

# Nevirapine (Viramune)

## Summary

Nevirapine is a type of anti-HIV drug from the group commonly called non-nukes. The most common side effect of nevirapine is skin rash. Nevirapine is taken at a dose of 200 mg twice a day, with or without food.

## What is nevirapine?

Nevirapine, sold under the brand name Viramune, is a type of anti-HIV drug (antiretroviral) called a non-nuke or NNRTI (non-nucleoside reverse transcriptase inhibitor). Nevirapine is used in combination with other anti-HIV drugs to treat (but not cure) HIV.

## How does nevirapine work?

To explain how nevirapine works, we need to first tell you some information about HIV. When HIV infects a cell, it takes control of that cell. HIV then forces the cell to make many more copies of the virus. To make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced the production of HIV slows.

Nevirapine belongs to a group or class of drugs called non-nucleoside reverse transcriptase inhibitors. Nevirapine interferes with an enzyme called reverse transcriptase (RT), which is used by HIV-infected cells to make new viruses. Since nevirapine inhibits, or reduces the activity of this enzyme, this drug causes HIV-infected cells to produce fewer viruses.

## How do people with HIV use nevirapine?

Nevirapine is used in combination with several other anti-HIV drugs, usually including drugs from different classes, such as protease inhibitors and/or nukes (nucleoside reverse transcriptase inhibitors). Combinations such as this 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 ART 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

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**Published**  
2014

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infection. Neither nevirapine 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

## Warnings

### 1. Skin reactions

Although they are rare, severe and life-threatening skin reactions have occurred in a small number of nevirapine users. A severe rash could be a sign of a rare allergic reaction, called Stevens-Johnson syndrome, that may be life threatening. If a rash occurs while you are taking nevirapine, tell your doctor right away. Along with a rash, the following may occur:

- fever
- blisters
- sores/lesions in the mouth
- itching or burning eyes, eyelids
- swelling of the face
- muscle or joint pain
- tiredness

If a rash is accompanied by any of these symptoms contact your doctor right away. Also, the manufacturer, Boehringer Ingelheim, recommends that you stop taking nevirapine and never take it again. This is because the rash may become severe and possibly fatal.

### 2. Liver damage

Although it is uncommon, severe and life-threatening liver damage has occurred in some people taking nevirapine. In a few cases, nevirapine has caused such severe liver inflammation (hepatitis) that people have died. It is therefore very important that you see your doctor regularly, particularly during the first 18 weeks that you are taking

nevirapine. Signs/symptoms of hepatitis can include one or more the following:

- loss of appetite
- nausea
- vomiting
- diarrhea
- pale stools
- yellowing of the skin and eyes (jaundice)
- abdominal pain or tenderness

If you have any of these symptoms, tell your doctor immediately. Blood tests may detect higher-than-normal levels of liver enzymes—a sign of liver damage. If this happens, you may have to stop taking nevirapine.

### 3. Co-infection with hepatitis B or C

People with HIV who are co-infected with hepatitis B or C and who use nevirapine are at increased risk of developing nevirapine-related side effects. Because alcohol damages the liver, researchers recommend users of nevirapine avoid drinking alcohol.

### 4. Women and pregnancy

There have been reports that HIV-positive women may be more likely to develop nevirapine-associated rash than men. Moreover, women who have more than 250 CD4+ cells when beginning therapy with nevirapine are at considerably increased risk of liver toxicity if they use nevirapine. Why this difference between men and women occurs is not clear. In one study, researchers found that on average, women had higher levels of nevirapine in their blood than men. The increased risk of serious side effects in women highlights the importance of careful monitoring by your doctor.

If you are pregnant or wish to become pregnant, talk to your doctor about the use of nevirapine.

## 5. Men and nevirapine

Men who have more than 400 CD4+ cells when starting therapy with nevirapine may be at increased risk of rash and liver toxicity.

## 6. Low body mass index

One study has found that both men and women who have low body mass index (BMI) are at increased risk for nevirapine-related toxicity. BMI is calculated by dividing a person's weight (in kg) by the square of their height (in m). Your doctor or nurse can calculate your BMI for you. People with HIV who have a BMI less than 18 are at risk for developing side effects from nevirapine.

