

# Cabenuva (injectable cabotegravir + rilpivirine)

## Summary

Cabenuva is the name given to an injectable formulation that combines the two anti-HIV drugs cabotegravir and rilpivirine (Edurant). Cabotegravir belongs to a group or class of drugs called integrase inhibitors. Rilpivirine belongs to a group of drugs called non-nucleoside reverse transcriptase inhibitors (“non-nukes”).

Cabenuva is a treatment option if you are already on successful HIV treatment and the amount of HIV in your blood is less than 50 copies/mL or “undetectable”.

Before starting Cabenuva injections, the two anti-HIV drugs in Cabenuva are taken in pill form once daily together with food for one month. These pills are called Vocabria (containing cabotegravir) and Edurant (containing rilpivirine). If Vocabria + Edurant continue to suppress the amount of HIV in your blood and you can tolerate them, your doctor will switch you to Cabenuva (the injectable formulations of these drugs). You will get two injections of Cabenuva into the buttocks, once a month for two consecutive months. After this, you may continue with monthly injections or switch to injections every two months depending on what you and your doctor have decided.

The pills (Vocabria + Edurant) and the injections of Cabenuva are generally well-tolerated. Common side effects from Cabenuva include temporary pain at the injection site, lack of energy and headache.

## FACT SHEET

**Published**  
2021

## CONTACT US

**by e-mail**  
info@catie.ca

**by mail**  
555 Richmond Street West  
Suite 505, Box 1104  
Toronto ON M5V 3B1

## How do the drugs in Cabenuva work?

Cabotegravir works by interfering with the integrase enzyme and rilpivirine works by interfering with the reverse transcriptase enzyme. Both these enzymes are needed by HIV to make copies of itself. Using these drugs greatly reduces HIV's ability to infect cells and make copies of itself.

## How do people with HIV use Cabenuva?

When starting the new treatment, the two pills Vocabria + Edurant are first taken daily as an oral replacement for your previous treatment. Prior to changing treatment to the combination of Vocabria + Edurant, your viral load should be less than 50 copies/mL or "undetectable". The combination of Vocabria + Edurant is a complete treatment but its use is temporary – usually for a month. The main purpose of initiating the temporary oral formulations of these drugs is to ensure that you can tolerate them and to maintain your viral suppression. At the end of this time, as long as your viral load is still suppressed and you are not having side effects, your doctor will change your treatment to Cabenuva, the injectable version of these anti-HIV drugs. Cabenuva consists of two injections, one into each buttock, initially once a month. The doses and schedule of Cabenuva will vary depending on whether you and your doctor have decided that you will receive the injections once a month or every two months. Cabenuva is considered a complete treatment for people with HIV.

For more information about HIV treatment, see CATIE's *Your Guide to HIV Treatment*.

For many people with HIV, the use of ART (HIV treatment or antiretroviral therapy) has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to greatly reduce the risk of developing a life-threatening infection or an AIDS-related cancer. Vocabria, Edurant or Cabenuva or any other treatment regimen (ART) is not a cure for HIV. It is therefore important that you see your doctor for checkups and lab tests on a regular basis.

Evidence shows that HIV-positive people who are on ART, engaged in care, and have an ongoing

undetectable viral load are substantially less likely to transmit HIV to others, be it through sex, when sharing equipment to use drugs or during pregnancy and birth. In fact, the evidence for sexual transmission shows that people on ART who maintain an undetectable viral load do not pass HIV to their sexual partners. For further information see the CATIE fact sheet *HIV treatment and an undetectable viral load to prevent HIV transmission*. However, it may still be a good idea to use condoms because they can reduce your risk for getting and passing on other sexually transmitted infections.

## Warnings

### Anxiety and depression

Although not common in clinical trials, a small proportion of people who took either Vocabria + Edurant (pills) or Cabenuva (injections) developed irritability, anxiety, depression and/or negative thoughts. Anxiety and depression are relatively common in HIV-positive people (regardless of whether they are on treatment or the type of treatment that they take). If you are taking either Vocabria + Edurant (pills) or Cabenuva (injections) and think that you may have developed anxiety or depression, speak to your doctor right away. Your doctor can help determine if you have anxiety or depression and if there is any relationship between them and the medicines that you are taking.

