CABENUVA

cabotegravir 200 mg/mL; rilpivirine 300 mg/mL

extended-release injectable suspensions

Dosing and Administration Guide

Please see full Prescribing Information, including Instructions for Use, for CABENUVA.

Introduction

CABENUVA is a once-monthly complete regimen[1]

- CABENUVA is a 2-drug, co-packaged product consisting of [1]:
  - cabotegravir, an HIV-1 INSTI
  - rilpivirine, an HIV-1 NNRTI
- Before initiation of CABENUVA, ensure that patients agree to the required monthly dosing schedule, and counsel patients about the importance of adherence to scheduled dosing visits[1]
- Prior to initiating treatment with CABENUVA, prescribe cabotegravir 30-mg and rilpivirine 25-mg oral tablets, both taken once daily with a meal, to assess tolerability[1]
- Patients will receive initiation injections on the last day of oral lead-in, followed by monthly continuation injections.[1] CABENUVA is for Healthcare Professional administration only

This guide will provide information on

- CABENUVA dosing kits and storage
- The oral lead-in and CABENUVA dosing schedule
- Managing missed injections
- Considerations prior to injection
- Preparing and administering injections
- Frequently asked questions

HIV-1=human immunodeficiency virus type 1; INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor.

INDICATION

CABENUVA is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Do not use CABENUVA in patients with previous hypersensitivity reaction to cabotegravir or rilpivirine
- Do not use CABENUVA in patients receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (>1 dose), and St John's wort

Please see additional Important Safety Information for CABENUVA throughout.
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How CABENUVA is supplied and stored

CABENUVA is supplied in 2 dosing kits, co-packaged as follows[1]

600-mg/900-mg kit for initiation injections[1]

- One single-dose vial containing 600 mg/3 mL of cabotegravir extended-release injectable suspension
- One single-dose vial containing 900 mg/3 mL of rilpivirine extended-release injectable suspension

400-mg/600-mg kit for continuation injections[1]

- One single-dose vial containing 400 mg/2 mL of cabotegravir extended-release injectable suspension
- One single-dose vial containing 600 mg/2 mL of rilpivirine extended-release injectable suspension

Each dosing kit also contains 2 syringes, 2 syringe labels, 2 vial adaptors, and 2 needles for IM injection (23-gauge, 1½ inch).[1] If 2-inch safety needles are required to reach the gluteus muscle, please order by visiting: http://www.fisherhealthcare.com/2inchsafetyneedle.

Storage

- Store CABENUVA in the refrigerator at 2°–8°C (36°–46°F) in the original carton until ready to use[1]
- Once the vials are removed from the refrigerator, they must be used or discarded. They cannot be cycled into and out of the refrigerator[2]

- Do not freeze or mix with any other product or diluent[1]

IM=intramuscular.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions:

- Hypersensitivity reactions, including cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), have been reported during postmarketing experience with rilpivirine-containing regimens. While some skin reactions were accompanied by constitutional symptoms such as fever, other skin reactions were associated with organ dysfunctions, including elevations in hepatic serum biochemistries

