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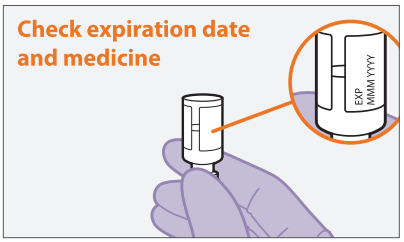
Instructions for use: preparation

PREPARATION

1 Inspect the vial

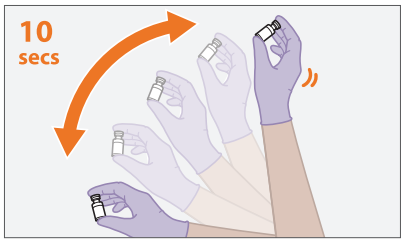


- Check that the expiration date has not passed
- Inspect the vial immediately. If you can see foreign matter, do not use the product

  Note: The vial has a brown tint to the glass.

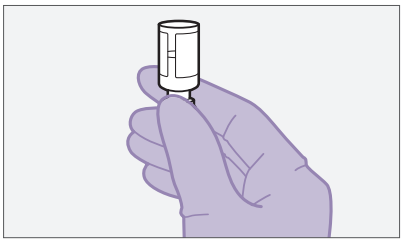
  Do not use if the expiration date has passed.
- If the pack has been stored in the refrigerator, allow the medication to come to room temperature

2 Shake the vial vigorously



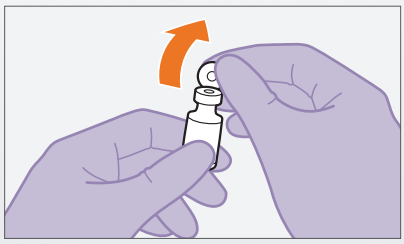
- Hold the vial firmly, and vigorously shake for a full 10 seconds

3 Inspect suspension



- Invert the vial and confirm the suspension is uniform. It should look uniform
- If the suspension is not uniform, shake the vial again
- It is also normal to see small air bubbles

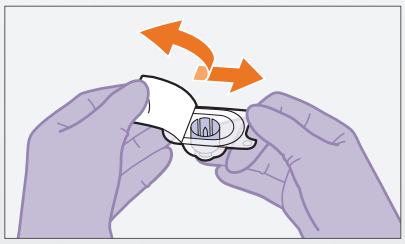
4 Remove the vial cap



- Remove the cap from the vial
- Wipe the rubber stopper with an alcohol wipe

  Do not allow anything to touch the rubber stopper after wiping it.

5 Peel open the vial adapter

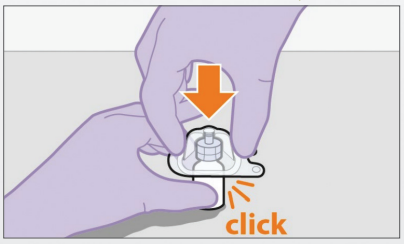


- Peel off the paper backing from the vial adapter packaging

  Note: Do not remove the adapter from its packaging for the next step.

  The adapter **will not** fall out when its packaging is turned upside down.

6 Place vial on flat surface and attach the vial adapter



- Ensure the vial is upright and on a flat surface
- Press the vial adapter straight down onto the vial, as shown
- The vial adapter should click securely into place

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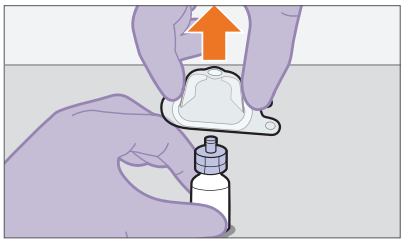
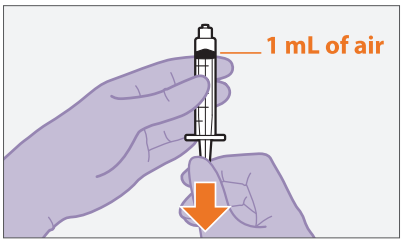
7 Lift off the packaging



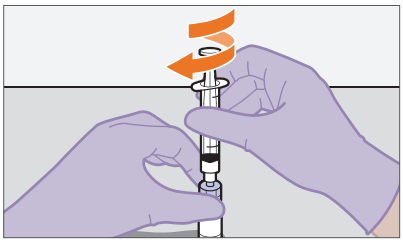
- Lift off the vial adapter packaging, as shown