Symptoms of anxiety and depression can include the following:

- becoming easily upset or angry
- feeling fearful
- excessive worry
- difficulty falling asleep or staying asleep, or waking up prematurely
- unexpected feelings of sadness
- recurrent nightmares
- prolonged feelings of sadness, anger or depression
- feeling hopeless
- loss of pleasure in everyday activities

- unexpectedly feeling tired or experiencing a lack of energy
- strange thoughts

If you have any of these feelings, contact your doctor or nurse right away.

If you have thoughts of harming yourself or others, dial 911 right away.

### Liver health

A small proportion of people who have taken cabotegravir (in Vocabria and Cabenuva) have developed liver inflammation. This was detected with blood tests. These tests found higher than normal levels of liver enzymes.

A small proportion of people who have taken rilpivirine (in Edurant and Cabenuva) have also developed elevated levels of liver enzymes in their blood.

These problems with elevated liver enzyme levels with cabotegravir and rilpivirine have occurred both in HIV-positive people without any history of liver problems, and in HIV-positive people who have pre-existing liver issues, such as co-infection with hepatitis B virus or hepatitis C virus.

The manufacturer recommends that people taking these drugs undergo regular tests to monitor the health of their liver.

### Immediate reactions after injection

Cabenuva is meant to be injected deep into muscle. It is released slowly and for a prolonged period (a couple of months) after injection into muscle. When it is not injected into muscle, some short-term problems can occur. There have been reports of rare cases of reactions occurring within minutes after an injection of rilpivirine (in Cabenuva). These reactions included the following:

- problems breathing
- agitation
- abdominal cramps
- flushing of the skin

- sweating
- numbness of the mouth
- feeling lightheaded or faint

Tell your doctor or nurse right away if you have any of these symptoms soon after an injection of Cabenuva. These problems should start to clear after a few minutes. The manufacturer of Cabenuva suggests that these problems have occurred when Cabenuva is accidentally and partially injected into a vein rather than deep into muscle tissue.

### Skin and hypersensitivity reactions

Over the past decade, there have been reports of skin and hypersensitivity reactions with integrase inhibitors and with rilpivirine (in Edurant). Symptoms of hypersensitivity reactions can include severe rash or rash with a fever, together with lack of energy and painful muscles or joints. There have not been reports of skin and hypersensitivity reactions to the integrase inhibitor cabotegravir (in Cabenuva and Vocabria). However, users of either Vocabria + Edurant (pills) or Cabenuva (injections) should remain vigilant about these potential side effects.

In clinical trials with Edurant-containing regimens, some severe cases of hypersensitivity with additional symptoms occurred, such as peeling of the skin, blisters on the lips, swollen eyes and face, stomach cramps and difficulty breathing. If symptoms suggestive of hypersensitivity occur, see your doctor or nurse immediately or go to the emergency room of your nearest hospital or medical centre.

### Pregnancy

Neither Vocabria + Edurant (pills) nor Cabenuva (injections) have been studied in pregnant women. The manufacturer recommends that these combinations of drugs “should not be used in pregnant women unless the potential benefits outweigh the potential risks to the fetus.”

### Age

Neither Vocabria + Edurant (pills) nor Cabenuva (injections) have been tested in people younger

than 18 years. This combination of drugs has also not been tested in large numbers of people who are 65 years or older so its effectiveness and safety in these populations is not known.

## Hepatitis B virus

Cabenuva cannot protect you from hepatitis B virus. Check with your healthcare provider to find out if you have been vaccinated against hepatitis B and whether it is still effective. If you have not been vaccinated against hepatitis B, talk to your healthcare provider about getting vaccinated. If you have hepatitis B, ask about your treatment options.

## Side effects

### General

In clinical trials, Vocabria + Edurant (pills) and Cabenuva (injections) were well tolerated, generally safe and effective. However, as with any treatment, there were side effects but these were uncommon and included the following:

- fever or feeling hot
- lack of energy or feeling weak
- headache
- muscle pain

Note that the HIV-positive people who are typically enrolled in pivotal clinical trials of HIV treatments, including either Vocabria + Edurant (pills) or Cabenuva (injection), are generally young and healthy. Once a drug is approved and more widely available, it gets used by populations who are not usually in pivotal clinical trials. These people may be older and may have other health issues—such as cardiovascular disease, liver injury, kidney injury, type 2 diabetes, anxiety, depression, and substance use—that require medications or that cause symptoms. As a result, their experience of side effects may be different from those reported in pivotal clinical trials.

