



AZT (Retrovir, zidovudine)

Summary

AZT is a type of anti-HIV drug called a nucleoside analogue (“nuke”). The most common side effects of AZT can include headache, nausea, and loss of appetite. More rarely, it can cause anemia and low white blood cell counts. It is usually taken at a dose of 300 mg twice daily, with or without food.

What is AZT?

AZT (zidovudine), sold under the brand name **Retrovir**, is a type of anti-HIV (antiretroviral) drug called a nucleoside analogue or “nuke”. AZT is used in combination with other anti-HIV drugs to treat (but not cure) HIV/AIDS.

AZT is usually taken as a component of **Combivir** and **Trizivir**, which are single tablets containing AZT plus one or more other anti-HIV drugs.

How does AZT work?

To explain how AZT 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. In order to make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced or blocked, production of HIV slows or stops.

AZT belongs to a group of drugs called nucleoside analogues. AZT interferes with an enzyme called reverse transcriptase (RT),

which is used by HIV-infected cells to make new viruses. Since AZT inhibits, or reduces the activity of this enzyme, this drug causes HIV-infected cells to produce fewer viruses.

How do people with HIV/AIDS use AZT?

AZT is used in combination with several other anti-HIV drugs, usually including drugs from different classes, such as protease inhibitors and/or non-nukes (non-nucleoside reverse transcriptase 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/AIDS (PHAs), 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 AZT nor any other



anti-HIV medication is a cure for HIV/AIDS. It is therefore important that you do the following:

- see your doctor regularly so that he/she monitors your health
- continue to practice safer sex and take other precautions so as not to pass HIV on to other people

AZT was originally approved under the brand name Retrovir, which is still available but is very rarely used as a separate medication. AZT is usually taken as a component in the “fixed-dose combinations” Combivir and Trizivir, which combine AZT with other anti-HIV drugs in a single tablet.

Women and childbirth

AZT is also used to help prevent the transmission of HIV from mother to child during pregnancy and childbirth. It was the first drug studied for this purpose and remains a cornerstone of this kind of prevention, although other drugs have also been investigated.

In 1994, a study found that HIV-positive mothers could lower the risk of passing HIV to their child by 70% by using AZT. The current standards for pregnant HIV-positive women include:

- Taking AZT orally, 300 mg twice daily or 200 mg three times daily, beginning 14 to 34 weeks into the pregnancy and continuing at least until birth.
- Receiving intravenous AZT during labour, until delivery.
- Oral infant doses of AZT given to the baby, beginning eight to twelve hours after birth and continuing for six weeks.

AZT is not used on its own, because single-drug therapy (monotherapy) leads to drug resistance: combination therapy is used instead. Specific treatments are geared to the individual woman. There is a great deal of evidence that AZT is safe for pregnant women and their unborn children when used according to guidelines.

There have been concerns that exposure of the fetus to AZT may result in long-term complications. Research to date shows that AZT is safe and effective when used during pregnancy. The benefit of this drug in reducing HIV transmission to the baby outweighs the risk.

Warnings

1. Anemia and bone marrow toxicity

AZT can be toxic to the bone marrow—the soft tissue inside bones where blood cells are made. As a result, AZT can cause anemia (lowered red blood cell levels) and neutropenia (lowered neutrophil or white blood cell counts). In serious cases, this can require blood transfusions, and AZT must be stopped.

People with abnormally low hemoglobin levels or neutrophil counts should not take AZT. People starting AZT should have their blood cell counts monitored closely. If anemia occurs at all, it usually happens within the first four to six weeks after starting AZT. Although it was previously thought to be more common, a recent large-scale review found that only about 1% to 2% of people taking AZT develop anemia. Estimates of neutropenia range from 1.8% to 8%.

2. Lactic acidosis and hepatic steatosis

Two related conditions, lactic acidosis (a buildup of lactic acid in the blood) and hepatic steatosis (excess fat in the liver), have occurred in some people who have used nucleoside analogues. These conditions can be serious or fatal. They have mostly been seen in women and people who are overweight or who have been on nucleosides a long time, and can cause the following symptoms:

- unexpected tiredness or weakness
- nausea and/or vomiting
- persistent abdominal pain
- painful inflammation of the pancreas (pancreatitis)



If any of these symptoms occur without apparent reason, call your nurse or doctor right away.