8 Prepare the syringe



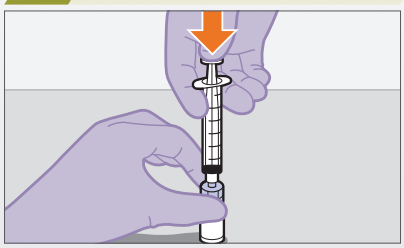
- Remove the syringe from its packaging
- Draw 1 mL of air into the syringe. This will make it easier to draw up the medicine later

9 Attach the syringe



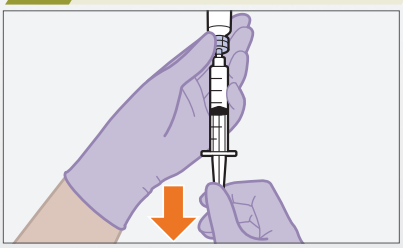
- Hold the vial adapter and vial firmly, as shown
- Screw the syringe firmly onto the vial adapter

10 Press the plunger



- Press the plunger all the way down to push the air into the vial

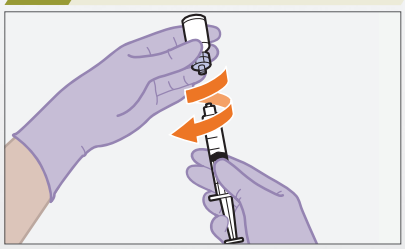
11 Slowly draw up the dose



- Invert the syringe and vial and slowly withdraw as much of the medicine as possible into the syringe. There may be more medicine than the dose amount

> **Note:** Keep the syringe upright to avoid leakage.

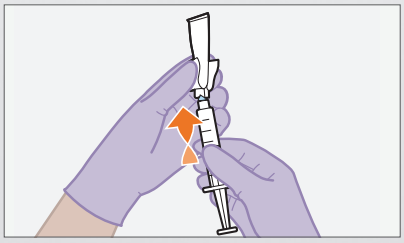
12 Unscrew the syringe



- Hold the syringe plunger firmly in place as shown to prevent leakage. It is normal to feel some back pressure
- Unscrew the syringe from the vial adapter, holding the vial adapter as shown

> **Note:** Check that the suspension looks uniform and milky white.

13 Attach the needle



- Peel open the needle packaging part way to expose the needle base
- Keeping the syringe upright, firmly twist the syringe onto the needle
- Remove the needle packaging from the needle

Injection instructions on the next page

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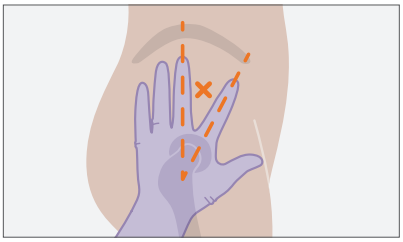
Instructions for use: injection and after injection

INJECTION

14 Prepare the injection site



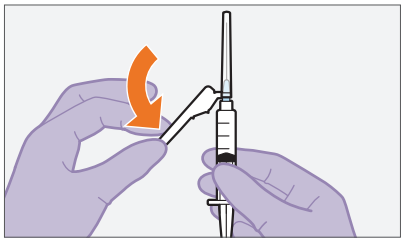
APRETUDE must be administered to a gluteal site. Select from the following areas for the injection:

- Ventrogluteal, as shown (recommended)
- Dorsogluteal, not shown (upper outer quadrant)

Note: For gluteal intramuscular use only.

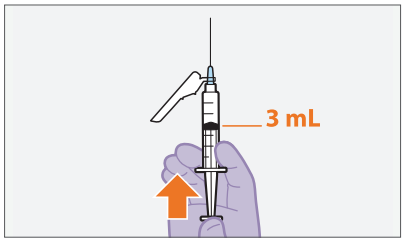
Do not inject intravenously.

15 Remove the cap



- Fold the needle guard away from the needle
- Pull off the injection needle cap

16 Remove extra liquid from the syringe



- Hold the syringe with the needle pointing up. Press the plunger to the 3 mL dosing mark to remove extra liquid and any air bubbles

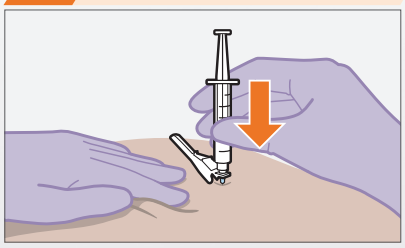
Note: Clean the injection site with an alcohol wipe. Allow the skin to air dry before continuing.

17 Stretch the skin

Use the z-track injection technique to minimize medicine leakage from the injection site.