## Injection site reactions

There will be some discomfort and pain from the injections of Cabenuva. In clinical trials, the vast majority of cases where such side effects occurred were of mild or moderate intensity. Also, these side effects usually resolve in a day or two. However, if pain and discomfort at the injection site persist, speak to your nurse or doctor.

## Weight gain

Research suggests that some people with the following features or characteristics tend to gain weight when on ART:

- women
- people of African, Black or Caribbean descent
- people whose CD4+ cell count fell below the 200 cell/mm<sup>3</sup> level at some point in the past

However, HIV-positive people without these features can also gain weight. The cause of increased weight in HIV-positive people is not clear because studies suggest that HIV-negative people of the same age and gender are also generally gaining weight even though they are not taking ART.

An increase of one or two kilograms in weight is normal when initiating ART and is what has been reported in clinical trials of Vocabria + Edurant (pills) and Cabenuva (injection). However, should you gain more than this amount of weight, speak to your nurse or doctor so that your weight gain can be assessed. Doctors and nurses also take into account a person's waist size and/or body mass index (BMI) – this is a number derived by dividing their height by the square of their weight. If your nurse or doctor has found that your BMI is increasing and is outside what is considered healthy then they will investigate possible causes for an increase in weight.

There may be one or more reasons that your BMI is increasing, including the following:

*Physical activity* – Are you getting enough daily physical activity, including walking and climbing stairs? If not, can you begin a program of exercise? Speak to your nurse or doctor about what kind of exercise is right for you.

*Sleeping problems* – Rest and sleep quality are sometimes overlooked aspects of health. A large observational study in HIV-negative people found that people who have sleeping problems tend to gain weight. If you are unexpectedly gaining weight, speak to your doctor or nurse to rule out any sleep problems.

*Emotional and mental health* – Are there factors in your life that can affect how you respond to stressful events? For instance, when stressed, some people eat more fat and carbohydrate-rich foods as a source of comfort. Repeated engagement in excessive intake of carbohydrates and fatty foods can lead to weight gain over time. Depression can affect appetite—some people gain weight, others lose weight. If you notice weight gain along with changes in your mood, speak to your doctor or nurse.

### Metabolic conditions, hormones and arthritis

Some conditions and life-stages are associated with weight gain, including the following:

- diabetes
- problems with the thyroid gland and its hormones
- being post-menopausal
- arthritis

### Diet

Not everyone follows a diet that is informed by dietary guidelines. If you have access to subsidized dietary counselling (sometimes this is provided in large hospitals and clinics), you may benefit from consulting a registered dietitian. Registered dietitians can assess the quality and quantity of meals, and if necessary, provide helpful advice about making healthy changes.

### Substance use

Alcohol contains calories. Is excess consumption of alcohol an issue for you? Excess consumption of alcoholic beverages could suggest unaddressed mental health and emotional issues.

### Prescription medicines

Some prescription medicines (for conditions other than HIV) have the potential to cause changes in weight, particularly increased weight. It can be useful to speak to a pharmacist about all the medicines that you are taking to see if any are associated with changes in weight. You can then discuss any medicines that your pharmacist has identified with your doctor.

### Bear in mind

While this list covers some potential causes of weight gain in HIV-positive people, it is not exhaustive.

### Uncommon symptoms

The following symptoms were generally uncommon (occurring in 3% or fewer participants) in clinical trials of Vocabria + Edurant (pills) or Cabenuva (injections). With the exception of muscle/bone pain it is not clear if these symptoms were caused by these drugs, the underlying disease process or something else:

- muscle soreness and/or bone pain
- nausea
- difficulty falling asleep and/or staying asleep; feeling sleepy during the daytime
- dizziness
- rash

### Drug interactions

Some drugs (including prescribed and over-the-counter), herbs and supplements can interfere with the absorption and/or effectiveness of either Vocabria + Edurant (pills) or Cabenuva (injections). Such interference is called a drug interaction. Some drugs or herbs and supplements can reduce the levels of the medicines in Vocabria + Edurant or Cabenuva in your blood. This can make Vocabria + Edurant or Cabenuva less effective and lead to treatment failure, reducing your future treatment options. Other drugs can raise the levels of medicines in Vocabria + Edurant or Cabenuva

in your blood, resulting in enhanced side effects or new side effects. Therefore it is important to disclose to your doctor, nurse and pharmacist all the supplements, drugs, and herbs you are taking.

