



## MARAVIROC (Celsentri)

### Summary

Maraviroc is a type of anti-HIV drug called a CCR5 antagonist or entry inhibitor. Common side effects of maraviroc can include cough, fever, muscle pain and rash. The dose of maraviroc used depends on the other medications in your combination. Maraviroc can be taken with or without food.

### What is maraviroc?

Maraviroc, sold under the brand name **Celsentri** (also known as Selzentry), is a type of anti-HIV drug (antiretroviral) drug called a CCR5 antagonist or entry inhibitor. Maraviroc is used in combination with other anti-HIV drugs to treat, but not cure, HIV/AIDS.

### How does maraviroc work?

Most currently approved therapies for the treatment of HIV infection work by interfering with HIV *after* it has infected a cell. Maraviroc is different because it acts *before* HIV has infected a cell. Maraviroc works by covering a molecule called CCR5 that is found on the surface of cells of the immune system. HIV needs to attach itself to CCR5 in order to enter and infect a cell. Maraviroc blocks access to CCR5 so HIV cannot get in, hence it belongs to a class of anti-HIV drugs called entry inhibitors. By using maraviroc as part of combination therapy, HIV's ability to infect cells is reduced and production of new copies of HIV is also greatly reduced.

### Know your co-receptors

HIV needs a number of different receptors to help it enter and infect a cell. The first of those receptors is called CD4. This receptor is found on many cells of the immune system, including T-cells and macrophages.

But HIV also needs at least one of two co-receptors—CXCR4 (or X4) and CCR5 (or R5)—to help it get into a cell. HIV that prefers R5 receptors is called R5 tropic and HIV that prefers X4 receptors is called X4 tropic. Some forms of HIV can attach to either receptor; these viruses are called dual or mixed tropic.

To help assess which kind of virus predominates in a person, the company Monogram Biosciences has developed a test called Trofile. Using this test, a sample of blood can be analysed to find out the tropism of HIV. Before using maraviroc, a Trofile test must be performed on a patient's blood sample to help physicians decide whether maraviroc is going to work.



## More about the Trofile assay

In order to profile the co-receptor tropism, maraviroc users will have their blood assessed with Trofile prior to starting therapy with this drug. This is an important step because some people have HIV that prefers to use CXCR4 or both CXCR4 and CCR5. Maraviroc only works against HIV that prefers to use CCR5, so the screening test with Trofile helps doctors decide who will benefit from the use of maraviroc.

Trofile results can be as follows:

- R5 tropic – only CCR5-tropic viruses; this means that maraviroc will work
- X4 tropic – this means that a person's HIV prefers the X4 co-receptor; maraviroc will not work
- dual/mixed tropism – this means that a person's HIV can attach to both X4 and R5 co-receptors; maraviroc will not have any significant benefit

## How do PHAs use maraviroc?

Maraviroc is used in combination with several other anti-HIV drugs, usually nukes (nucleoside analogues), non-nukes (NNRTIs) and drugs from other groups (classes) such as protease inhibitors. Combinations such as this are called highly active antiretroviral therapy, or HAART. For more information on HAART, see CATIE's *Practical Guide to HAART for People Living with HIV/AIDS* at [www.catie.ca/PG\\_HAART\\_e.nsf](http://www.catie.ca/PG_HAART_e.nsf).

For many people with HIV/AIDS (PHAs), the use of HAART has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to reduce the risk of developing a life-threatening infection. Neither maraviroc nor any other anti-HIV medication is a cure for HIV/AIDS. It is therefore important that you do the following:

- see your doctor regularly so that he/she monitors your health
- continue to practise safer sex and take other precautions so as not to pass HIV on to

other people and, protect yourself from different strains of HIV and other germs

Before starting maraviroc, potential users have a sample of their blood sent for a Trofile test. Trofile is an expensive test, costing hundreds of dollars. However, because the use of maraviroc depends on knowing a person's HIV co-receptor preference, Pfizer is paying for the cost of Trofile in Canada. Trofile is expected to be available in major treating centres across Canada.

## Warnings

Bear in mind that maraviroc is a relatively new medication. The full range of its side effects may not be known for many years.

### 1. Liver health

Liver damage has occurred in some people who have used maraviroc. In some cases, an allergic reaction has occurred before the liver was damaged. The following symptoms can accompany the allergic reaction:

- an itchy rash on your body
- your skin or eyes look yellow and your urine becomes dark in colour
- vomiting
- stomach pain

If these occur, contact your doctor right away.

