Trizivir

Summary

Trizivir is a combination of three anti-HIV drugs commonly called nukes. Each Trizivir tablet contains 300 mg of abacavir, 150 mg of 3TC and 300 mg of AZT. Common side effects of Trizivir can include unexpected tiredness, diarrhea, nausea, loss of appetite and headache. Trizivir is usually taken at a dose of one tablet twice a day, with or without food.

Note: Some people who take Trizivir may have a serious allergic ("hypersensitivity") reaction to the abacavir it contains: please see the "Warnings" section. There is now a screening test to help predict whether you are likely to have an abacavir hypersensitivity reaction. See CATIE’s fact sheet Abacavir hypersensitivity screening.

What is Trizivir?

Trizivir is the brand name of three anti-HIV drugs—abacavir (Ziagen), 3TC (lamivudine) and AZT (zidovudine, Retrovir)—that are combined together in one tablet. These three drugs belong to a group or class of anti-HIV drugs (antiretrovirals) called nucleoside analogues or "nukes.” Trizivir is used in combination with other anti-HIV drugs to treat, but not cure, HIV.

How does Trizivir work?

To explain how Trizivir 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.

Trizivir contains abacavir, 3TC and AZT, three drugs that belong to a class of anti-HIV drugs called nukes. These drugs interfere with an enzyme called reverse transcriptase (RT), which is used by HIV-infected cells to make new viruses. Since abacavir, 3TC and AZT inhibit, or reduce the activity of this enzyme, Trizivir causes HIV-infected cells to slow down or stop producing new viruses.
How do people with HIV use Trizivir?

Trizivir is used in combination with another anti-HIV drug from a different class, such as protease inhibitors or non-nukes (NNRTIs). Combinations such as this are called antiretroviral therapy, or ART. For more information on ART, see CATIE’s Your Guide to HIV 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 Trizivir 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/she monitors your health.
- Continue to practice safer sex and take other precautions so as not to pass HIV on to other people and protect yourself from different strains of HIV and other germs.

Women and children

Trizivir is not recommended for children because there is no data on its use in this population. Trizivir has not been well studied in pregnant women. The manufacturer suggests that Trizivir only be used in pregnant women if the “benefit to the mother outweighs the risk to the fetus.”

Warnings

1. Hypersensitivity reaction

Up to 8% of people with HIV who use Trizivir experience an exaggerated immune reaction against the abacavir component of the combination. This reaction, called the abacavir hypersensitivity reaction, is very serious and can be fatal.

Although the hypersensitivity reaction can occur at any time while a person is taking Trizivir, on average it occurs within the first six weeks of use. The manufacturer, ViiV Healthcare, states that you should stop using Trizivir if you have signs or symptoms from two or more of the following groups:

1. Fever
2. Rash
3. Gastrointestinal symptoms (including nausea, vomiting, diarrhea or belly pain)
4. General symptoms (including fatigue, lack of energy, achiness)
5. Respiratory symptoms (sore throat, shortness of breath, cough, unusual findings on X-rays of the chest)

If you develop symptoms from two or more of these groups while you are taking Trizivir or any drug containing abacavir, you should stop taking this medicine and contact your doctor right away. If a hypersensitivity reaction to abacavir has indeed occurred, then Trizivir should never be restarted, as a fatal reaction could occur within hours. You should also never take any other drug that contains abacavir.

There is now a screening test to help predict whether you are likely to have an abacavir hypersensitivity reaction. See CATIE’s fact sheet Abacavir hypersensitivity screening.

2. Restarting treatment

Trizivir should never be restarted following a hypersensitivity reaction, as a fatal reaction could occur within hours. You should also never take any other drug that contains abacavir (this includes Ziaxen and Kivexa).

This hypersensitivity reaction has even occurred among people who did not have any problems when they first took abacavir-containing drugs, but who then stopped and restarted.

3. Cardiovascular risk

There are conflicting data from some studies about a link between heart attacks and the initial use of abacavir-containing products (Ziaxen and in Kivexa). However, a review by the U.S. Food and Drug Administration (FDA) of randomized clinical trials has not found any link between...
abacavir use and an increased risk of heart attack. If you or your close family members (mother, father, brother, sister) have a history of heart problems, let your doctor know. Before using abacavir-containing medicines, always speak to your doctor about getting tested for abacavir hypersensitivity.

