Abacavir (Ziagen)

FACT SHEET

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Summary

Abacavir is a type of anti-HIV drug called a nucleoside analogue ("nuke"). The most common side effects of abacavir include headache, nausea, vomiting, unexpected tiredness and sleeping problems. In adults, It is usually taken at a dose of 600 mg daily, with or without food.

Note: Up to 8% of the people who take abacavir may have a serious allergic ("hypersensitivity") reaction to it: please see the "Warnings" section.

What is abacavir?

Abacavir, sold under the brand name Ziagen (and available in Kivexa, Triumeq and Trizivir), is a type of antiretroviral (anti-HIV) drug called a nucleoside analogue or "nuke." Abacavir is used in combination with other antiretroviral drugs to treat (but not cure) HIV.

How does abacavir work?

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 infected cell uses proteins called enzymes. When the activity of these enzymes is reduced, the production of HIV greatly slows.

Abacavir belongs to a class of antiretrovirals called nucleoside analogues. Abacavir interferes with an enzyme called reverse transcriptase (RT), which is used by HIV-infected cells to make new viruses. Since abacavir inhibits, or reduce the activity of this enzyme, this drug causes HIV-infected cells to produce fewer viruses.

How do people with HIV use abacavir?

Abacavir is no longer commonly used. However, when it is prescribed, abacavir is used in combination with several other antiretroviral drugs. Such combinations 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.

CATIE Canada's source for HIV and hepatitis C information

Neither abacavir nor any other antiretroviral medication is a cure for HIV. It is therefore important that you see your doctor for checkups and lab tests on a regular basis.

Evidence shows that HIV-positive people who are on ART, engaged in care, and have an ongoing undetectable viral load are substantially less likely to transmit HIV to others, be it through sex, when sharing equipment to use drugs or during pregnancy and birth. In fact, the evidence for sexual transmission shows that people on ART who maintain an undetectable viral load do not pass HIV to their sexual partners. For further information see the CATIE fact sheet *HIV treatment and an undetectable viral load to prevent HIV transmission*. However, it is still a good idea to use condoms because they can reduce your risk of getting and passing on other sexually transmitted infections.

Warnings

1. Hypersensitivity reaction

In up to 8% of people with HIV who use abacavir, an exaggerated reaction against abacavir by the immune system—abacavir hypersensitivity—can occur. **This reaction is very serious and can be fatal.**

Although the hypersensitivity reaction can occur at any time while a person is taking abacavir, on average it occurs within the first six weeks of use. The manufacturer, ViiV Healthcare, states that you should stop using abacavir 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 abacavir 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 abacavir 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

Abacavir 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 Kivexa, Triumeq and Trizivir).

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

Data from a well-designed trial (called Reprieve) of 7,769 people with HIV have been analysed. This was a study that recruited people at low to moderate risk of cardiovascular disease. Participants were randomly assigned to receive the cholesterol-lowering medicine pitavastatin or placebo. After an average of five years of monitoring, researchers found that people who received pitavastatin had a 35% reduced risk of major symptoms of cardiovascular disease (heart attack, stroke and so on).

Although people in Reprieve were not randomly assigned to receive their HIV treatment (they were all on treatment), the randomization used in the study helps to reduce the possibility of drawing biased conclusions when analyzing the data. The researchers are able to further analyse the information captured from the Reprieve study to answer important research questions. One such

question is the potential risk associated with the use of the drug abacavir.

Since 2008, some observational studies have reported that there has been an increased risk of a heart attack in some people with HIV who used abacavir. However, because these studies were observational in design, they could not prove that use of abacavir was linked to an increased risk of a heart attack. Furthermore, most of these analyses from observational studies appeared to have issues – missing data or not being able to take into account factors such as smoking and substance use.

Now that has changed. An analysis from the very well-designed Reprieve study has found that recent or past use of abacavir was linked to a 50% increased risk for heart attack and other major symptoms of severe cardiovascular disease.

The analysis from Reprieve was able to consider factors such as sex, smoking, age, substance use, kidney health and so on. Even when the Reprieve researchers adjusted for these and other factors, abacavir was still linked to a significantly increased risk for heart attack and related issues.

These results from Reprieve have again heightened concern about the safety of abacavir-containing medicines.

Therefore, as a precaution, before starting Ziagen or any abacavir-containing medicine, let your doctor know if you have any of these or other risk factors for cardiovascular disease:

- your close family members (mother, father, brother, sister) have a history of problems such as heart attack or stroke
- you have any of these: high blood pressure, abnormal cholesterol or triglyceride levels in your blood, have pre-diabetes or diabetes, or kidney injury/disease.
- you use tobacco or smoke drugs
- you inject drugs or use stimulants (e.g. cocaine, crystal meth, MDMA/ecstasy, amphetamine or speed)

Your doctor can help you find ways to reduce your risk factors for cardiovascular disease. Your doctor can also help you decide if abacavir is right for you.

4. Lactic acidosis and hepatic steatosis

In the current era, in very rare cases, 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 was seen by doctors in the 1990s and early 2000s in some people on ART. However, today it is extremely rare as ART is much safer. 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

General

Common side effects that have been reported by some abacavir users include: headache, nausea, vomiting, unexpected tiredness, diarrhea, loss of appetite, fever, and skin rash. Many people find that side effects caused by antiretrovirals improve or go away after the first several weeks of treatment.

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 abacavir, 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 abacavir 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 antiretroviral drugs or other medications
- prescribe different antiretroviral drugs for you

Drug interactions for abacavir

The following drugs interact or have the potential to interact with abacavir. This list may not be exhaustive.

- In men, the use of alcohol in combination with abacavir causes an increase of abacavir in the blood, which could cause an increase in toxic effects. This has not been studied in women.
- Abacavir interacts with riociguat (used to treat pulmonary arterial hypertension) and can raise levels of riociguat in the blood about three times above its normal level. The manufacturer of abacavir, ViiV Healthcare, recommends that both drugs should be used with caution. They note that the dose of riociguat may need to be reduced in people who use abacavir.

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

Dosage and formulations

Abacavir is available as 300 mg tablets and 20 mg/mL liquid. The standard adult dose of abacavir is either one tablet twice daily, or two tablets once daily, with or without food, for a total of 600 mg per day. Formulations can change, and dosages may need to be customized. All medications should always be taken as prescribed and directed.

Availability

Abacavir is licensed in Canada for the treatment of HIV infection in combination with other antiretroviral drugs. Your doctor can tell you more about the availability and coverage of abacavir in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

Also see CATIE's fact sheets on Kivexa, Triumeq and abacavir hypersensitivity screening.

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Author(s): Hosein SR, Thaczuk D, Ziegler B

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