Maraviroc (Celsentri)

Summary
Maraviroc is a type of anti-HIV drug called a CCR5 antagonist or entry inhibitor. Common side effects of maraviroc include cough, fever, muscle pain and rash. The dose of maraviroc prescribed 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 (or Selzentry in the U.S.), is a type of anti-HIV drug called a CCR5 antagonist or entry inhibitor. Maraviroc is used in combination with other anti-HIV (antiretroviral) drugs to treat, but not cure, HIV.

How does maraviroc work?
Whereas most currently approved drugs used to treat HIV infection work by interfering with HIV after it has infected a cell, maraviroc acts before HIV has infected a cell. Maraviroc works by covering a molecule called CCR5, which is found on the surface of cells of the immune system. Maraviroc blocks access to CCR5 so HIV cannot enter and infect that cell; hence, it belongs to a class of anti-HIV drugs called entry inhibitors. Using maraviroc as part of combination therapy reduces HIV's ability to infect cells and reduces the virus's ability to make copies of itself.

Know your co-receptors
To enter and infect a cell, HIV needs a number of different molecules on the surface of the cell—these are called receptors. One of these receptors is called CD4. HIV also needs at least one of two co-receptors—CXCR4 (or X4) or 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. Maraviroc only works against HIV that prefers CCR5 (or R5) receptors.
Tropism testing

Tropism testing is used to determine which kind of virus a person has. For this test, a sample of blood is analyzed to find out the tropism of the virus. Before using maraviroc, tropism testing must be done to help a physician decide whether maraviroc is going to work.

The result of tropism testing can be as follows:

- **R5**—this means that the HIV in your body tends to use CCR5 co-receptors and that you can use maraviroc.
- **Non-R5**—this means that the HIV in your body tends to use CXCR4 co-receptors and that maraviroc will not work.
- **Non-reportable**—this means that the test did not work for some reason (for example, there was not enough virus to test in the sample).

How do people with HIV use maraviroc?

Maraviroc is used in combination with other anti-HIV drugs, usually nukes (nucleoside analogues), non-nukes (NNRTIs) and drugs from other classes, such as protease inhibitors. Such combinations are called antiretroviral therapy, or ART. For more information on ART, see CATIE's Your Guide to HIV Treatment.

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

- See your doctor regularly so that he or she can monitor your health.
- Continue to practise safer sex and take other precautions to avoid passing HIV on to other people and protect yourself from different strains of HIV as well as other germs.

Warnings

1. Liver health

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

- an itchy rash
- your skin or eyes look yellow
- 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 a person’s risk of developing infections and possibly cancer. In studies of people who took maraviroc, there appeared to be a slightly increased risk of herpes infections. The manufacturer of maraviroc recommends that people taking the drug be monitored for symptoms of infection.

Studiees of people who took maraviroc for one year found no increased risk of cancer. However, the long-term risks of maraviroc use are not known.

3. Cardiovascular

According to the manufacturer, maraviroc should be “used with caution” by patients with a history of cardiovascular disease and people who are at risk for a heart attack, stroke or other cardiovascular-related complications.

Maraviroc should also be used with caution by people who have low blood pressure and people who are taking medication to lower their blood pressure.
Side effects

Because maraviroc is a relatively new medication, the full range of its side effects may not be known for many years.

1. General

The most commonly reported side effects include the following:

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

If any side effects are severe or do not go away, let your doctor know about them.

If you experience any of the following symptoms, call your doctor immediately:

- signs of infection, such as sore throat, fever or chills
- pain, pressure or discomfort in the chest
- pain in your arm, back, neck, jaw or stomach
- shortness of breath
- sweating

2. Cardiovascular

People who have low blood pressure and use maraviroc may experience dizziness, lightheadedness or fainting when they stand up. If this happens to you, rest your feet on the ground for a few minutes before you stand up and try getting up slowly. If this problem happens again, let your doctor know.

3. Hepatitis

Maraviroc has not been well studied in people co-infected with HIV and hepatitis B or C. Hepatitis viruses cause liver damage and if liver disease grows worse while a person is taking maraviroc, the manufacturer notes that doctors must consider interrupting or stopping the use of maraviroc.

4. Pregnancy

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

5. Lipodystrophy syndrome

HIV lipodystrophy syndrome is the name given to a range of symptoms that can develop over time when people use anti-HIV drugs. So far, there does not appear to be any link between maraviroc and lipodystrophy syndrome.