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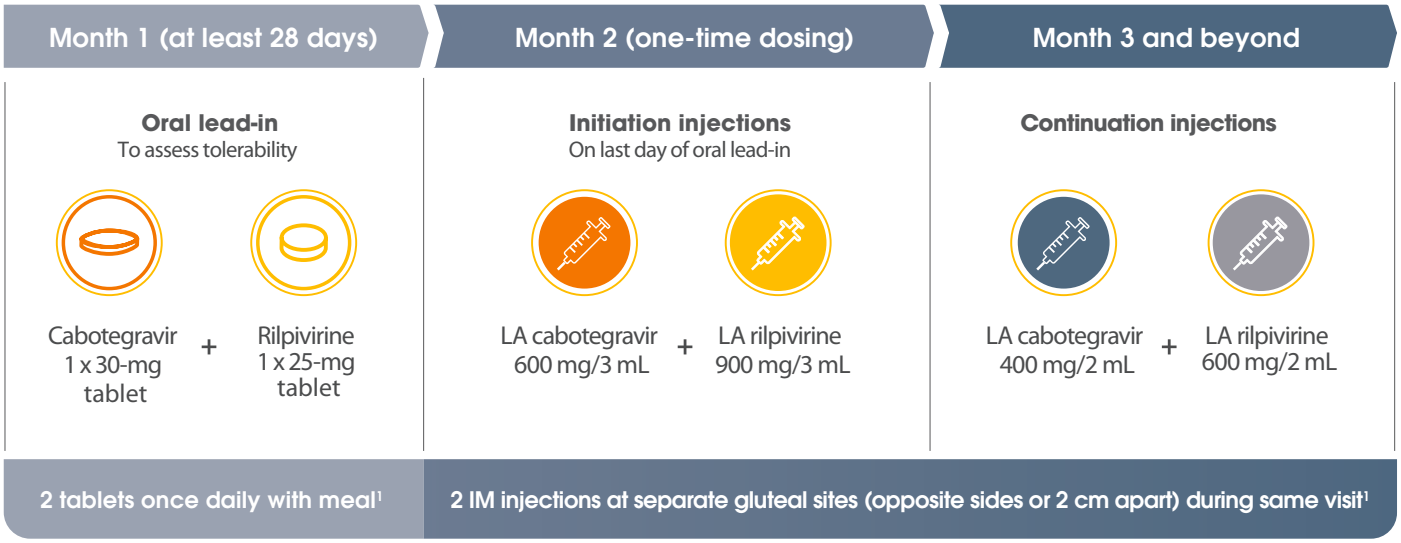
Recommended dosing schedule for CABENUVA



LA=long-acting.

Setting a Target Treatment Date that works for you and your patients

- It is important that patients set a consistent monthly injection date to be their **Target Treatment Date**
- It is recommended that patients pick a day **between the 1st and the 28th** of the month and adhere to monthly scheduled appointments for that date
- It is recommended that patients keep their **Target Treatment Date** for monthly dosing[1]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hypersensitivity Reactions (cont'd):

- Serious or severe hypersensitivity reactions have been reported in association with other integrase inhibitors and could occur with CABENUVA
- Discontinue CABENUVA immediately if signs or symptoms of hypersensitivity reactions develop. Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated. Prescribe the oral lead-in prior to administration of CABENUVA to help identify patients who may be at risk of a hypersensitivity reaction

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Recommended dosing schedule for CABENUVA (cont'd)

CABENUVA has dosing flexibility, allowing for injections to be given up to 7 days before or up to 7 days after the Target Treatment Date[1]

- If patients receive their injection within the dosing window (up to 7 days before or 7 days after their Target Treatment Date) but not on the Target Treatment Date, the following monthly dose should be scheduled for the original Target Treatment Date
- If a patient plans to miss a scheduled injection visit by more than 7 days, prescribe daily oral therapy with cabotegravir and rilpivirine to replace up to 2 consecutive monthly injection visits[1]
- Patients who miss a scheduled injection visit should be clinically reassessed to ensure resumption of therapy remains appropriate[1]

Adherence to the monthly injection dosing schedule is strongly recommended.[1] Setting a consistent injection date, the Target Treatment Date, can help keep your patients on track.

If injection dosing will be continued after a patient misses a monthly injection, see pages 6 and 7 for detailed dosing recommendations on reinitiating CABENUVA after missed injections.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Post-Injection Reactions:

- Serious post-injection reactions (reported in less than 1% of subjects) were reported within minutes after the injection of rilpivirine, including dyspnea, agitation, abdominal cramping, flushing, sweating, oral numbness, and changes in blood pressure. These events may have been associated with inadvertent (partial) intravenous administration and began to resolve within a few minutes after the injection
- Carefully follow the Instructions for Use when preparing and administering CABENUVA to avoid accidental intravenous administration. Observe patients briefly (approximately 10 minutes) after the injection. If a post-injection reaction occurs, monitor and treat as clinically indicated