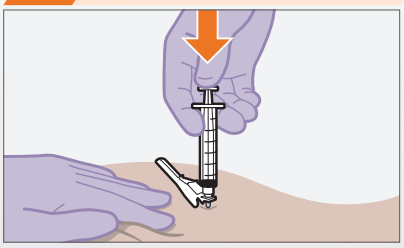
- Firmly drag the skin covering the injection site, displacing it by about an inch (2.5 cm)
- Keep it held in this position for the injection

18 Insert the needle



- Insert the needle to its full depth, or deep enough to reach the muscle

19 Inject the dose of medicine



- Still holding the skin stretched—slowly press the plunger all the way down
- Ensure the syringe is empty
- Withdraw the needle and release the stretched skin immediately

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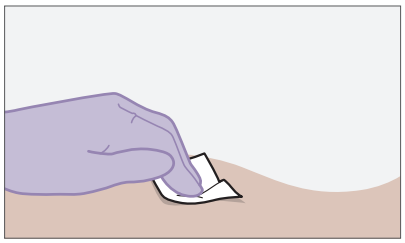
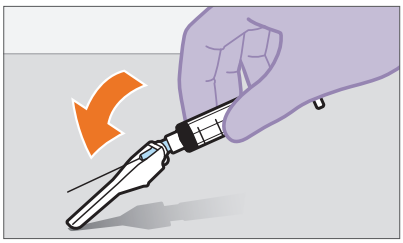
20 Assess the injection site

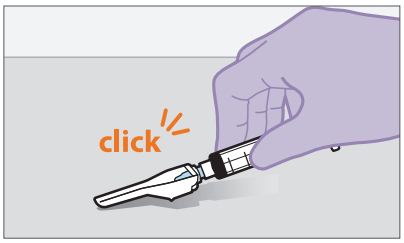


- Apply pressure to the injection site using a gauze pad
- A small bandage may be used if bleeding occurs

Do not massage the area.

21 Make the needle safe

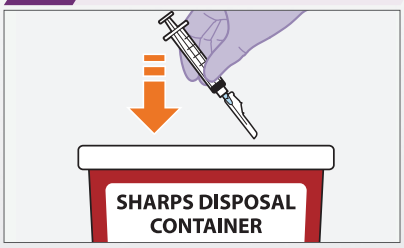




- Fold the needle guard over the needle
- Gently apply pressure using a hard surface to lock the needle guard in place
- The needle guard will make a click when it locks

AFTER INJECTION

22 Dispose safely



- Dispose of used needle, syringe, vial, and vial adapter according to local health and safety laws

Please see additional Important Safety Information throughout. Please click on the accompanying full Prescribing Information, including Boxed Warning and Instructions for Use, for APRETUDE.

Apretude
cabotegravir 200 mg/mL
extended-release injectable suspension

ViiV Healthcare

Questions and answers

If the pack has been stored in the refrigerator, is it safe to warm the vial up to room temperature more quickly?

- The vial should be brought to room temperature before you are ready to give the injection, but make sure the vial does not get above 86°F (30°C)
- **Do not** use any heating methods, other than using the warmth of your hands

How long can APRETUDE be left in the syringe?

- It is best to inject (room temperature) APRETUDE as soon as possible after drawing it up. However, APRETUDE can remain in the syringe for up to 2 hours before injection
- If the medicine remains in the syringe for more than 2 hours, the filled syringe and needle must be discarded

Why do I need to inject air into the vial?

- Injecting 1 mL of air into the vial makes it easier to draw up the medicine into the syringe. Without the air, some liquid may flow back into the vial unintentionally, leaving less medicine than intended in the syringe

Why is the ventrogluteal administration approach recommended?

- The ventrogluteal approach into the gluteus medius muscle is recommended because it is located away from major nerves and blood vessels. A dorsogluteal approach into the gluteus maximus muscle is acceptable, if preferred by the healthcare professional. The injection should not be administered in any other site

Learn more about APRETUDE (cabotegravir) by visiting APRETUDEHCP.com

INDICATION

APRETUDE is indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating APRETUDE (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF APRETUDE FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED HIV-1 INFECTION

Individuals must be tested for HIV-1 infection prior to initiating APRETUDE or oral cabotegravir, and with each subsequent injection of APRETUDE, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of APRETUDE by individuals with undiagnosed HIV-1 infection. Do not initiate APRETUDE for HIV-1 PrEP unless negative infection status is confirmed. Individuals who acquire HIV-1 while receiving APRETUDE for PrEP must transition to a complete HIV-1 treatment regimen.

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Produced in USA.

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