



TRUVADA

Summary

Truvada is the name of a fixed-dose co-formulation of two anti-HIV drugs: tenofovir and FTC all in one pill. Truvada is used as part of combination therapy for people with HIV/AIDS. Common side effects of Truvada can include dizziness, headache, nausea and vomiting. Truvada is taken once-daily with or without food.

What is Truvada?

Truvada is the name of a fixed-dose co-formulation of two anti-HIV drugs: tenofovir (**Viread**) and FTC (emtricitabine, **Emtriva**) all in one pill.

How does Truvada work?

To explain how Truvada 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.

The two medications inside Truvada are as follows:

- tenofovir – this belongs to a group or class of drugs called *nucleotide* analogues
- FTC – this belongs to a group of drugs called *nucleoside* analogues or *nukes*

Both medicines inside Truvada interfere with an enzyme called reverse transcriptase, which is used by HIV-infected cells to make new

viruses. Since Truvada inhibits, or reduces the activity of this enzyme, this drug causes HIV-infected cells to slow down or stop producing new viruses.

How do people with HIV/AIDS use Truvada?

Truvada is taken in combination with other anti-HIV drugs such as non-nukes (NNRTIs) or protease inhibitors. Such combinations 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 Truvada 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 practise 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

Warnings

1. Lactic acidosis

Higher-than-normal levels of lactic acid can occur in the blood. This condition is called lactic acidosis and has happened in some people who have used tenofovir, FTC or related anti-HIV drugs. Women who are overweight are at increased risk for lactic acidosis. Sometimes the livers of people with lactic acidosis become swollen because of fatty deposits. Signs and symptoms of lactic acidosis may include the following:

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

If these symptoms persist, see your doctor right away.

2. Hepatitis B

The safety of Truvada in people co-infected with both HIV and hepatitis B virus (HBV) is not known. Truvada contains tenofovir and FTC. Both of these drugs have anti-HBV activity. Co-infected people who take Truvada and then later stop may experience worsening HBV co-infection. People who are co-infected with HIV and hepatitis-causing viruses and who take HAART are at increased risk for liver toxicity. It is important to have regular blood tests so that your doctor can assess the health of your liver.

If you have HBV co-infection, talk to your doctor before you start Truvada. If you are not sure if

you have HBV, ask your doctor about getting tested. If you later need to change your therapy from Truvada, remind your doctor that you have HBV.

3. Pancreatitis

Painfully swollen pancreas glands have been reported in some people taking tenofovir as part of HAART. Higher-than-normal levels in the blood of the enzyme amylase (made by the pancreas gland) have been detected in some people taking tenofovir. This increase may be suggestive of inflammation in the pancreas gland. Symptoms of pancreatitis can include the following:

- abdominal pain, particularly when laying down
- nausea
- vomiting
- unexpected sweating
- fever
- anxiety

If these symptoms occur, talk to your doctor right away.

4. Kidney toxicity

Tenofovir can cause kidney dysfunction and damage. If you or a close family member has kidney problems, tell your doctor. For more about tenofovir and the kidney, please see the section on side effects later in this fact sheet.

Side effects

1. General side effects

Common side effects that have occurred in Truvada users include the following:

- dizziness
- headache
- nausea
- vomiting
- flatulence



2. Kidney health

Truvada contains tenofovir and tenofovir belongs to a group of drugs called nucleotide analogues. This group of drugs is broken down by the kidneys and is associated with kidney dysfunction. There have been reports of cases of kidney dysfunction in some people who used tenofovir. People who use this drug may wish to have regular blood and urine tests done so that their doctors can assess the health of their kidneys. These tests can include the following:

- creatinine
- e-GFR (estimated-glomerular filtration rate)
- calcium
- phosphorus
- bicarbonate

In addition to tenofovir, there are other medications which are processed by the kidneys and have the potential to damage these organs. Many of these medications are antibiotics and are grouped as follows:

- beta-lactams – penicillin, amoxicillin
- quinolones – ciprofloxacin and related compounds
- aminoglycosides – amikacin, gentamicin
- macrolides – erythromycin
- tetracyclines – minocycline
- anti-tuberculosis agents – rifampin, ethambutol
- other antibiotics – co-trimoxazole (**Septa/Bactrim**), vancomycin (**Vanocin**)

Bear in mind that there are other medications with the potential to damage the kidneys. The following is a list of medications with this potential, this list is not exhaustive:

- antiviral agents – acyclovir (**Zovirax**), valacyclovir (**Valtrex**), cidofovir (**Vistide**), foscarnet (**Foscavir**), indinavir (**Crixivan**)
- antifungal agents – amphotericin B (**Fungizone**), intravenous pentamidine

- anti-seizure drugs – phenytoin, carbamazepine, valproic acid
- NSAIDs (non-steroidal anti-inflammatory drugs) – acetaminophen (**Tylenol**), ibuprofen (**Advil, Motrin**), indomethacin (**Indocid**), naproxen (**Naprosyn**)

3. Bone health

Truvada contains tenofovir. In experiments on monkeys using tenofovir at doses 10 to 30 times greater than would be used in people, the animals' bones became thinner over a period of one year.