## Side effects

### 1. General

The most common side effects reported in users of nevirapine include the following:

- rash
- nausea
- fatigue
- headache
- sleepiness
- diarrhea
- abdominal pain
- muscle pain

### 2. Rash and liver toxicity

Although uncommon, nevirapine can cause skin rashes and/or liver damage. These side effects can be severe and life threatening. If you experience these side effects, tell your doctor immediately. For more information about rash and liver damage please see "Warnings."

### 3. Central nervous system (CNS)

There have also been rare reports of nevirapine being associated with depression and delusions.

These symptoms cleared once nevirapine was stopped.

## 4. Lipodystrophy syndrome

The HIV lipodystrophy syndrome is the name given to a range of symptoms that can develop over time when people use ART. 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 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 ART 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*.

For more information on side effects, see also Warnings.

## Drug interactions

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

Some drugs can interact with nevirapine, 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.

It may also be necessary to avoid drugs that do not affect nevirapine drug levels, but cause similar side effects.

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 for nevirapine

The following drugs interact or have the potential to interact with nevirapine. These lists are not exhaustive.

The following drugs can *increase* levels of nevirapine in the blood:

- antibiotics – erythromycin (Eryc)
- antifungal drugs – fluconazole (Diflucan, Triflucan)

The following drugs can *decrease* levels of nevirapine in the blood:

- herbs – St. John's wort
- antibiotics / anti-tuberculosis drugs – rifampin (Rifadin, Rifater): the manufacturer suggests that an alternative antibiotic, rifabutin (Mycobutin), be used instead

Nevirapine can *decrease* levels of the following drugs:

- anti-HIV drugs – efavirenz (Sustiva, Stocrin), indinavir (Crixivan), saquinavir (Invirase), lopinavir (in Kaletra); an increase in the dose of Kaletra is necessary if you are also taking nevirapine
- antibiotics – clarithromycin (Biaxin); the manufacturer suggests considering alternative antibiotics
- anti-cancer drugs – cyclophosphamide (Cytoxan, Procytox)
- anti-fungal drugs – itraconazole (Sporanox), ketoconazole (Nizoral)
- anti-seizure drugs – carbamazepine (Tegretol), phenytoin (Dilantin), phenobarbital (Dilantin)
- birth control medication – ethinyl estradiol, norethindrone
- drugs for abnormal heart rhythms – amiodarone (Codarone), bepridil (Vasacor) flecainide (Tambocor), propafenone (Rhythmol), quinidine

- methadone – nevirapine can cause levels of methadone in the blood to drop so low that people experience withdrawal symptoms. (Methadone users may have to have their dose increased if they take nevirapine.)
- migraine drugs (ergot derivatives) – dihydroergotamine (Migranal), Ergomar (ergotamine), Ergonovine
- transplant drugs – cyclosporine (Neoral), tacrolimus (Prograf), sirolimus (Rapamune)

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

If you stop taking nevirapine, low levels of this drug can remain in your body for up to two weeks. In the absence of combination therapy, these low levels of nevirapine are not high enough to suppress HIV. Therefore, if you are taking nevirapine and need to interrupt your therapy, speak to your specialist

about ways of minimizing the chance that HIV in your body might become resistant to nevirapine. HIV that is resistant to nevirapine will usually also be resistant to other NNRTIs such as delavirdine (Rescriptor) and efavirenz.

### Therapeutic drug monitoring (TDM)

In some parts of Canada your doctor may have access to therapeutic drug monitoring (TDM). This is a process whereby a sample of your blood is taken and the amount of nevirapine in it is assessed. If your nevirapine levels are too low or too high, your doctor may adjust your dose of nevirapine. TDM can be a useful tool to ensure that nevirapine levels in your blood are appropriate particularly if you are replacing a protease inhibitor with nevirapine or if you are taking a complex treatment regimen. Feel free to speak to your doctor about whether TDM is an option for you and if you will have to pay for it.

### Dosage and formulations

Nevirapine is available as 200 mg tablets and in a 10 mg/mL liquid. In the first two weeks of treatment, the usual standard adult dose of nevirapine is 200 mg (1 tablet), daily. After this, the dose is 200 mg (1 tablet), twice daily. Nevirapine can be taken with or without food. Nevirapine is also available as Viramune XR extended release tablets. The extended release tablets should not be broken or chewed. Formulations can change, and dosages may need to be customized. All medications should always be taken as prescribed and directed.

### Availability

Nevirapine 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 nevirapine in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

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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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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.

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