This factsheet is *not* comprehensive and only lists some of the potential and actual drug interactions with the pills Vocabria and Edurant and with the injectable formulation Cabenuva. Speak to your pharmacist to find out more about drug interactions with Vocabria, Edurant or Cabenuva.

### Drug interactions with Vocabria

People taking Vocabria should not use the following drugs:

- antiseizure drugs – carbamazepine, oxcarbazepine, phenobarbital, and phenytoin.
- antibiotics for TB (tuberculosis) or Mycobacterium complex – rifampin and rifapentine should not be used by people taking Vocabria.
- other antibiotics – clarithromycin, erythromycin or telithromycin. The manufacturer of Vocabria, ViiV, recommends that where possible, doctors should consider alternative antibiotics such as azithromycin.

### Acid-reducing agents, laxatives, metal supplements and buffered medicines

ViiV recommends that acid-reducing agents and similar drugs/metal supplements/buffered medicines should be taken “at least two hours before or four hours after taking Vocabria.” Examples of acid-reducing agents include:

- Alka-Seltzer
- Calcium and/or magnesium supplements
- Gaviscon (tablets and syrup)
- Maalox (liquid and tablets)
- Milk of Magnesia
- Pepto-Bismol and Pepto Bismol Children’s
- Roloids

- Tums
- Zantac (ranitidine), Tagamet (cimetidine)

### Drug interactions with Edurant

Rilpivirine (in Edurant and Cabenuva) interacts with many medicines. Always speak to your pharmacist about its potential to interact with over the counter or prescription drugs. Here are a few more interactions with rilpivirine (this list is not exhaustive):

- antifungal agents – azole antifungal drugs such as fluconazole (Diflucan), itraconazole (Sporanox), posaconazole (Spirafil) and voriconazole (Vfend) can all increase levels of rilpivirine in the blood. This increase in rilpivirine levels may affect the health of the heart. Also, rilpivirine can reduce the concentration of these drugs in the blood leading to new or recurring fungal infections. Therefore, the manufacturer of rilpivirine recommends that azole antifungal drugs be used “cautiously” in people who are taking rilpivirine.
- herbs – St. John’s wort or the active ingredients – hypericin or hyperforin; this herb or substances in St. John’s wort has the potential to reduce levels of rilpivirine in the blood and increase the risk of treatment failure.
- methadone – the manufacturer states that no dose adjustment of methadone is needed when starting therapy with Edurant. However, it encourages doctors to monitor people who use methadone as the dose of this drug may need adjustment in the future.

### Drug interactions with Cabenuva

ViiV recommends that the following drugs and herbs should not be used by people who take Cabenuva:

- anti-seizure drugs – carbamazepine, oxcarbazepine, phenobarbital or phenytoin
- antibiotics – rifabutin, rifampin or rifapentine



- steroids – more than one dose of dexamethasone (oral or intravenous)
- herbs – St. John’s wort or the active ingredients – hypericin or hyperforin

### Methadone

No interaction is expected between methadone and Cabenuva. However, ViiV cautions that doctors monitor people who are taking methadone as its dose may need to be adjusted.

### Resistance and cross-resistance

Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes, called mutations, can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you. ViiV states that Vocabria and Cabenuva should not be used in people with “known or suspected resistance to cabotegravir or rilpivirine.”

To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken exactly as prescribed and directed. If doses are delayed, missed or not taken as prescribed, the level of medicines inside Vocabria + Edurant (pills) or Cabenuva (injections) in the blood may fall too low. If this happens, the HIV in your body can become resistant to the medication. If you find you are having problems taking your medications as directed, speak to your doctor, nurse or pharmacist about this. They can find ways to help you.

When HIV becomes resistant to one drug in a class, it sometimes becomes resistant to other drugs in that class. This is called cross-resistance. Feel free to talk with your doctor about your current and future treatment options. To help you decide what these future options might be, at some point your doctor can have a small sample of your blood analyzed to test for resistance.

### Dosage

The dosing, formulation, schedule and administration of injectable therapy can seem complex at first. The drugs need to be injected deep

into muscular tissue in the buttocks and need to be injected by a health care professional.

