



3TC (lamivudine, Epivir)

Summary

3TC is a type of antiretroviral drug called a nucleoside analogue (“nuke”). 3TC can cause nausea, headache, diarrhea, vomiting, and weakness; however, it causes few side effects compared to many other antiretroviral drugs. It is usually taken at a dose of 300 mg daily or 150 mg twice daily, with or without food.

What is 3TC?

Lamivudine, sold under the brand name **3TC** (**Epivir** in the US), is a type of antiretroviral (anti-HIV) drug called a nucleoside analogue or “nuke”. 3TC is used in combination with other antiretroviral drugs to treat (but not cure) HIV/AIDS.

How does 3TC work?

To explain how 3TC 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.

3TC belongs to a group of drugs called nucleoside analogues. 3TC interferes with an enzyme called reverse transcriptase (RT), which is used by HIV-infected cells to make new viruses. Since 3TC 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 3TC?

3TC is used in combination with several other antiretroviral 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 3TC nor any other antiretroviral 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



3TC is one of the most widely used components of HAART, because it is easy to take and one of the least toxic antiretrovirals. 3TC is also a component in several “fixed-dose combinations” (**Combivir**, **Trizivir**, and **Kivexa**) that combine 3TC with other antiretrovirals in a single tablet.

Lamivudine and hepatitis B

A 100 mg formulation of lamivudine is also approved as a treatment for chronic hepatitis B infection. This formulation is sold under the brand name **Heptovir** in Canada, and **Epivir HBV** in the US. Neither of these is interchangeable with 3TC. People with both HIV and hepatitis B virus (HBV) should use 3TC as prescribed for HIV. (Also see “Warnings – Hepatitis B”.)

Warnings

1. 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.

2. Hepatitis B

If someone with hepatitis B infection is taking 3TC, the hepatitis can “flare up” if the medication is stopped. People with hepatitis B who are taking 3TC should be carefully monitored if they stop taking the drug.

Side effects

1. General

3TC is generally one of the most easily-tolerated antiretrovirals, but it may cause some side effects. Common side effects reported by some 3TC users include headaches, malaise, tiredness, and diarrhea. Other reported side effects include nausea, vomiting, abdominal pain and discomfort, and coughing. 3TC generally adds little to the side effects caused by other antiretrovirals. Many people find that side effects caused by antiretrovirals improve or go away after the first several weeks of treatment.

Less common, but more serious, side effects may include **peripheral neuropathy** (a numbness, tingling or burning sensation in the hands or feet), **neutropenia** (a decrease in the number of white blood cells called neutrophils), and **anemia** (a decrease in hemoglobin or red blood cells).

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.

There is little evidence that 3TC is especially likely to cause or contribute to lipodystrophy.

Drug interactions

No significant drug interactions have been reported with 3TC. However, you should

always consult your doctor and pharmacist about taking any other prescription or non-prescription medication, including herbs, supplements, and recreational drugs.

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 antiretroviral drugs, which means those drugs will no longer work for you. Combining 3TC with at least two other antiretroviral drugs delays the development of drug resistance.

To reduce the risk of developing drug resistance, all antiretroviral drugs should be taken every day exactly as prescribed and directed. If doses are delayed, missed, or not taken as prescribed, levels of 3TC 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 3TC, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

There is a single mutation (known as “M184V”) which causes HIV to become highly resistant to 3TC. However, it is generally considered worth continuing 3TC even if this has happened, because the mutated, 3TC-resistant virus:

- is less “fit” (i.e., does not reproduce itself as well)



- is still controlled by 3TC to some degree
- is actually more vulnerable to certain other antiretrovirals, including AZT

Dosage and formulations

3TC is available as 150 mg and 300 mg tablets, and as an oral solution (10 mg/mL). The usual standard adult dose of 3TC is either one 150 mg tablet twice daily or one 300 mg tablet once daily. 3TC may be taken with or without food.

The fixed-dose combinations **Combivir**, **Trizivir**, and **Kivexa** are single tablets which combine 3TC with other antiretrovirals, 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**). Kivexa contains 300 mg 3TC plus 600 mg abacavir.

Formulations can change, and dosages may need to be customized. All medications should always be taken as prescribed and directed.

Availability

3TC is licensed in Canada for the treatment of HIV infection in adults, in combination with other antiretroviral drugs. Your doctor can tell you more about the availability and coverage of 3TC 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, Trizivir and Kivexa.

Credits

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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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