### 2. Infections and cancer

In theory, it is possible that maraviroc and similar drugs may affect the immune system, increasing the risk of developing infections and possibly, cancer. In studies with people given maraviroc, there appeared to be a slightly increased risk of herpes infections. The manufacturer recommends that people taking maraviroc need to be monitored for symptoms of infection.

There were no reports of an increased risk of cancer with maraviroc in studies with people for one year. The long-term risks of exposure to maraviroc are not known.



# Side effects

## 1. General

Common side effects that have been reported by some maraviroc users include the following:

- cough
- fever
- lung infections
- rash
- muscle pain
- stomach pain
- dizziness
- constipation
- itching
- difficulty sleeping

## 2. Cardiovascular

According to the manufacturer, maraviroc should be “used with caution” in patients with a history of cardiovascular disease or who are at risk for a heart attack, stroke or another cardiovascular-related complication.

Maraviroc should also be used with caution in people who have low blood pressure or who are taking medication to lower their blood pressure. People who have low blood pressure and who use maraviroc may experience dizziness or fainting when they stand up.

## 3. Hepatitis

Maraviroc has not been well studied in people co-infected with HIV and hepatitis-causing viruses such as hepatitis B virus or hepatitis C virus. These viruses cause liver damage and if liver disease grows worse while on maraviroc, the manufacturer notes that doctors must consider interrupting or stopping the use of maraviroc.

## 4. Pregnancy

If you are pregnant or want to have a baby, tell your doctor. The manufacturer recommends that maraviroc should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

## 5. Lipodystrophy syndrome

The HIV lipodystrophy syndrome is the name given to a range of symptoms that can develop over time when people use HAART regimens. Some features of the lipodystrophy syndrome include:

- loss of fat just under the skin (subcutaneous fat) in the face, arms, and legs
- bulging veins in the arms and/or legs due to the loss of fat under the skin
- increased waist and belly size
- fat pads at the back of the neck (“buffalo hump”) or at the base of the neck (“horse collar”)
- small lumps of fat in the abdomen
- increased breast size (in women)

Together with these physical changes, lab tests of your blood may detect the following:

- increased levels of fatty substances called triglycerides
- increased levels of LDL-cholesterol (low-density lipoprotein), or “bad” cholesterol
- increased levels of sugar (glucose)
- increased levels of the hormone insulin
- decreased sensitivity to insulin (insulin resistance)
- decreased levels of HDL-cholesterol (high-density lipoprotein), or “good” cholesterol

The precise causes of the HIV lipodystrophy syndrome are not clear and are difficult to understand because in some PHAs there may be one or more aspects of the syndrome taking place. For instance, some people may experience fat wasting, others fat gain, and others may experience both fat gain and wasting. What is becoming increasingly clear is that unfavourable changes in the lab readings of glucose, cholesterol, and triglycerides over a period of several years increase the risk of diabetes and cardiovascular disease. So far, however, the many benefits of HAART are much greater than the increased risk of cardiovascular disease or other side effects.



Maintaining a normal weight, eating a healthy diet, exercising regularly and quitting smoking are all important in helping you to reduce your risk of diabetes, heart disease, and other complications. Regular visits to your doctor for checkups and blood tests are a vital part of staying healthy. If necessary, your doctor can prescribe lipid-lowering therapy.

Researchers are studying the lipodystrophy syndrome to try to discover ways of helping PHAs avoid or reduce this problem. To find out more about options for managing aspects of the lipodystrophy syndrome, see CATIE's Practical Guide to HIV Drug Side Effects at [www.catie.ca/sideeffects\\_e.nsf](http://www.catie.ca/sideeffects_e.nsf).

## Drug interactions

Always consult your doctor and pharmacist about taking any other prescription or non-prescription medication, including over-the-counter medicines, herbs, supplements, and street drugs.

Some drugs can interact with maraviroc, increasing or decreasing its levels in your body. Increased drug levels can cause you to experience side effects or make pre-existing side effects worse. On the other hand, if drug levels become too low, HIV can develop resistance and your future treatment options may be reduced.

