

Zidovudine (AZT, Retrovir)

reprinted from www.aidsmeds.com, united states

What is Retrovir?

- Retrovir is an anti-HIV medication. It is in a category of HIV medications called nucleoside reverse transcriptase inhibitors (NRTIs). Retrovir prevents HIV from altering the genetic material of healthy T-cells. This prevents the cells from producing new virus and decreases the amount of virus in the body.
- Retrovir, manufactured by GlaxoSmithKline, was the first drug approved for the treatment of HIV, in 1987.
- Retrovir must be used in combination with at least two other anti-HIV drugs.
- There are actually five ways that Retrovir can be prescribed:
 - a syrup formula for babies and young children who have a difficult time swallowing pills;
 - as a tablet containing 300mg Retrovir (used in combination with at least two other anti-HIV drugs);
 - as a tablet that combines a single dose of Retrovir with a single dose of Efavirenz® (3TC) (sold as Combivir®; used in combination with at least one other anti-HIV drug);
 - as a tablet that combines single doses of Retrovir, Efavirenz, and Zalcitabine® (abacavir) (sold as Trizivir®; can be used alone by some HIV-positive people or used in combination with at least one other anti-HIV drug);
 - as a liquid that can be administered intravenously (though an IV line), used mostly to treat babies and

children who are hospitalized or pregnant women at the time of delivery.

What is known about Retrovir?

- For HIV-positive adults, the Retrovir dose is 600mg a day, taken by mouth. The usual dose is 300mg, taken twice a day, combined with other anti-HIV drugs. The manufacturer of Retrovir is conducting studies to see if Retrovir can be taken once a day, but these have not yet been completed.
- Retrovir can be taken either with or without food.
- Babies and children can also take Retrovir, using the syrup formulation. The dose depends on a baby's size or a child's weight. If you are caring for a child who is HIV-positive and has been prescribed Retrovir, be sure that you understand the correct dose to give the child. As a child grows, the dose of Retrovir will need to be increased on a regular basis.
- Numerous studies have demonstrated that Retrovir is effective for the treatment of HIV when combined with other anti-HIV drugs, usually at least one other nucleoside reverse transcriptase inhibitor (NRTI) and either a protease inhibitor or non-nucleoside reverse transcriptase inhibitor (NNRTI). Retrovir should not be taken alone (as monotherapy) or with just one other anti-HIV drug.

- The United States Department of Health and Human Services (DHHS) lists Retrovir as a “preferred” NRTI for HIV-positive people starting anti-HIV treatment for the first time. For best results, the DHHS recommends combining Retrovir with the NRTIs Epivir® (3TC) or Emtriva® (emtricitabine) plus either the NNRTI Sustiva® (efavirenz) or the protease inhibitor Kaletra® (lopinavir/ritonavir).
- Retrovir is safe and effective when used during the second and third trimesters of pregnancy (the last six months), during the time of delivery, and in babies born to HIV-positive mothers. HIV-positive women who do not take anti-HIV medications while they are pregnant or at the time of delivery have a 30% chance of giving birth to an HIV-positive baby. One important clinical trial conducted by the U.S. government (ACTG 076) demonstrated that AZT treatment during pregnancy can reduce this risk to 8%. This requires taking Retrovir by mouth during pregnancy, and receiving Retrovir through an IV line at the time of delivery. After delivery, the baby will take Retrovir syrup, by mouth, four times a day for six weeks.
- Therapy with Retrovir can cause certain changes (mutations) in HIV’s structure to occur. Some mutations will prevent Retrovir from working against HIV. Many of these mutations will also prevent Zerit® (d4T) from working against HIV. Some mutations can also prevent all of the NRTIs from working against HIV. If your viral load does not go undetectable or becomes detectable (and increases) while you are taking an anti-HIV drug regimen that contains Retrovir, your doctor can order a drug-resistance test to determine if your HIV has mutations that are causing resistance to Retrovir and to help you figure out which NRTIs your HIV is still sensitive to.
- Some laboratory studies have suggested that Retrovir should not be combined with either Rebetol® or Copegus®, two brand-name versions of ribavirin. Ribavirin is an oral medication used to treat hepatitis C. In these studies, ribavirin appeared to affect the way Retrovir is broken down by the body into its active form. This can make Retrovir less effective against HIV. However, many doctors report that this hasn’t been in a problem in their patients taking both drugs.
- Retrovir can interact with some medications used to treat TB, MAC and other bacterial infections. Rifadin® (rifampin) and Mycobutin® (rifabutin) can lower levels of Retrovir in the bloodstream, which can cause the drug to be less effective against HIV. If you need to take Rifadin or Mycobutin, it might be necessary to switch your Retrovir for another nucleoside reverse transcriptase inhibitor (NRTI) that does not interact with these drugs.