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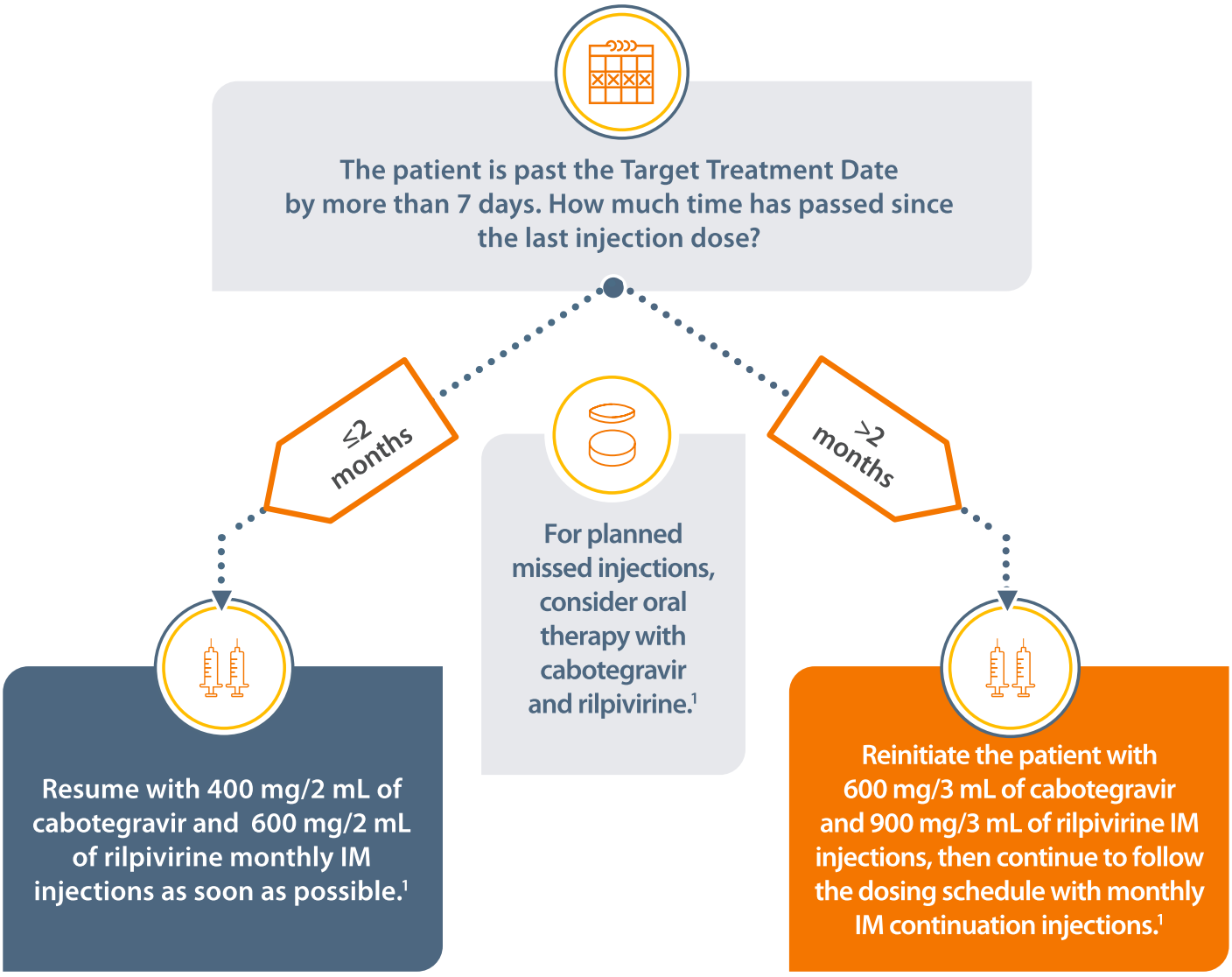
Continuing after missed injections



IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hepatotoxicity:

- Hepatotoxicity has been reported in patients receiving cabotegravir or rilpivirine with or without known pre-existing hepatic disease or identifiable risk factors
- Patients with underlying liver disease marked elevations in transaminases prior to treatment may be at increased risk for worsening or development of transaminase elevations
- Monitoring of liver chemistries is recommended and treatment with CABENUVA should be discontinued if hepatotoxicity is suspected

