What is delavirdine?

Delavirdine, sold under the brand name Rescriptor, is a type of antiretroviral drug called a non-nucleoside reverse transcriptase inhibitor. Antiretroviral drugs fight HIV infection by interfering with the life cycle of the virus. At each stage of this cycle, chemicals called enzymes help the virus make copies of itself (replicate). Some drugs can inhibit (slow down or stop) the actions of these enzymes. When these enzymes can’t perform effectively, the virus does not replicate as efficiently, thus slowing the progression of HIV disease.

How does delavirdine work?

HIV infects cells and then replicates with the help of its own enzymes. In the first stage of replication, the enzyme reverse transcriptase converts the genetic material of the virus (RNA) to match the genetic material of the cell (DNA). Non-nucleoside reverse transcriptase inhibitors (NNRTIs or “non-nukes”) like delavirdine interfere directly with the action of the reverse transcriptase enzyme, preventing it from working properly.

Summary

Delavirdine is a type of anti-HIV drug called a non-nucleoside reverse transcriptase inhibitor. The most common side effect is a skin rash that usually goes away on its own. Delavirdine is taken three times a day, with or without food.

CD4+ counts and viral load measures as well as reduce opportunistic infections. The International AIDS Society–USA suggests that a combination of delavirdine plus two nucleoside analogues may be a useful first combination for treating HIV infection.

Health Canada has granted conditional approval for the sale of delavirdine. This approval is based on studies that showed a statistically significant (that is, not due to chance alone) drop in viral load when delavirdine was combined with AZT and 3TC. When delavirdine was added to AZT + ddI, no statistically significant change in viral load was seen. To receive unconditional approval to market delavirdine, the manufacturer must submit to Health Canada study results that show clinical benefit (improved survival, decreased opportunistic infections).

Resistance and cross-resistance

Over time, as HIV makes copies of itself, the virus can change its structure. These changes allow HIV to resist the effects of antiretroviral drugs. Resistance to non-nukes, when used alone, appears as early as two weeks after treatment begins. Combining delavirdine with at least two other drugs may delay the

Combination therapy

For many people, combination therapy with three or more anti-HIV drugs can improve CD4+ counts and viral load measures as well as reduce opportunistic infections. The International AIDS Society–USA suggests that a combination of delavirdine plus two nucleoside analogues may be a useful first combination for treating HIV infection.

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development of drug resistance. To limit the risk of resistance, all antiretroviral drugs should be taken every day, exactly as prescribed. This strict schedule is necessary because resistant virus can develop if the level of drug in the blood drops. This may happen if doses are delayed or skipped.

It's generally believed that all non-nukes may be cross-resistant. This means that, if HIV becomes resistant to one non-nuke, it may also be able to resist the effects of the other non-nukes. In other words, if the virus has become resistant to delavirdine it will probably be resistant to nevirapine and efavirenz.

## Side effects

The most common side effect of delavirdine is a skin rash. The rash appears as red, slightly raised patches on the skin and may be itchy. Rash usually develops within the first three weeks of taking delavirdine. Although it often disappears on its own after a couple of weeks, anyone who develops a rash while using delavirdine should consult their doctor as soon as possible. If the rash is accompanied by fever, skin blisters, itching or burning eyes, swelling, muscle or joint pain, delavirdine must be stopped.

Other side effects include headache, nausea, diarrhea, fatigue, fever, and changes in dreams.

Blood tests may show higher than usual levels of liver enzymes.

To date, there have been no reports of side effects unique to women.

## Drug interactions

Delavirdine is metabolized (broken down and processed) by the liver through the actions of the p450 cytochrome enzymes. Taking delavirdine with drugs that are metabolized the same way may change blood levels of each drug. As a result of these drug interactions, blood levels of some drugs may drop too low to be of benefit, or they may rise so high they cause serious side effects. Dosages of other drugs may therefore have to be raised or lowered, or some drugs may have to be changed.

Drugs that should not be taken with delavirdine include terfenadine (Seldane) and astemizole (Hismanal), phenytoin, phenobarbital, carbamazepine (Tegretol), triazolam (Halcion), alprazolam (Xanax), midazolam (Versed), rifampin, rifabutin (Mycobutin), cimetidine (Tagamet), ranitidine (Zantac), nizatidine (Aixd), famotidine (Pepcid), quinidine, dapsone, and cisapride (Prepulsid). If you’re starting a new drug, check with your doctor or pharmacist about potential interactions with delavirdine.

Delavirdine should be taken at least one hour before or one hour after taking ddI or any antacid (Maalox, Rolaid, Tums, etc.).

## Delavirdine and protease inhibitors

The interaction studies of delavirdine with saquinavir hard-gel capsules (Invirase), indinavir, and nelfinavir were done with HIV-negative volunteers.

Saquinavir (600 milligrams (mg) three times a day) in combination with delavirdine (400 mg three times a day) produced a slight reduction of delavirdine levels. However, saquinavir levels were increased more than five times. Two of the thirty volunteers had serious increases in blood levels of the liver enzymes ALT and AST.

Indinavir was given as a single 400 mg or 600 mg dose with 400 mg of delavirdine three times a day. Delavirdine appeared to double the amount of indinavir in the blood. For this combination to be useful, Pharmacia and Upjohn (which manufactures delavirdine) suggest reducing indinavir dosage from 800 mg every eight hours to 400 mg every eight hours.

Ritonavir (600 mg twice a day) with delavirdine (400 mg three times a day) reduced delavirdine levels but increased ritonavir levels.
Dosage
The recommended dose of delavirdine is 400 mg taken three times daily, with or without food. The tablets can be dissolved in three ounces of any room-temperature liquid: water, juices, even carbonated drinks can be used to dissolve the tablets, although delavirdine tends to make pop foam up — like a Coke float.

Availability
Delavirdine received conditional marketing approval in June 1998. This conditional approval may affect provincial drug coverage.

Credits
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References

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