Rilpivirine (Edurant)

Summary

Rilpivirine is a type of anti-HIV drug called a non-nuke, or NNRTI. Rilpivirine is approved for use only in people who have never used anti-HIV drugs. Common side effects of rilpivirine include headache, nausea and sleep problems. The dose of rilpivirine used is usually 25 mg once daily. This medication should always be taken with a meal.

What is rilpivirine?

Rilpivirine, sold under the brand name Edurant (also called TMC125), belongs to a class of anti-HIV drugs called non-nukes or NNRTIs (non-nucleoside reverse transcriptase inhibitors). Rilpivirine is used in combination with other anti-HIV drugs (or antiretrovirals) to treat, but not cure, HIV infection.

How does rilpivirine work?

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.

Rilpivirine interferes with an enzyme called reverse transcriptase, which is used by HIV-infected cells to make copies of the virus. Because rilpivirine inhibits or reduces the activity of this enzyme, this drug causes HIV-infected cells to produce less HIV.

Rilpivirine is licensed for use against HIV-1, the most common form of HIV.

How do people with HIV use rilpivirine?

Rilpivirine is used in combination with anti-HIV drugs from other classes, usually nukes (nucleoside analogues) and protease inhibitors or integrase inhibitors. Combinations such as these are called antiretroviral therapy, or ART. (For more information on these drug combinations, see CATIE’s Your Guide to HIV Treatment.)

For many people with HIV, the use of HIV drug treatment has increased their CD4 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 rilpivirine 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 prevent passing HIV on to other people and protect yourself from different strains of HIV and other germs.

**Warnings**

Because rilpivirine is a relatively new medication, the full range of its side effects may not be known for many years. The following potentially serious side effects are uncommon; you may not experience any of them. However, if you do, report them to your doctor. This is not a complete list. Talk to your doctor and pharmacist about side effects that might occur with your use of rilpivirine.

1. **Cardiovascular health**

The manufacturer advises that rilpivirine should be used cautiously in people who might have cardiovascular health complications, including abnormal heart rhythms, heart failure and poor circulation of blood to the heart. In clinical trials, researchers found that exposure to rilpivirine gradually affected the hearts of some volunteers and that they were more likely to develop abnormal heart rhythms.

Symptoms of abnormal heart rhythms can include the following:

- dizziness
- fainting
- palpitations (a feeling that your heart is pumping very hard or fast when you are at rest)
- seizures

If you develop any of these symptoms, talk to your doctor right away.

If you have cardiovascular disease, including abnormal heart rhythms, or have a parent, brother or sister with any type of heart problem, let your doctor(s) know.

2. **Mental health**

In clinical trials, problems related to depressive illness, including depression, anxiety and negative thoughts, were reported. In less than 5% of participants, the severity of these symptoms ranged from moderate to life-threatening. However, only about 1% of rilpivirine users in clinical trials needed to stop taking this drug because of these symptoms.

While taking rilpivirine, if you have any of the following symptoms, see your doctor right away:

- you become easily upset or angry
- you have unexpected feelings of sadness
- you feel hopeless
- you have strange thoughts
- you have thoughts about harming yourself or others
- you have thoughts about suicide

3. **Hepatitis and liver health**

The manufacturer recommends that rilpivirine should not be used in people with severe liver damage. Rilpivirine has been tested in only a small number of people with mild-to-moderate liver damage. Therefore, the manufacturer recommends that it be used cautiously in people with mild-to-moderate liver damage.

In clinical trials, HIV-positive patients co-infected with hepatitis B or C viruses who received rilpivirine had increased levels of liver enzymes in the blood. The levels of these enzymes were higher in participants who were co-infected with HIV and hepatitis B or C than in other clinical trial participants who were not co-infected with hepatitis B or C.