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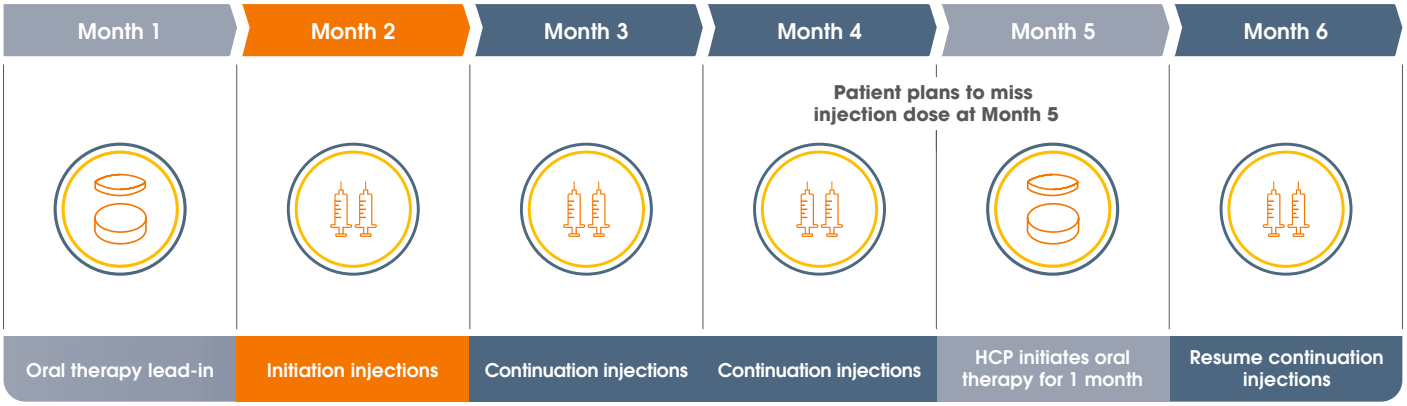
Planned missed injections

- **If a patient plans to miss a scheduled injection visit by more than 7 days, prescribe daily oral therapy with cabotegravir and rilpivirine to replace up to 2 consecutive monthly injection visits**[1]
  - The first dose of oral therapy (one 30-mg cabotegravir tablet and one 25-mg rilpivirine tablet once daily with a meal) should be taken approximately 1 month after the last injection dose of CABENUVA and continued until the day injection dosing is restarted[1]
- If oral treatment will continue for more than 2 months, an alternative fully suppressive regimen should be chosen based on treatment history and the availability of resistance testing results[1,3]

Hypothetical treatment plan if a patient plans to miss their injections[1]



HCP=healthcare professional.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Depressive Disorders:

- Depressive disorders (including depressed mood, depression, major depression, mood altered, mood swings, dysphoria, negative thoughts, suicidal ideation or attempt) have been reported with CABENUVA or the individual products
- Promptly evaluate patients with depressive symptoms

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Pre-injection considerations

Tips for your patients

Communicate

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

Empower

- Include patients in decision-making, timing, and preferred position for injection

Encourage relaxation

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

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:

- The concomitant use of CABENUVA and other drugs may result in known or potentially significant drug interactions (see Contraindications and Drug Interactions)
- Rilpivirine doses 3 and 12 times higher than the recommended oral dosage can prolong the QTc interval. CABENUVA should be used with caution in combination with drugs with a known risk of Torsade de Pointes

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Pre-injection overview

Preparation overview[2]

- A complete dose of CABENUVA requires 1 dose each of cabotegravir and rilpivirine
- Cabotegravir and rilpivirine are suspensions that do not need further dilution or reconstitution
- The preparation steps for both medicines are the same
- Cabotegravir and rilpivirine are for gluteal IM use only. Each injection must be administered to separate gluteal sites (on opposite sides or at least 2 cm apart). The administration order is not important

Note: The ventrogluteal site is recommended for injection.

Prior to administration[2]

- It is recommended to label the syringe with the time that the medication has been drawn into the syringe if the medication is not administered immediately
- See FAQs on pages 14-15 for other considerations prior to administration

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Long-Acting Properties and Potential Associated Risks with CABENUVA:

- Residual concentrations of cabotegravir and rilpivirine may remain in the systemic circulation of patients for prolonged periods (up to 12 months or longer). Select appropriate patients who agree to the required monthly injection dosing schedule because non-adherence to monthly injections or missed doses could lead to loss of virologic response and development of resistance
- To minimize the potential risk of developing viral resistance, it is essential to initiate an alternative, fully suppressive antiretroviral regimen no later than 1 month after the final injection doses of CABENUVA. If virologic failure is suspected, switch the patient to an alternative regimen as soon as possible

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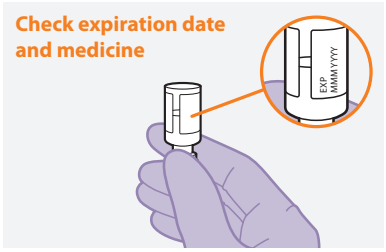
Instructions for use: Preparation

1 Inspect both vials[2]



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

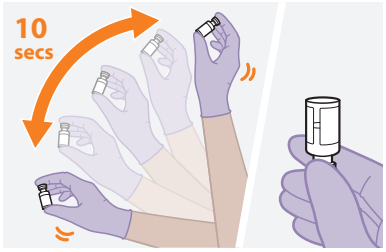
Note: The cabotegravir vial has a brown tint to the glass.

