

# Tenofovir (Viread)

## Summary

Tenofovir is a type of anti-HIV drug from a class of drugs called nucleotide analogues (nukes). Tenofovir is used as part of combination therapy for people with HIV. Common side effects include nausea, diarrhea and vomiting. The adult dose is 300 mg (one tablet) per day.

## What is tenofovir?

Tenofovir, sold under the brand name Viread, is a once-daily treatment for HIV infection. Tenofovir is also co-formulated with other medicines:

- Truvada: tenofovir + FTC
- Atripla: tenofovir + FTC + efavirenz
- Complera: tenofovir + FTC + rilpivirine
- Stribild: tenofovir + FTC + cobicistat + elvitegravir

## How does tenofovir 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 cell uses proteins called enzymes. When the activity of these enzymes is reduced the production of HIV slows.

Tenofovir belongs to a group (or class) of drugs called nucleotide analogues. Tenofovir interferes with an enzyme called reverse transcriptase, which is used by HIV-infected cells to make new viruses. Since tenofovir 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 use tenofovir?

Tenofovir is used in combination with several other anti-HIV drugs, usually nukes (nucleoside analogues) and sometimes drugs from other classes such as protease inhibitors. 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.

# FACT SHEET

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Neither tenofovir 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 or she can monitor your health.
- Continue to practise safer sex and take other precautions to prevent passing HIV on to other people and protect yourself from different strains of HIV as well as other germs.

## Tenofovir to prevent HIV infection

Clinical trials have found that Truvada (tenofovir + FTC), when taken as part of a package of HIV prevention tools (frequent screening for HIV and other sexually transmitted infections, safer sex counselling, use of condoms), can *reduce* the risk of HIV transmission in some people. For more information about this, see CATIE's fact sheet on Pre-exposure prophylaxis (PrEP).

## Warnings

### 1. Lactic acidosis

Some people who have used tenofovir or related anti-HIV drugs have experienced a condition called lactic acidosis—higher-than-normal levels of lactic acid in 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

Tenofovir has activity against hepatitis B virus (HBV) and is approved for treating this infection. Co-infected people who take tenofovir and then later stop it may experience worsening HBV co-infection. If you have this co-infection, talk to your doctor before you start or stop tenofovir. If you later need to change your therapy, remind your doctor that you have HBV. People who are co-infected with HIV and hepatitis-causing viruses and who take ART may be at increased risk for liver injury. It is important to have regular blood tests so that your doctor can assess the health of your liver. If lab tests reveal that you do not have HBV, speak to your doctor about getting a vaccine to protect you from HBV.

### 3. Pancreatitis

Painfully swollen pancreas glands have been reported by some people taking tenofovir as part of ART. Higher-than-normal levels in the blood of the enzyme amylase (made by the pancreas gland) have been detected in people taking tenofovir. This increase may suggest 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 injury

Tenofovir can cause kidney dysfunction and injury. If you or a close family member have kidney problems, tell your doctor. See the section on side effects that follows.

## Side effects

### 1. General side effects

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

- weakness
- diarrhea
- nausea

### 2. Kidney health

Tenofovir belongs to a class 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
- protein (albumin)

In addition to tenofovir, there are other medications that are processed by the kidneys and have the potential to cause or amplify kidney dysfunction. 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 (Septra/Bactrim), vancomycin (Vanocin)

Bear in mind that there are other medications that have the potential to cause kidney dysfunction. These include (but are not limited to):

- antiviral agents – acyclovir (Zovirax), valacyclovir (Valtrex), valganciclovir (Valcyte) cidofovir (Vistide), foscarnet (Foscavir), indinavir (Crixivan)
- antifungal agents – amphotericin B (Fungizone), intravenous pentamidine
- anti-seizure drugs – phenytoin, carbamazepine, valproic acid
- boosting agents – cobicistat (in Stribild)
- NSAIDs (non-steroidal anti-inflammatory drugs) – acetaminophen (Tylenol), ibuprofen (Advil, Motrin), indomethacin (Indocid), naproxen (Naprosyn), diclofenac (Arthrotec)
- transplant drugs – cyclosporine (Neoral, Sandimmune)

### 3. Bone health

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 thinner-than-normal bones (osteopenia or osteoporosis) or other bone problems, or if your parents, brothers or sisters have bone problems.

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 blood. In the cases of tenofovir-associated bone loss, injured kidneys may not be able to

restore bone-building nutrients back to the blood. Bone pain and muscle weakness has also been reported by some tenofovir users.

Bear in mind that some people with HIV can develop thinner-than-normal bones without ever using tenofovir. This sometimes occurs in people who use ART. The decrease in bone density tends to stabilize within one or two years after starting ART. 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, talk to your doctor about your intake of calcium and vitamin D<sub>3</sub>. Regular monitoring of bone density may also be useful.

For more information about vitamin D and bones, see CATIE's *A Practical Guide to Nutrition for People Living with HIV*.

#### 4. Pregnancy

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

#### 5. Lipodystrophy syndrome

The HIV lipodystrophy syndrome is the name given to a range of symptoms that can develop over time when people use ART.

Tenofovir is **not** associated with fat wasting (lipoatrophy).

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, blood tests 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 some people living with HIV may experience one or more aspects of the syndrome. For instance, some people may experience fat wasting, others fat gain, and others may experience both fat wasting and gain. What is becoming increasingly clear is that unfavourable changes in levels 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 far outweigh 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 to help 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*.

## 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, 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 levels of tenofovir, 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 the dose of either your anti-HIV drugs or other medications; or
- prescribe different anti-HIV drugs for you.

The following lists contain drugs that interact or have the potential to interact with tenofovir. 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 (Kaletra)
- ddl, didanosine (Videx, Videx EC)

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

- atazanavir – this medication can increase levels of tenofovir in the blood. Higher levels of tenofovir could lead to tenofovir-related toxicity. People receiving this combination 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 this combination of medications need monitoring for this toxicity.
- Didanosine, ddl (Videx, Videx EC) – tenofovir increases levels of ddl in the blood by between 40% and 60%. Such a large increase could cause signs and symptoms such as a painfully swollen pancreas gland, 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.

The manufacturer recommends that tenofovir should not be used together with the anti-hepatitis B drug adefovir (Hepsera).

## Resistance and cross-resistance

Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes, called mutations, can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you. Combining tenofovir 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 tenofovir 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 analyzed using resistance testing.

Should HIV in your body become resistant to tenofovir, your doctor, with the help of resistance testing, can help put together a new treatment regimen for you.

## Dosage and formulations

Tenofovir (Viread) is available in 300 mg tablets. The standard adult dose is 300 mg (one tablet) once daily. Tenofovir can be taken with or without food.

## Availability

Tenofovir is licensed in Canada for the treatment of HIV infection in adults, in combination with other anti-HIV drugs. This drug is also licensed for the treatment of hepatitis B virus (HBV) infection. Your doctor can tell you more about the availability and coverage of tenofovir in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

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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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