Increased levels of liver enzymes may suggest liver inflammation and dysfunction; talk to your doctor about your test results.
4. High HIV viral load

In clinical trials of rilpivirine, some volunteers had high viral loads (more than 100,000 copies/ml) before receiving this drug. Such people were more likely to develop virologic failure when given rilpivirine-based ART, than people whose pre-study viral loads were less than 100,000 copies/ml. Moreover, volunteers whose rilpivirine-based regimens failed developed HIV that was resistant not only to rilpivirine and other non-nukes, such as efavirenz (Sustiva and in Atripla), etravirine (Intelence) and nevirapine (Viramune), but to other nukes as well. Taking this information into account, the United States Department of Health and Human Services (DHHS), which writes comprehensive HIV treatment guidelines, has stated that “caution should be exercised when using rilpivirine in patients [whose viral load is greater than] 100,000 copies/ml.”

5. Pregnancy

As rilpivirine is a new drug, there is no information from large numbers of pregnant women on the safety of rilpivirine for these women or their fetuses. Studies in animals do not suggest that rilpivirine can damage the fetus. However, the manufacturer recommends that rilpivirine “should not be used during pregnancy unless the potential benefits outweigh the potential risks.”

Side effects

1. General

Rilpivirine is a relatively new drug so the full range of its side effects are not yet known. However, data from clinical trials suggest that rilpivirine is generally well-tolerated. Monitoring of long-term rilpivirine use is underway. In clinical trials, rilpivirine was used as part of combination therapy so it is difficult to be certain which side effects are caused by this drug.

Here is a list of some symptoms reported by rilpivirine users in clinical trials:

- dizziness
- feeling sleepy during the daytime
- headache
- rash
- nausea
- stomach pain

2. Depression (see also Warnings, above)

Rilpivirine, like all non-nukes, has the potential to cause depression and anxiety, although in clinical trials, less than 10% of people reported such problems. Before severe depression occurs, more subtle symptoms may appear, such as:

- difficulty concentrating
- problems falling asleep
- problems staying asleep
- persistent irritability
- difficulty remembering
- fatigue
- changes in appetite
- persistent nightmares

If you notice these or changes to your mood, speak to your doctor right away.

3. 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. Although rilpivirine is a new drug, so far, there is no link between the use of rilpivirine and lipodystrophy syndrome.

Some features of lipodystrophy include:

- loss of 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)

In addition to 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 blood 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 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 the risk of diabetes and cardiovascular disease. So far, however, the many benefits of anti-HIV drugs far outweigh 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 ways of helping people with HIV avoid or reduce this problem. (To find out more about options for managing lipodystrophy syndrome, see CATIE’s A Practical Guide to HIV Drug Side Effects.)

**Food interactions**

Rilpivirine must always be taken with a meal so that it is absorbed. Avoid eating grapefruit or drinking grapefruit juice as these will increase the concentration of rilpivirine in your body leading to side effects.

**Drug and herb 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 rilpivirine, 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 become drug-resistant 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 the dose of either your anti-HIV drugs or other medications; or
- prescribe different anti-HIV drugs.

The manufacturer warns that rilpivirine should not be used with the following drugs or herbs because they can severely reduce the concentration of rilpivirine in the blood and cause HIV to become resistant to rilpivirine and other anti-HIV medicines. Note that the following lists are not exhaustive:

**Antiseizure drugs**

- carbamazepine, oxcarbazepine, phenobarbital and phenytoin.

**Antibiotics for TB (tuberculosis) or MAC (mycobacterium avium complex)**

- rifabutin (Mycobutin), rifampin (Rifadin, Rofact and in Rifater), rifampicin and rifapentene.
**Corticosteroids**
- Dexamethasone given as pills, injection or intravenously. Given in these forms, high doses of corticosteroids can accumulate in the body and interact with rilpivirine.

**Herbs**
- St. John’s wort (hypericin, hyperforin).

**Non-nukes**
- efavirenz (Sustiva, also in Atripla), etravirine (Inteligible) and nevirapine (Viramune).

**Proton pump inhibitors**
- esomeprazole (Nexium), lansoprazole (Prevacid), omeprazole (Losec), pantoprazole (Pantoloc), rabeprazole (Pariet).

The manufacturer warns that the following drug should not be used with rilpivirine because it can greatly increase rilpivirine levels (and can therefore cause side effects):

**Delavirdine**
- Unlike the other non-nukes listed above, delavirdine (Rescriptor) can increase levels of rilpivirine and should not be used by people taking rilpivirine.