Do not use if the expiration date has passed.

2 Wait 15 minutes[2]

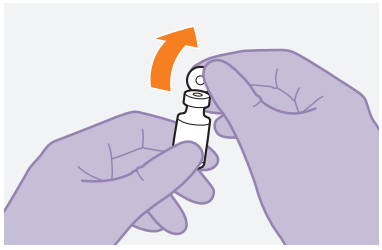
- Wait at least 15 minutes before you are ready to give the injection to allow the medication to come to room temperature

3 Shake the vial vigorously[2]



- Hold the vial firmly, and vigorously shake for a full 10 seconds
- Invert the vial and confirm the suspension is uniform
- If the suspension is not uniform, shake the vial again
- It is also normal to see small air bubbles

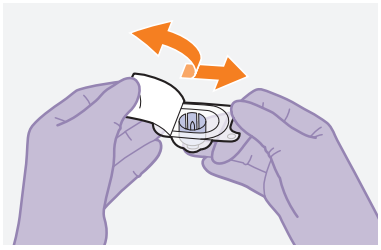
4 Remove the vial cap[2]



- 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.

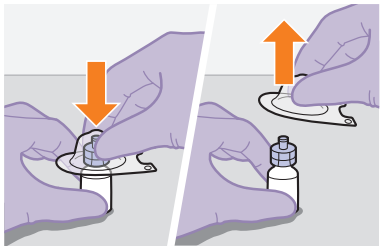
5 Peel open the vial adaptor[2]



- Peel off the paper backing from the vial adaptor packaging

Note: Keep the adaptor in place in its packaging for the next step.

6 Attach the vial adaptor[2]



- Press the vial adaptor straight down onto the vial using the packaging, as shown
- The vial adaptor should snap securely into place
- When you are ready, lift off the vial adaptor packaging

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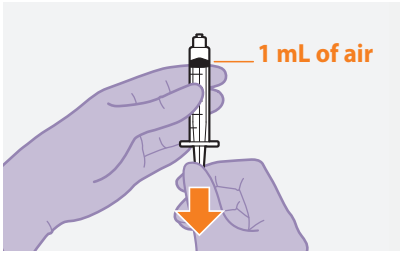
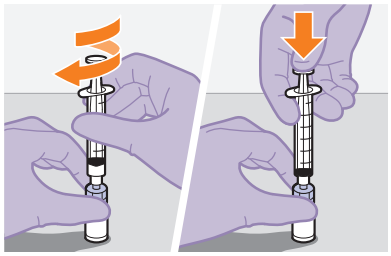
Instructions for use: Preparation (cont'd)

7 Prepare the syringe[2]



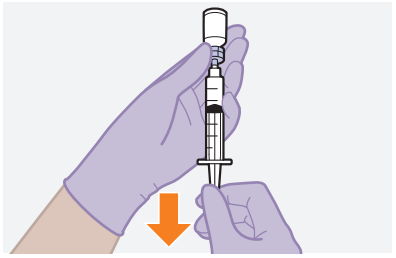
- Remove the syringe from its packaging
- Draw 1 mL of air into the syringe. This will make it easier to draw up the medicine later

8 Attach the syringe[2]



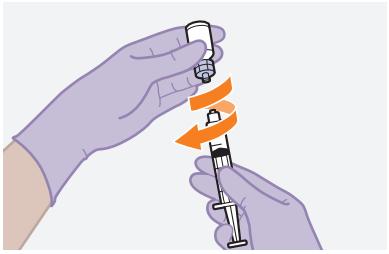
- Hold the vial adaptor and vial firmly
- Screw the syringe firmly onto the vial adaptor
- Press the plunger all the way down to push the air into the vial

9 Slowly draw up the dose[2]



- 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

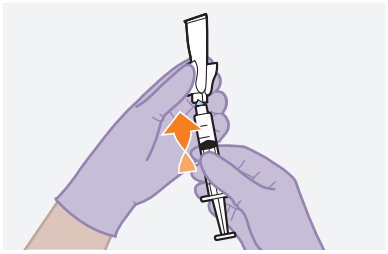
10 Unscrew the syringe[2]



- Unscrew the syringe from the vial adaptor, holding the vial adaptor

Note: Keep the syringe upright to avoid leakage. Check that the suspension looks uniform and milky white.

