



FACTSHEET

Raltegravir (Isentress)

Summary

Raltegravir is a type of anti-HIV drug called an integrase inhibitor. Common side effects of raltegravir can include cough, headache and rash. The dose of raltegravir used is usually 400 mg twice daily. Raltegravir can be taken with or without food.

What is raltegravir?

Raltegravir, sold under the brand name **Isentress**, is a type of anti-HIV (antiretroviral) drug called an integrase inhibitor. Raltegravir is used in combination with other anti-HIV drugs to treat, but not cure, HIV.

How does raltegravir work?

Raltegravir is the first integrase inhibitor approved for treatment of HIV. This drug works by interfering with an enzyme needed by HIV called integrase. By interfering with this enzyme, raltegravir helps to reduce the ability of HIV to infect cells and take over cells. So using raltegravir as part of combination therapy helps to reduce HIV's ability to infect cells and production of new copies of HIV is also greatly reduced.

How do people with HIV use raltegravir?

Raltegravir 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.

For many people with HIV, 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 raltegravir 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/she monitors your health;
- continue to practise safer sex and take other precautions so as not to pass HIV on to other people and to protect yourself from different strains of HIV and other germs.

Warnings

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

1. Pregnancy

Raltegravir has not been studied in large numbers of pregnant, HIV-positive women. Therefore, the manufacturer does not recommend the use of this drug in pregnant women. If you are pregnant or want to have a baby, talk to your doctor so that you can find medicines that are safe for you and your baby.

2. Other medicines

The manufacturer recommends that raltegravir be used cautiously with drugs such as the antibiotic rifampin (used to treat TB). Levels of raltegravir may fall considerably when it is taken by people who are also taking rifampin.

3. Cancer risk

In the early stages of clinical trials with raltegravir there were reports of an apparent increase in cancers seen in some raltegravir users. Concerned about this finding, researchers compared cancer cases seen in several raltegravir trials over time. The researchers found that after 12 months there was no statistically significant difference in rates of cancer between people receiving raltegravir and others who received placebo. This suggests that there is no significantly increased risk of cancer due to raltegravir exposure.

People taking raltegravir will continue to be monitored for the development of cancer to ensure that raltegravir has no potential cancer-causing effects. For more information on cancer risk with raltegravir see CATIE's *Treatment Update 173* at www.catie.ca/tu.nsf.

Side effects

1. General

Raltegravir is a relatively new drug and so its full range of side effects is not known. Long-term monitoring of raltegravir users is underway, as are many clinical trials. Raltegravir is generally well-tolerated. In clinical trials, raltegravir was used as part of combination therapy and so it is

difficult to be certain about the side effects caused by this drug. Here is a list of some symptoms reported by raltegravir users in clinical trials:

- cough;
- fever;
- rash;
- muscle pain;
- stomach pain;
- dizziness;
- constipation;
- itching;
- difficulty sleeping.

2. Hepatitis

Raltegravir has not been well studied in people co-infected with HIV and hepatitis-causing viruses, such as hepatitis B virus or hepatitis C virus. In clinical trials, only about 16% of people taking raltegravir were co-infected with these viruses. Liver enzymes (AST and ALT) were somewhat higher in co-infected people after taking raltegravir.

3. 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 people with HIV there may be one or more aspect 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 people with HIV 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.

So far, there is no link between raltegravir and the lipodystrophy syndrome.

4. Depression

According to regulatory authorities in the European Union as well as doctors in British Columbia, there have been reports of worsening of pre-existing depression and in some cases thoughts of suicide in some people who took raltegravir. If you have been depressed in the past or think you might have depression, let your doctor know.

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 raltegravir, 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 raltegravir

In general, raltegravir tends not to interact with other anti-HIV drugs. Raltegravir does not interact with female hormonal contraceptives (the pill). However, raltegravir can interact with the antibiotic rifampin / rifampicin, which is used for TB treatment.

Antibiotics

- rifampin / rifampicin - this drug can reduce levels of raltegravir in the blood.

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 raltegravir 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 raltegravir 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 raltegravir, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

There are other integrase inhibitors in development, one of which is elvitegravir. If your HIV becomes resistant to raltegravir, it will also likely be resistant to elvitegravir.

Raltegravir is licensed for use against HIV-1—the most common form of HIV. But laboratory experiments suggest that it should be effective against HIV-2.

Dosage and formulations

Raltegravir (**Isentress**) is available in 400 mg pink tablets. The dose of raltegravir used in adults with HIV is 400 mg twice daily. The drug may be taken with or without food.

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

Availability

Raltegravir is licensed in Canada for the treatment of treatment-experienced adult HIV-positive patients, in combination with other anti-HIV drugs. Your doctor can tell you more about the availability and coverage of raltegravir in your region. CATIE's online module Federal, Provincial and Territorial Drug Access Programs (on CATIE's Web site at www.catie.ca/eng/Publications/drugaccess/drugaccessIndex.shtml) also contains information about Canadian drug coverage.

Credits

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Date: 2009

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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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Funding has been provided by the Public Health Agency of Canada.