Some features of lipodystrophy 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, blood tests may detect the following:

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

The precise causes of HIV lipodystrophy syndrome are not clear and are difficult to understand. Some people living with HIV may experience one or more aspects of the syndrome. For instance, some people may experience fat wasting, others fat gain, and others may experience both fat wasting and gain. What is becoming increasingly clear is that increases in a person’s levels of glucose, cholesterol and triglycerides over a period of several years increase their risk of diabetes and cardiovascular disease. So far, however, the many benefits of anti-HIV drugs are much greater than the increased risk of cardiovascular disease or other side effects.

To reduce your risk of diabetes, heart disease and other complications, it is important to maintain a normal weight, eat a healthy diet, exercise regularly and, if you smoke, quit smoking. Regular visits to your doctor for checkups and blood tests are also a vital part of staying healthy. If necessary, your doctor can prescribe lipid-lowering therapy.

Researchers are studying lipodystrophy syndrome to try to discover how it might be avoided or minimized. To find out more options for managing lipodystrophy syndrome, see CATIE’s Practical Guide to HIV Drug Side Effects.

**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. An interaction may increase or decrease the amount of maraviroc you have in your body. Increased drug levels can cause you to experience more side effects or make pre-existing side effects worse. On the other hand, if drug levels become too low, HIV can become drug-resistant and your future treatment options may become more limited.

If you must take a drug that could potentially interact with maraviroc, your doctor may do the following:

• adjust the dose of either the maraviroc or your other medication
• prescribe different anti-HIV drugs for you

Do not use the herbal supplement St. John’s Wort with maraviroc. St. John’s Wort lowers the level of maraviroc in the blood.

The following is a list of drugs that can interact with maraviroc. Your doctor may need to adjust your dose of maraviroc if you are also taking any of these drugs (this list is not exhaustive):

**Non-nukes**

• efavirenz (Sustiva, also in Atripla) — the dose of maraviroc should be increased.
• delavirdine (Rescriptor) — the dose of maraviroc should be decreased.
• etravirine (Intelence) — the dose of maraviroc should be increased.

**Protease inhibitors**

• atazanavir (Reyataz) with or without ritonavir (Norvir) — the dose of maraviroc should be decreased.
• darunavir (Prezista) with ritonavir — the dose of maraviroc should be decreased.
• saquinavir (Invirase) with ritonavir — the dose of maraviroc should be decreased.
• nelfinavir (Viracept) — the dose of maraviroc should be decreased.

**Non-nukes and protease inhibitors**

• lopinavir/ritonavir (Kaletra) and efavirenz — the dose of maraviroc should be decreased.
• saquinavir/ritonavir and efavirenz — the dose of maraviroc should be decreased.
• efavirenz and ddl-EC (Videx EC) and tenofovir (Viread)—the dose of maraviroc should be increased.

• etravirine (Integrelin) and darunavir/ritonavir—the dose of maraviroc should be decreased.

Other combinations of anti-HIV medications
• efavirenz and Combivir (AZT and 3TC)—the dose of maraviroc should be increased.

• lopinavir/ritonavir, 3TC and d4T (stavudine, Zerit)—the dose of maraviroc should be decreased.

Antifungal agents
• ketoconazole (Nizoral)—when 400 mg/day of ketoconazole is taken, the dose of maraviroc should be reduced.

• itraconazole (Sporanox)—the dose of maraviroc used should be reduced.

• voriconazole (Vfend)—should be used with caution.

• fluconazole (Diflucan)—should be used with caution.

Antibiotics
• rifampin/rifampicin—the dose of maraviroc should be increased.

• clarithromycin (Biaxin) or telithromycin (Ketek)—the dose of maraviroc should be decreased.

Erectile dysfunction agents
• sildenafil (Viagra)—people taking either drug have reported low blood pressure; therefore, 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, called mutations, can cause HIV to resist the effects of anti-HIV drugs. If this occurs, those drugs may 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. If doses are delayed, missed or not taken as prescribed, the level of maraviroc in the blood may fall too low. If this happens, the virus can become drug resistant. If 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 analyzed to test for resistance. Should HIV in your body become resistant to maraviroc, your doctor can recommend a new treatment combination for you.

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

Dosage and formulations
Maraviroc is available in 150 and 300 mg tablets. The dose of maraviroc prescribed depends on the other medications in your combination.

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

Maraviroc can be taken with or without food. Tablets should be swallowed whole—avoid splitting, chewing or crushing them.

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 also contains information about drug coverage in Canada.

References


Holst PJ, Orskov C, Qvortrup K et al. CCR5 and CXCR3 are dispensable for liver infiltration, but CCR5 protects against virus-induced T-cell-mediated hepatic steatosis. Journal of Virology. 2007;81(18):10101-10112.


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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.

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