11 Attach the needle and affix syringe label[2]



- 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
- Write the name of the medicine on the syringe label. Affix the label to the syringe, making sure the gradations remain visible

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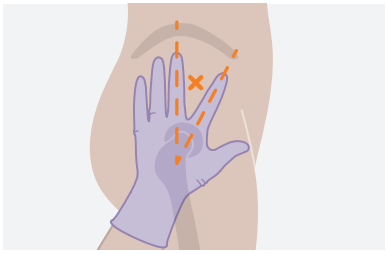
Instructions for use: Injection

12 Prepare the injection site[2]

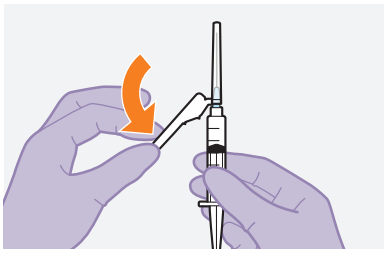


- Injections must be administered to the gluteal sites
- Select from the following areas for the injection:
  - Ventrogluteal, as shown (recommended) or dorsogluteal (upper outer quadrant)

Note: For gluteal intramuscular use only.

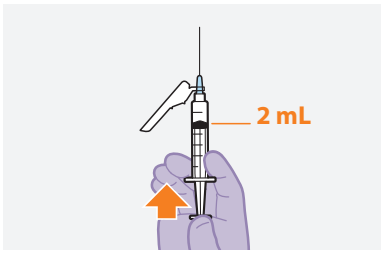
Do not inject intravenously.

13 Remove the cap[2]



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

14 Remove extra liquid from the syringe[2]

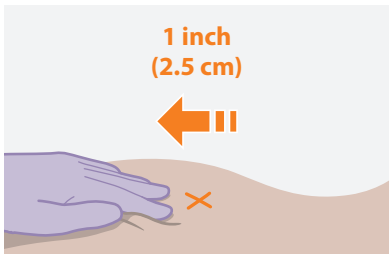


- Hold the syringe with the needle pointing up
- Press the plunger to the appropriate volume to remove extra liquid and any air bubbles

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

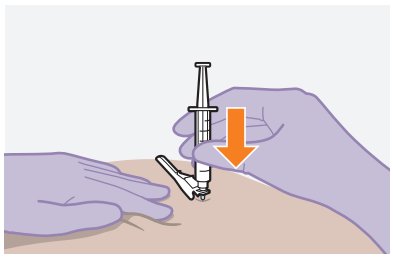
Figure 14 represents a 2-mL continuation injection. A 3-mL initiation injection is also available.

15 Stretch the skin[2]



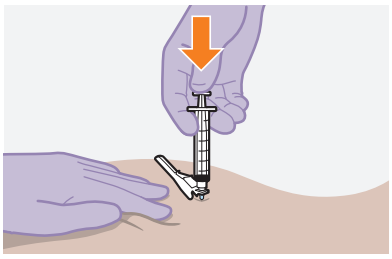
- Use the z-track injection technique to minimize medicine leakage from the injection site
- Firmly drag the skin covering the injection site, displacing it by about an inch (2.5 cm)
- Keep it held in this position for the injection

16 Insert the needle[2]



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

17 Inject the dose of medicine[2]



- 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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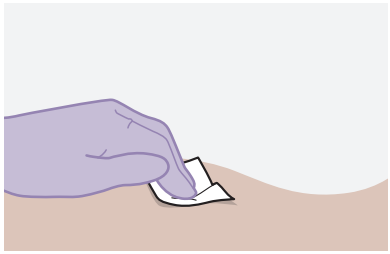
Instructions for use: Injection (cont'd)

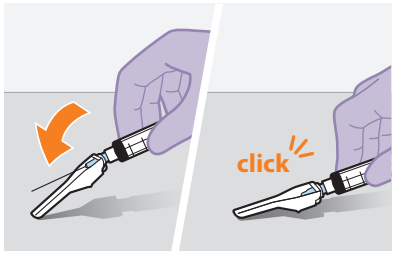
18 Assess the injection site[2]



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

Do not massage the area.