If you must take a drug that has the potential to interact with your existing medications, your doctor can do the following:

- adjust your dose of either your anti-HIV drugs or other medications
- prescribe different anti-HIV drugs for you

## Drug interactions with maraviroc

Maraviroc has the potential to interact with many commonly used medications. The manufacturer has made relevant suggestions when different medications are used at their standard doses with maraviroc. There are

several lists in this fact sheet about dose adjustments; bear in mind that these lists are not exhaustive.

### Non-nukes

- efavirenz (**Sustiva**, also in **Atripla**) – the dose of maraviroc should be increased to 600 mg twice daily
- delavirdine (**Rescriptor**) – the dose of maraviroc should be decreased to 150 mg twice daily

### Protease inhibitors

- atazanavir (**Reyataz**) with or without ritonavir (**Norvir**) – the dose of maraviroc should be decreased to 150 mg twice daily
- darunavir (**Prezista**) with ritonavir – the dose of maraviroc should be decreased to 150 mg twice daily
- saquinavir (**Invirase**) with ritonavir – the dose of maraviroc should be decreased to 150 mg twice daily

### Non-nukes and protease inhibitors

- lopinavir/ritonavir (**Kaletra**) and efavirenz – the dose of maraviroc should be decreased to 150 mg twice daily
- saquinavir/ritonavir and efavirenz – the dose of maraviroc should be decreased to 150 mg twice daily
- efavirenz and ddI-EC (**Videx EC**) and tenofovir (**Viread**) – the dose of maraviroc should be increased to 600 mg twice daily
- nevirapine (**Viramune**), 3TC and tenofovir – the dose of maraviroc should be 300 mg twice daily

### Other combinations of anti-HIV medications

- efavirenz and **Combivir** (AZT and 3TC) – the dose of maraviroc should be increased to 600 mg twice daily
- lopinavir/ritonavir, 3TC and d4T (stavudine, **Zerit**) – the dose of maraviroc should be decreased to 150 mg twice daily



## Antifungal agents

- ketoconazole (**Nizoral**) – when 400 mg/day of ketoconazole is taken, the dose of maraviroc should be reduced to 150 mg twice daily
- itraconazole (**Sporanox**) – the dose of maraviroc used should be reduced to 150 mg twice daily
- voriconazole (**Vfend**) – the manufacturer recommends that a dose of 300 mg twice daily be used with caution

## Antibiotics:

- rifampin / rifampicin – the dose of maraviroc should be increased to 600 mg twice daily when rifampin at a dose of 600 mg per day is used.
- clarithromycin (**Biaxin**) or telithromycin (**Ketek**) – the dose of maraviroc should be decreased to 150 mg twice daily

## Erectile dysfunction agents

- sildenafil (**Viagra**) – people taking either drug have reported low blood pressure. Therefore, the dose of maraviroc 300 mg twice daily should be used with caution.

## Resistance, cross-resistance and treatment interruption

Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes are called mutations and can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you. Combining maraviroc with at least two other anti-HIV drugs delays the development of drug resistance.

To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken every day exactly as prescribed and directed. If doses are delayed, missed, or not taken as prescribed, levels of maraviroc in the blood may fall too low. If this happens, resistant virus can develop. If you find you are having

problems taking your medications as directed, speak to your doctor and nurse 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 therapies might be, at some point your doctor can have a small sample of your blood analysed using resistance testing. Should HIV in your body become resistant to maraviroc, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

There are other CCR5 receptor blockers in development. It is not clear if HIV resistant to maraviroc will be sensitive to these other receptor blockers.

## Dosage and formulations

Maraviroc (**Celsentri**) is available in 150 and 300 mg tablets. The dose of maraviroc used depends on the other medications in your combination; check the “Drug interactions with maraviroc” section for more specific information.

Formulations can change, and dosages may need to be customized. All medications should always be taken as prescribed and directed.

## Availability

Maraviroc is licensed in Canada for the treatment of HIV infection in adults, in combination with other anti-HIV drugs. Your doctor can tell you more about the availability and coverage of maraviroc in your region. CATIE’s online module Federal, Provincial and Territorial Drug Access Programs (on CATIE’s website at [www.catie.ca/eng/Publications/drugaccess/drugaccessIndex.shtml](http://www.catie.ca/eng/Publications/drugaccess/drugaccessIndex.shtml)) also contains information about Canadian drug coverage.



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## Credits

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## Disclaimer

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

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