The manufacturer warns that the following drugs can increase rilpivirine levels and suggests that physicians exercise “caution” when prescribing these drugs to patients who are taking rilpivirine:

**HIV protease inhibitors**
- Atazanavir (Reyataz), darunavir (Prezista), fosamprenavir (Telzir), lopinavir-ritonavir (Kaletra), ritonavir (Norvir), saquinavir (Fortovase), tipranavir (Aptivus). Rilpivirine should not increase levels of these other drugs.

**Antacids**
- containing aluminum, magnesium hydroxide or calcium carbonate. The manufacturer warns that these drugs should be used with caution as they can affect the acidity of the stomach and greatly decrease absorption of rilpivirine and reduce its levels in the blood.

The manufacturer recommends that antacids should only be used “either at least two hours before or at least four hours after” a person takes rilpivirine.

**Antifungal agents**
- azole antifungal drugs, such as fluconazole (Diflucan), itraconazole (Sporanox), posaconazole (Spiralizil) and voriconazole (Vfend) can all increase levels of rilpivirine in the blood. Also, rilpivirine can reduce the concentration of these drugs in the blood leading to new or recurring fungal infections. Therefore, these drugs should not be used by people taking rilpivirine.

**Macrolide antibiotics**
- Clarithromycin (Biaxin), erythromycin and troleandomycin can all increase rilpivirine levels leading to side effects. The manufacturer suggests that when possible, physicians should consider prescribing an alternative macrolide, such as azithromycin (Zithromax).

The following drugs can decrease rilpivirine levels and must be used cautiously:

**Histamine2-receptor antagonists**
- cimetidine (Tagamet), famotidine (Pepcid), nizatidine, ranitidine (Zantac). These drugs reduce the acidity of the stomach and can therefore significantly reduce absorption of rilpivirine. This can lead to HIV becoming resistant to rilpivirine and other anti-HIV drugs. The manufacturer suggests that these drugs should be used with caution and if they must be used, then they should only be taken “at least 12 hours before or at least four hours after rilpivirine.”
Other drugs

Medicines that cause people to urinate (water pills, diuretics) excessively or have diarrhea (laxatives or enemas) or other drugs such as amphotericin B (Fungizone, Abelcet) can upset the balance of minerals in your blood and this could affect your heart’s rhythm. The manufacturer recommends that these drugs be used cautiously in people taking rilpivirine.

Interactions are not expected

The manufacturer does not expect rilpivirine to interact with these drugs:

- methadone
- certain HIV and hepatitis drugs—specifically, nukes for treating HIV (abacavir, 3TC, FTC, tenofovir and similar drugs); co-receptor blockers, such as maraviroc (Celsentri); and nukes for treating hepatitis C, such as ribavirin; integrase inhibitors such as raltegravir (Isentress). The drug ddl (Videx) needs to be taken on an empty stomach at least two hours before or at least four hours after taking rilpivirine
- erectile dysfunction drugs such as sildenafil (Viagra), tadalafil (Cialis) or vardenafil (Levitra)
- lipid-lowering agents called statins, including atorvastatin (Lipitor), rosuvastatin
- (Crestor) and similar drugs
- oral contraceptives (“the pill”)

Dosage and formulations

Rilpivirine (Edurant) is available in 25 mg tablets. The usual dose of rilpivirine for adults with HIV is 25 mg once daily. The drug should always be taken right after a meal to ensure absorption. Taking it on an empty stomach may make it less effective.

Rilpivirine must always be taken with a meal. The tablets should be swallowed whole, with water or another liquid.

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

Availability

Rilpivirine, in combination with other anti-HIV drugs, is licensed in Canada for the treatment of HIV-1 infection in adults who have never previously used ART. Your doctor can tell you more about the availability and coverage of rilpivirine in your region. CATIE’s online module Federal, Provincial and Territorial Drug Access Programs also contains information about drug coverage.

References


Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents. Recommendations for NNRTI use in antiretroviral treatment-naïve patients with HIV-1 infection. 16 August, 2011.


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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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