Before you start taking tenofovir, tell your doctor if you have bone problems or thinner-than-normal bones (osteopenia or osteoporosis).

In clinical trials of regimens containing tenofovir, thinner bones in the spine and elsewhere have occurred. Thinner bones are generally weaker and are at increased risk for breaking (fractures) should accidents or trauma occur.

Researchers are not certain why bone thinning may occur in some people exposed to tenofovir. One theory is that bones became thinner because tenofovir appears to have caused the kidneys to malfunction. The kidneys filter blood, putting waste materials into the urine and returning nutrients back to the blood. In the cases of tenofovir-associated bone loss, damaged kidneys may not be able to restore bone-building nutrients back to the blood.

Bear in mind that some people with HIV/AIDS can develop thinner-than-normal bones without ever using tenofovir. It may be useful for you to discuss with your doctor the possibility of having bone density assessments done before you begin taking tenofovir or any other anti-HIV therapy. If your bones are thin, your doctor may suggest that you increase your intake of calcium and vitamin D₃. Regular monitoring of bone density may also be useful.

For further information about vitamin D and bones, see CATIE's *Practical Guide to Nutrition for People Living with HIV* at www.catie.ca/ng_e.nsf.



4. Pregnancy

There are no well-controlled studies of Truvada in pregnant HIV-positive women. Therefore, the manufacturer recommends that Truvada “should be used in pregnant women only if the potential benefits outweigh the potential risks.”

5. Skin discolouration

In rare cases, darker skin has developed on the palms and the soles of the feet in people exposed to FTC. The reason for this is not clear. However, this side effect is harmless.

6. 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.

Truvada is not associated with fat wasting (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 tenofovir or FTC, increasing or decreasing their 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 levels of the medications contained in Truvada, 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 anti-HIV drugs or other medications
- prescribe different anti-HIV drugs for you

Drug interactions with Truvada

The following lists contain drugs that interact or have the potential to interact with the medications in Truvada (tenofovir and FTC). These lists are not exhaustive.

The manufacturer recommends that caution be used with the following drugs as there is the potential for serious drug interactions:

- atazanavir (**Reyataz**)
- lopinavir/ritonavir (in **Kaletra**)
- ddl (**Videx, Videx EC**)

Here is what the manufacturer of Truvada recommends when using these medications with Truvada:

- atazanavir – this medication can increase levels of tenofovir in the blood. Higher levels of tenofovir could lead to tenofovir-related toxicity. People receiving these combinations of medications need monitoring for this toxicity. Also, tenofovir decreases levels of atazanavir in the blood. People taking this combination need to take the drug ritonavir (**Norvir**) to maintain their levels of atazanavir. All three medications should be taken with food, once-daily.
- lopinavir/ritonavir – this medication can increase levels of tenofovir in the blood.

Higher levels of tenofovir could lead to tenofovir-related toxicity. People receiving these combinations of medications need monitoring for this toxicity.

- ddl – tenofovir increases levels of ddl in the blood between 40% and 60%. Such a large increase could cause signs and symptoms of ddl-related toxicity such as painfully swollen pancreas glands, excessive levels of lactic acid in the blood and damaged nerves in the hands and feet (peripheral neuropathy). If both ddl and tenofovir must be used, then a reduced dose of ddl is needed. Speak to your HIV specialist about the dose of ddl that is right for you.

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 Truvada with at least one other anti-HIV drug, such as a non-nuke or protease inhibitor, 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 efavirenz and FTC 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 the medicines in Truvada, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

Here are some additional points to note:

- Truvada should not be used as part of a triple nuke regimen as this has not been proven to be effective against HIV.
- Also, reports of treatment failure have occurred among people new to HIV therapy who had high viral loads and were treated with a combination of ddI, tenofovir and a non-nuke.
- Truvada should not be used with FTC or tenofovir as these drugs are already inside Truvada.
- Doctors caring for treatment-experienced patients are encouraged by the manufacturer to consider the treatment history, resistance testing and other lab tests when considering the use of Truvada.

Dosage and formulations

Truvada is available as tablets, each containing 200 mg FTC and 300 mg tenofovir. The standard adult dose of Truvada is one tablet daily, with or without food, in combination with other anti-HIV medications. All medications should always be taken as prescribed and directed.

Availability

Truvada 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 Truvada 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.

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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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