Lactic acidosis is rare (less than one case per year for every thousand patients), and has mostly been seen with nucleoside analogues other than AZT. If you do develop any of these symptoms, it does not necessarily mean you have lactic acidosis, but you should still let your doctor know right away.

Side effects

1. General

Common side effects that have been reported by some AZT users include headaches, nausea, vomiting, insomnia, tiredness, muscle pain, and loss of appetite. Many people find that side effects caused by anti-HIV drugs improve or go away after the first several weeks of treatment.

AZT may also cause myopathy, a weakness or loss of muscle mass, especially with long-term use. Some people of colour have experienced darkening of the skin and/or nails while using AZT.

2. 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 PHAs 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 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 PHAs 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.

The drugs AZT and d4T are nukes that belong to a group of drugs called thymidine analogues. Thymidine analogues, particularly d4T and to



a lesser extent AZT, have been associated with loss of the fatty layer just under the skin—lipoatrophy.

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 AZT, 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 AZT 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 medication
- prescribe different anti-HIV drugs for you

Drug interactions for AZT

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

AZT should never be combined with d4T (**Zerit**, stavudine), as these drugs have been proven to interfere with each other.

The following drugs can affect the bone marrow, decreasing the production of white and/or red blood cells. Using AZT with these or other drugs that affect the bone marrow can increase the risk of infections and/or anemia:

- dapsone (**Avlosulfon**)
- ganciclovir (**Cytovene**)
- interferon-alpha and ribavirin (used as treatment for hepatitis C)

- valganciclovir (**Valcyte**)
- valproic acid (**Depakene**, **Divalproex**, other brand names)

AZT should be used cautiously with these drugs, or not at all.

For some people, but not all, methadone increases the blood level of AZT. Aspirin, codeine, morphine and a number of other drugs can also affect the metabolism of AZT, so use of these drugs should be discussed with your doctor.

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



Dosage and formulations

AZT is available as capsules (as **Retrovir** and generic formulations; 100 mg), as a solution for intravenous (IV) infusion (10 mg/mL), and as a syrup (50 mg/ 5 mL).

The fixed-dose combinations **Combivir** and **Trizivir** are single tablets which combine AZT with other anti-HIV drugs, reducing the number of pills that need to be taken. Combivir combines 300 mg AZT with 150 mg 3TC into a single twice-a-day pill. Trizivir contains the same combination as Combivir, plus 300 mg abacavir (**Ziagen**).

The usual standard adult dose of AZT is 600 mg per day, taken as 300 mg twice a day, with or without food. Formulations can change, and dosages may need to be customized. All medications should always be taken as prescribed and directed.

AZT was the first anti-HIV drug introduced. It was originally used as a single drug (monotherapy), at much higher doses (1200 mg or 1500 mg per day). Monotherapy is now strictly avoided because it leads to drug resistance. The higher AZT doses were reduced after they were found to be much more toxic, and no more effective, than the 600 mg daily dose (especially as part of combination therapy). A 500 mg per day dose was also in use for some time, and a 300 mg AZT tablet was introduced but is now unavailable due to low demand.

Availability

Retrovir 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 Retrovir in your region. CATIE's online module, Federal, Provincial and Territorial Drug Access Programs (on CATIE's website at www.catie.ca/eng/Publications/drugaccess/drugaccessIndex.shtml) also contains information about Canadian drug coverage.

Also see CATIE's fact sheets on Combivir and Trizivir.

Credits

Author: Derek Thaczuk

Design: Renata Lipovitch

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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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Contact CATIE

by telephone
1.800.263.1638
416.203.7122

by fax
416.203.8284

by e-mail
info@catie.ca

on the Web
<http://www.catie.ca>

by mail
505-555 Richmond Street West
Box 1104
Toronto ON M5V 3B1
Canada



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