What is d4T?
d4T (stavudine), sold under the brand name Zerit, is a type of anti-HIV (antiretroviral) drug called a nucleoside analogue or “nuke.” d4T is used in combination with other anti-HIV drugs to treat, but not cure, HIV.

How does d4T work?
To explain how d4T 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.

d4T interferes with an enzyme called reverse transcriptase (RT), which is used by HIV-infected cells to make new viruses. Since d4T inhibits, or reduces, the activity of this enzyme, this drug causes HIV-infected cells to slow down or stop the production of new viruses.

How do people with HIV use d4T?
d4T is used in combination with several other anti-HIV drugs, including nukes (nucleoside analogues) and drugs from other groups (classes) of drugs, such as non-nukes (NNRTIs) and protease inhibitors (PIs). Combinations such as these are called antiretroviral therapy, or ART. For more information on ART, see CATIE’s A Practical Guide to HIV Drug 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 infection. Neither d4T nor any other anti-HIV drug 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.

Summary
d4T (stavudine, Zerit) is a type of anti-HIV drug called a nuke or nucleoside analogue. Common side effects of d4T can include headache, nausea, vomiting and diarrhea. d4T is taken twice daily, every 12 hours, with or without food. The appropriate dose of d4T depends on your weight.
Warnings

1. Lactic acidosis

Higher-than-normal levels of lactic acid can occur in the blood. This condition is called lactic acidosis and has happened in some people who have used nukes, including d4T. Women who are overweight are at increased risk for lactic acidosis. Sometimes the livers of people with lactic acidosis become swollen because of fatty deposits. Signs and symptoms of lactic acidosis may include the following:

- nausea
- vomiting
- abdominal pain
- diarrhea
- unexpected weight loss
- unexpected tiredness
- unexpected muscle pain
- feeling cold especially in the arms and legs
- feeling dizzy or light-headed

Because there have been fatal cases of lactic acidosis related to the use of d4T, if you have these symptoms, see your doctor right away.

2. Liver health

d4T should be used with caution in people who have a history of liver dysfunction or who have risk factors for liver disease including hepatitis co-infection. In some cases of d4T-related liver damage, the liver has become swollen and fatty. This has not been accompanied by higher-than-normal levels of liver enzymes in the blood. People who take the combination of d4T, ddI (didanosine, Videx EC) and hydroxyurea (Hydrea) are at increased risk for severe liver toxicity and death.

3. Neuro-muscular syndrome

There have been reports of rare cases of loss of control of, and difficulty coordinating, muscles and movement in users of d4T. Most of these cases have occurred in people who have had symptoms of lactic acidosis. The d4T neuro-muscular syndrome resembles a neurologic condition called Guillain-Barré syndrome. Guillain-Barré usually starts with these symptoms:

- unexpected muscle weakness
- tingling or loss of sensation in the feet and legs. This later spreads to the upper body and arms
- in some cases, tingling and loss of sensation may begin in the face

As the disorder gets worse, muscles become very weak and eventually paralysis can set in. If you have any of these symptoms, see your doctor right away.

4. Pancreatitis

Painful swelling of the pancreas gland has been reported in some people taking d4T as part of ART. Symptoms of pancreatitis can include the following:

- abdominal pain, particularly when laying down
- nausea
- vomiting
- unexpected sweating
- fever
- anxiety

If left untreated, pancreatitis can be fatal. If you think that you may have pancreatitis, consult your doctor right away.

The risk for pancreatitis may be increased for people who:

- have a CD4+ cell count less than 200
- have kidney problems
- drink alcohol
- use another nuke called ddI (didanosine, Videx EC)
• use intravenous pentamidine
• have higher-than-normal levels of triglycerides in the blood

**Side effects**

1. **General side effects**

Side effects that have occurred in d4T users include the following:

- headache
- nausea
- vomiting
- diarrhea
- loss of appetite
- difficulty falling asleep
- rash

Note that d4T contains milk sugar (lactose). Lactose intolerance is the name of the condition when people are unable to process milk sugar. Lactose intolerance can result in nausea and diarrhea. It is therefore possible that some d4T users who are lactose intolerant have the potential to develop nausea and/or diarrhea when using d4T. If this problem persists, speak to your doctor or nurse.

For more information about dealing with lactose intolerance, please see the section on gas and bloating in CATIE’s *Practical Guide to HIV Drug Side Effects*.

2. **Peripheral neuropathy**

Peripheral neuropathy (PN)—damage to the nerves in the hands, feet and/or legs—can occur in people taking d4T. When a person has PN, they usually experience one or more of the following symptoms in their hands, feet and/or legs:

- pain
- numbness
- tingling

If you have had PN in the past, let your doctor know before you start taking d4T. While taking d4T if you notice any of these symptoms of PN, tell your doctor immediately. Taking the nuke ddl with d4T can increase the risk of peripheral neuropathy.

3. **Pregnancy**

If you are pregnant or want to have a baby, speak to your doctor.

There are no well-controlled studies of d4T in pregnant HIV-positive women. Therefore, the manufacturer recommends that d4T “should be used in pregnancy only if the potential benefit justifies the potential risk.”

Note that cases of fatal lactic acidosis have occurred in pregnant women who received both d4T and ddl. This combination should be avoided in pregnant women.

4. **Lipodystrophy syndrome**

Because of its potential to cause fat wasting resulting in changes in body shape, leading HIV treatment guidelines do not recommended using d4T for the initial treatment of HIV infection. In some cases, when d4T users were switched to another therapy such as tenofovir (Viread) or abacavir (Ziagen and also found in the combination pill Kivexa)), this fat wasting stopped and was somewhat reversed. However, there have not been studies demonstrating complete recovery from d4T-associated fat wasting because of switching therapy.

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.

**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 d4T, 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 levels of d4T 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 d4T**

The following is a list of drugs that interact or have the potential to interact with d4T. This list is not exhaustive.

The manufacturer of d4T recommends that it not be used with the following drugs:

• AZT (zidovudine, Retrovir and also found in the combination pills Combivir and Trizivir)
• ribavirin
• doxorubicin (Adriamycin, Caelyx, Myocet)
Resistance and cross-resistance

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 d4T 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 d4T 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 d4T, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

Please note that d4T should not be used as part of a triple nuke regimen as this has not been proven to be effective against HIV.

Dosage and formulations

d4T is available as capsules, in the following strengths:

- 15 mg
- 20 mg
- 30 mg
- 40 mg

The adult dosage of d4T depends on your weight as follows:

- people who weigh 60 kg (132 pounds) or more—40 mg twice daily, every 12 hours
- people who weigh less than 60 kg—30 mg twice daily, every 12 hours

Note that d4T can be taken with or without food.

Availability

d4T 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 d4T in your region. CATIE’s online module Federal, Provincial and Territorial Drug Access Programs also contains information about Canadian drug coverage.

References


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