What about side effects?

- Bone marrow problems, such as decreased production of red blood cells and/or white blood cells, can occur in people taking Retrovir. Contact your doctor immediately if you develop unusual fatigue, pale skin, sore throat, fever, or chills, which may be signs of bone marrow problems. These problems are more likely to occur if you combine Retrovir with other drugs that cause these same side effects. Examples of other drugs that can cause bone marrow problems include ganciclovir (Cytovene®), SMX-TMP (Bactrim™; Septra®), and various chemotherapy drugs used to treat cancer.
 - A rare but potentially serious side effect of Retrovir is myopathy (damage to the muscles, including the heart). People who use Retrovir for a long period of time, meaning several years, are at the greatest risk for myopathy. General symptoms of myopathy include weakness of limbs, usually proximal (located close to the center of the body).
 - Lactic acidosis, which can be fatal, and severe liver problems (fatty liver) have been reported in people taking nucleoside reverse transcriptase inhibitors
- What about drug interactions?
- Retrovir should not be combined with Zerit® (d4T). They are “antagonistic,” which means that they do not work well together and can cause additional side effects.

(NRTIs). Contact your doctor immediately if you experience nausea, vomiting, or unusual or unexpected stomach discomfort; weakness and tiredness; shortness of breath; weakness in the arms and legs; yellowing of the skin or eyes; or pain in the upper stomach area. These problems are more likely to occur in HIV-positive people taking Zerit® (d4T), or Zerit in combination with Videx®/Videx EC® (ddI). However, there have been some reports of these potentially serious side effects occurring in people taking Retrovir.

- Feeling tired (fatigue), rash, trouble sleeping (insomnia), nausea, and headache can also be caused by Retrovir. Side effects are more likely to occur in people who have low T-cell counts at the time therapy with Retrovir is started.
- Anti-HIV drug regimens containing NRTIs, including Retrovir, can cause increased fat levels (cholesterol and triglycerides) in the blood, abnormal body-shape changes (lipodystrophy; including increased fat around the abdomen, breasts, and back of the neck, as well as decreased fat in the face, arms, and legs), and diabetes.

Who should not take Retrovir?

- Before taking this medication, tell your doctor if you have kidney disease, liver disease, a history of pancreatitis, or decreased activity of your bone marrow (low red blood cells [anemia] or low white blood cells). You may not be able to take Retrovir, or you may require lower doses or special monitoring during treatment, if you have any of these conditions.
- Retrovir is classified by the FDA as a pregnancy category C drug. All the FDA-approved anti-HIV drugs are classified as either category B or C. Pregnancy category B means that animal studies have failed to demonstrate a risk to the fetus, but there are no adequate and well-controlled studies in pregnant women. Pregnancy category C means that animal studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may

warrant use of the drug in pregnant women despite potential risks. HIV-positive women who become pregnant should discuss the benefits and possible side effects of anti-HIV treatment to help protect their babies from HIV.

- It is not known whether Retrovir passes into breast milk and what effects it may have on a nursing baby. However, to prevent HIV transmission of the virus to uninfected babies, it is recommended that HIV-positive mothers not breast-feed.

Where can I learn more about clinical trials that are using Retrovir?

- If you would like to find out if you are eligible for any clinical trials that include Retrovir, there is an interactive web site run by amfAR, the American Foundation for AIDS Research.
- Another useful service for finding clinical trials is *AIDSinfo.nih.gov*, a site run by the U.S. National Institutes of Health. They have “health information specialists” you can talk to at their toll-free number at 1-800-HIV-0440 (1-800-448-0440).

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TEXT LAST UPDATED: FEBRUARY 2004



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