4. 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 nukes. These conditions can be serious or fatal. They have mostly been seen in women and people who are overweight or who have been on nukes a long time. Symptoms of lactic acidosis can include the following:

- unexpected tiredness or weakness
- nausea and/or vomiting
- persistent abdominal pain
- diarrhea
- unexpected muscle pain
- feeling cold, especially in the arms and legs
- feeling dizzy or light-headed

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). 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.

5. Hepatitis B

Trizivir contains 3TC, a drug that is used in the treatment of hepatitis B virus infection (HBV). The manufacturer of Trizivir advises that people with HIV should get tested for HBV infection before starting ART. Be aware that discontinuing Trizivir (and therefore 3TC) can have the effect of making HBV infection temporarily worse. If you are co-infected with HBV, talk to your doctor about how best to treat this co-infection.

6. Pancreatitis

Some people taking two of the medications found in Trizivir—abacavir and 3TC—have developed a painful inflammation of their pancreas gland. Talk to your doctor right away if these symptoms occur as they may be suggestive of pancreatitis:

- abdominal pain
- nausea
- vomiting
- fever
- anxiety
- unexpected sweating

7. 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% of people taking AZT.

Side effects

1. General

The general side effects that occur in people with HIV taking AZT, 3TC and abacavir separately may also occur in people taking Trizivir. These side effects can include:

- gastrointestinal effects – diarrhea, nausea, vomiting, loss of appetite
• neurologic effects – headache, insomnia
• other effects – unexpected tiredness, muscle pain

Many people find that side effects caused by anti-HIV drugs improve or go away after the first several weeks of treatment.

Less common, but more serious, side effects may include neutropenia (a decrease in the number of white blood cells called neutrophils), and anemia (a decrease in hemoglobin or red blood cells).

In rare cases, the AZT in Trizivir over many years may also cause myopathy, a weakness or loss of muscle mass, especially with long-term use. Some people of color have experienced darkening of the skin and/or nails while using AZT.

2. Lipodystrophy syndrome

Trizivir contains AZT. Use of AZT may be associated with the loss of the fatty layer under the skin, a process called lipoatrophy. Lipoatrophy is one part of the lipodystrophy syndrome.

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 unfavorable 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 A Practical Guide to HIV Drug Side Effects.

Of all the anti-HIV drugs, 3TC and abacavir (two components of Trizivir) appear to be among the least likely to cause or contribute to lipodystrophy.

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 the abacavir in Trizivir, 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.

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 with Trizivir

1. Specific drug interactions: AZT

The following drugs can affect the bone marrow, decreasing the production of white and in some cases, red blood cells. Use of Trizivir with these or other drugs that affect the bone marrow can further reduce levels of these cells. This increases the risk of developing infections and/or anemia:

- dapsone (Avlosulfon)
- ganciclovir (Cytovene) or valganciclovir (Valcyte)
- interferon-alpha (Pegasys and Pegetron) and ribavirin
- valproic acid (Depakene)

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

The antibiotic clarithromycin can reduce the absorption of AZT. This can be avoided by taking the two medications at least two hours apart.

For some people, methadone increases the blood level of AZT. Aspirin, codeine and morphine can also affect the metabolism of AZT, so use of these drugs should be discussed with your doctor.

AZT should never be combined with d4T.

2. Specific drug interactions: abacavir

In men, the use of alcohol in combination with abacavir causes an increase of abacavir in the blood, which could cause an increase in toxicity. This has not been studied in women.

Abacavir can reduce levels of methadone in the blood, which might require an adjustment to your dose of methadone.

3. Specific drug interactions: 3TC

No significant drug interactions have been reported with 3TC.

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 Trizivir with another anti-HIV drug 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 abacavir, 3TC or 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 abacavir, 3TC and/or AZT, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

Dosage and formulations

Trizivir is available as tablets, each containing 300 mg abacavir and 150 mg 3TC (lamivudine) and 300 mg AZT. The usual standard adult dose of Trizivir is one tablet twice daily, with or without
food. Trizivir is not recommended for people who weigh less than 50 kg (110 lbs). All medications should always be taken as prescribed and directed.

**Availability**

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

See also fact sheets on abacavir, 3TC, AZT and abacavir hypersensitivity screening.

**References**


**Author(s):** Hosein SR, Ziegler B
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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