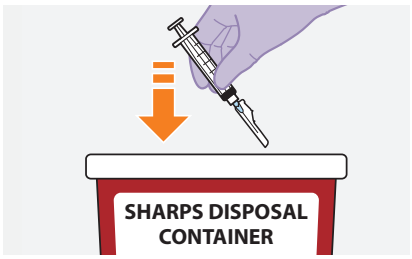
19 Make the needle safe[2]



- 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

Instructions for use: After injection

20 Dispose safely[2]



- Dispose of used needles, syringes, vials, and vial adaptors according to local health and safety laws

21 Repeat for 2nd medicine[2]

Repeat all steps for 2nd medicine

- If you have not yet injected both medicines, use the same steps for preparation and injection of the other medicine
- The second medicine must be injected into a separate gluteal intramuscular site (on opposite sides or at least 2 cm apart)

Observe patients for approximately 10 minutes after the injections.[1]

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Frequently asked questions

1. How long can the medicine be left out of the refrigerator?[2]

It is best to inject the medicine as soon as it reaches room temperature. However, the vials may sit in the carton at room temperature (maximum temperature of 25°C [77°F]) for up to 6 hours. If not used within 6 hours, the medication must be discarded.

Note: Once the vials are removed from the refrigerator, they must be used or discarded. They cannot be cycled in and out of the refrigerator.

2. How long can the medicine be left in the syringe?[2]

It is best to inject the (room temperature) medicine as soon as possible after drawing it up. However, the medication can remain in the syringe for up to 2 hours before injecting.

If 2 hours are exceeded, the medication, syringes, and needles must be discarded.

Note: The syringes and medicine cannot be cycled in and out of the refrigerator.

3. Why do I need to inject air into the vial?[2]

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.

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Frequently asked questions (cont'd)

4. Does the order in which I give the medicines matter?[2]

No, the order is unimportant.

5. Is it safe to warm the vials up to room temperature more quickly?[2]

It is best to let the vials come to room temperature naturally. However, you can use the warmth of your hands to speed up the warm-up time, but make sure the vials do not get above 25°C (77°F).

Do not use any other heating methods.

Please see Important Safety Information for CABENUVA throughout.
Please see full Prescribing Information, including Instructions for Use, for CABENUVA.

CABENUVA
cabotegravir 200 mg/mL; rilpivirine 300 mg/mL
extended-release injectable suspensions

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥2%, all grades) with CABENUVA were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash.

DRUG INTERACTIONS

- Refer to the applicable full Prescribing Information for important drug interactions with CABENUVA, VOCABRIA, or EDURANT
- Because CABENUVA is a complete regimen, coadministration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended
- Drugs that are strong inducers of UGT1A1 or 1A9 are expected to decrease the plasma concentrations of cabotegravir. Drugs that induce or inhibit CYP3A may affect the plasma concentrations of rilpivirine
- CABENUVA should be used with caution in combination with drugs with a known risk of Torsade de Pointes

USE IN SPECIFIC POPULATIONS

- **Pregnancy**: There are insufficient human data on the use of CABENUVA during pregnancy to adequately assess a drug-associated risk for birth defects and miscarriage. Discuss the benefit-risk of using CABENUVA during pregnancy and conception and consider that cabotegravir and rilpivirine are detected in systemic circulation for up to 12 months or longer after discontinuing injections of CABENUVA. An Antiretroviral Pregnancy Registry has been established
- **Lactation**: The CDC recommends that HIV-1–infected mothers in the United States not breastfeed their infants to avoid risking postnatal transmission of HIV-1 infection. Breastfeeding is also not recommended due to the potential for developing viral resistance in HIV-positive infants, adverse reactions in a breastfed infant, and detectable cabotegravir and rilpivirine concentrations in systemic circulation for up to 12 months or longer after discontinuing injections of CABENUVA

Please see additional Important Safety Information for CABENUVA throughout.
Please see full Prescribing Information, including Instructions for Use, for CABENUVA.

References: 1. CABENUVA [package insert]. Research Triangle Park, NC: ViiV Healthcare; 2021. **2.** Data on File. ViiV Healthcare group of companies. Research Triangle Park, NC. **3.** Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Accessed January 15, 2021.

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Learn more about the dosing and administration of CABENUVA by visiting **CABENUVAhcp.com**

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