Below is a brief outline of how people are switched to first the oral formulations of cabotegravir and rilpivirine and then the injectable formulations. Speak to your doctor or nurse about dosing and other concerns you may have about Cabenuva.

First patients are given oral therapy (pill formulations of the drugs that will eventually be injected) and then if there are no problems, about a month later they are switched to injectable therapy.

The dose of oral therapy is one tablet of Vocabria and one tablet of Edurant, taken together, once daily with a meal. ViiV notes that a protein shake is not equivalent to a meal in this case. Edurant requires fat in food to ensure its absorption.

If these drugs continue to suppress HIV and you can tolerate them, doctors proceed to the next phase which involves regular injections of Cabenuva and cessation of Vocabria and Edurant.

The doses and schedule of Cabenuva will vary depending on whether you and your doctor have decided that you will receive the injections once a month or every two months. Your doctor or clinic nurse will inject the drugs or refer you to a nurse who will do so. If a nurse will be injecting the drugs, note that your doctor will continue to provide your overall care so regular doctor visits and lab tests are important.

Speak to your nurse or doctor about your schedule of visits to get future injections. If you cannot attend your next appointment for an injection, let your doctor or nurse know right away. ViiV indicates that there is some flexibility about the timing of injections by up to seven days. However, repeatedly missing appointments for injections may increase the risk of that HIV can develop resistance to Cabenuva.

### Missed doses of Vocabria + Edurant

If you miss a dose of Vocabria or Edurant pills, ViiV advises to take a dose as soon as you remember. The company further states, “if your next dose is due within 12 hours, skip the dose you missed and take the next one at your usual time. Then continue

your treatment as before. Don't take a double dose to make up for the missed dose."

## Changing your regimen

If you want to stop taking Vocabria + Edurant (pills) or Cabenuva (injections) first speak to your doctor or nurse. They can listen to your reasons for quitting and either advise you about resolving the issues you have raised or help you find a new regimen. According to ViiV, small amounts of rilpivirine and cabotegravir will remain in your body for "up to 12 months or longer" after you stop getting injections. It is therefore important that you adhere to your new regimen so that your viral load stays suppressed and your HIV does not become resistant to Cabenuva or other treatments.

## Bear in mind

Cabenuva is not for everyone. There are risks and benefits with every combination of ART. Leading HIV treatment guidelines in the U.S. have stated that Cabenuva can be considered for use in the following people with HIV whose viral loads have been suppressed for at least three months and meet the following criteria:

- have no pre-existing resistance to cabotegravir or rilpivirine
- have never experienced virological failure
- do not have active hepatitis B virus (HBV) infection (unless also receiving an oral HBV active regimen),
- are not pregnant and are not planning on becoming pregnant
- are not receiving medications with significant drug interactions with either the oral or injectable forms of medicines used with this therapy

If you are thinking about changing your regimen from pills to injectable formulations, speak with your doctor or nurse to find out if these medicines are right for you.

## Availability

Vocabria, Edurant and Cabenuva are licensed in Canada. Cabenuva is meant to replace the current HIV treatment in people whose viral loads are less than 50 copies/mL ("undetectable"). Your doctor or pharmacist can tell you more about the availability and coverage of Cabenuva in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

## References

1. Vocabria cabotegravir tablets and Cabenuva extended release injectable suspension (cabotegravir and rilpivirine). *Product Monograph*. 18 March 2020.
2. Edurant (rilpivirine) tablets. *Product Monograph*. 4 March, 2019.
3. Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV*. 03 June, 2021. Available at <https://clinicalinfo.hiv.gov/sites/default/files/inline-files/AdultandAdolescentGL.pdf>.

**Author(s): Hosein SR**



## Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to consult as broad a range of sources as possible. Users relying on this information do so entirely at their own risk. Neither CATIE, nor any of its partners, funders, employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE do not necessarily reflect the policies or opinions of CATIE nor the views of its partners and funders.

## Permission to reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: *This information was provided by the Canadian AIDS Treatment Information Exchange (CATIE). For more information, contact CATIE at 1-800-263-1638.*

Production of this document has been made possible through a financial contribution from the Public Health Agency of Canada. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.

CATIE fact sheets are available for free at [www.catie.ca](http://www.catie.ca)

## CONTACT US

### by e-mail

[info@catie.ca](mailto:info@catie.ca)

### by mail

555 Richmond Street West  
Suite 505, Box 1104  
Toronto ON M5V 3B1

