



A Service of the U.S. Department
of Health and Human Services

Fact Sheets

Side Effects of Anti-HIV Medications

Health Information for Patients

October 2005

P.O. Box 6303, Rockville, MD 20849-6303

Telephone: 1-800-448-0440

International: 301-519-0459

Fax: 301-519-6616

TTY/TTD: 888-480-3739

Live Help: <http://aidsinfo.nih.gov/LiveHelp>

E-mail: ContactUs@aidsinfo.nih.gov

Web: <http://aidsinfo.nih.gov>

Side Effects of Anti-HIV Medications

Anti-HIV medications help people infected with HIV lead longer, healthier lives. The goal of HIV treatment is to reduce the amount of virus in a person's body and prevent destruction of the immune system.

Twenty-one anti-HIV medications have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of HIV. These medications must be given in combination, and all of the drugs may cause negative side effects. Such side effects range from mild to life-threatening.

This series of fact sheets discusses some of the major side effects of anti-HIV medications. The information in this series is based on the U.S. Department of Health and Human Services' *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents* (available at <http://aidsinfo.nih.gov/guidelines>) and *Management of Metabolic Complications Associated with Antiretroviral Therapy for HIV-1 Infection: Recommendations of an International AIDS Society-USA Panel* (available at <http://www.iasusa.org/pub/metcomp.html>).

Table of Contents

- [Hepatotoxicity](#)
- [Hyperglycemia](#)
- [Hyperlipidemia](#)
- [Lactic Acidosis](#)
- [Lipodystrophy](#)
- [Osteonecrosis, Osteoporosis, Osteopenia](#)
- [Skin Rash](#)

Hepatotoxicity

What is hepatotoxicity?

Hepatotoxicity is a general term for liver damage. Medications, including those used to treat HIV infection, may cause hepatotoxicity. Hepatotoxicity has developed in HIV infected people taking anti-HIV medications from three classes: **nucleoside reverse transcriptase inhibitors (NRTIs)**, **non-nucleoside reverse transcriptase inhibitors (NNRTIs)**, and **protease inhibitors (PIs)**.

There are several specific conditions that all fall within the general category of hepatotoxicity. These conditions include:

- hepatitis—inflammation of the liver
- hepatic necrosis—death of liver cells
- hepatic steatosis—too much fat in the liver; may be associated with a life-threatening condition called *lactic acidosis* (see [Lactic Acidosis Fact Sheet](#))

What are the symptoms of hepatotoxicity?

The first sign of damage to the liver is an increase in liver **enzyme** levels in the blood. When the liver is damaged, its enzymes are released into the bloodstream, where the levels can be measured by blood tests. These are called **liver function tests (LFTs)**. Enzyme levels that are routinely checked as part of LFTs include:

- alanine aminotransferase (ALT)
- aspartate aminotransferase (AST)
- gamma-glutamyltransferase (GGT)

The signs and symptoms of hepatotoxicity vary depending on how badly the liver is damaged. Symptoms of liver damage include:

- nausea
- vomiting
- abdominal pain
- loss of appetite
- diarrhea

Terms Used in This Fact Sheet:

Enzyme: a special protein that speeds up chemical reactions.

Liver function tests (LFTs): tests that measure the blood levels of liver enzymes (proteins made and used by the liver) to determine if your liver is working properly.

Non-nucleoside reverse transcriptase inhibitor (NNRTI): class of anti-HIV medication. NNRTIs work by blocking reverse transcriptase, a protein that HIV needs to make copies of itself. The NNRTIs approved by the FDA are Rescriptor, Sustiva, and Viramune.

Nucleoside reverse transcriptase inhibitor (NRTI): class of anti-HIV medication. NRTIs are faulty versions of the building blocks (nucleosides) used by reverse transcriptase, a protein that HIV needs to make copies of itself. The NRTIs approved by the FDA are Combivir, Emtriva, Epivir, Epzicom, Hivid, Retrovir, Trizivir, Truvada, Videx, Viread, Zerit, and Ziagen.

Protease inhibitor (PI): class of anti-HIV medication. PIs work by blocking protease, a protein that HIV needs to make copies of itself. The PIs approved by the FDA are Agenerase, Aptivus, Crixivan, Fortovase, Invirase, Kaletra, Lexiva, Norvir, Reyataz, and Viracept.

- feeling tired or weak
- jaundice (yellowing of the skin and eyes)
- hepatomegaly (liver enlargement)

Which anti-HIV medications cause hepatotoxicity?

All FDA-approved NRTIs, NNRTIs, and PIs are associated with hepatotoxicity.

NRTIs, especially Zerit (stavudine), Videx (didanosine), and Retrovir (zidovudine), are associated with lactic acidosis and hepatic steatosis.

NNRTIs, especially Viramune (nevirapine), are associated with hepatitis and hepatic necrosis. If you and your doctor decide to use Viramune in your HIV treatment regimen, you will likely be instructed to take only one pill a day for the first 14 days, then to increase

Hepatotoxicity (continued)

to two pills a day. This dosing schedule may decrease your risk of developing hepatotoxicity. Virmune-associated hepatotoxicity usually occurs within the first 12 weeks of taking the drug. Women appear to be at increased risk of liver damage. All patients starting therapy with Virmune should have LFTs every 2 weeks for the first month, then every month for the next 2 months, and then every 1 to 3 months throughout treatment.

PIs, especially full-dose Norvir (ritonavir) and Norvir-boosted Aptivus, are also associated with hepatotoxicity. Unlike Virmune, PIs may cause hepatotoxicity at any time. Patients infected with both HIV and hepatic C virus (HCV) may be at particular risk for developing hepatotoxicity while taking PIs.

Are there other risk factors for developing hepatotoxicity?

Yes. Other risk factors include:

- infection with hepatitis B or C virus
- high levels of certain liver enzymes prior to starting anti-HIV medications
- alcohol use
- use of other medications that damage the liver
- pregnancy

Can hepatotoxicity be prevented?

Because hepatotoxicity is poorly understood, it is not clear how it can be prevented. If you are worried about hepatotoxicity, one of the most important things you can do is to get checked for liver disease before starting anti-HIV medications. If you have liver disease or any risk factors for developing hepatotoxicity, you and your doctor may choose an HIV treatment regimen that minimizes the risk of liver damage. You should have LFTs performed frequently, especially when you first start your HIV treatment regimen.

What should I do if I develop hepatotoxicity?

Call your doctor if you develop any of the symptoms of hepatotoxicity. In some cases, hepatotoxicity goes away without changes in anti-HIV medications. Most cases, however, require that medications be stopped or changed. It is important that you do not stop or make any changes to your treatment regimen before talking with your doctor.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.

Hyperglycemia

What is glucose?

Glucose, commonly called blood sugar, is the body's main energy source. Your body breaks down the food you eat and converts it to glucose. Your cells take glucose from your blood and use it to make energy.

What is hyperglycemia?

Hyperglycemia occurs when you have a higher than usual level of glucose in your blood. This can happen shortly after you have eaten a big meal and is not a problem if your glucose level returns to normal.

Cells remove glucose from the blood in response to **insulin**. If your pancreas doesn't make enough insulin, glucose can't enter the cells and remains in the blood. Blood glucose levels can also get too high if cells are unable to respond to insulin properly (**insulin resistance**). Without glucose, your cells are unable to make energy and can't function properly.

Is hyperglycemia the same as diabetes?

Diabetes mellitus is a disease that occurs when the body can't use glucose properly. Hyperglycemia is a symptom of diabetes; however, you can have hyperglycemia without having diabetes.

What are the symptoms of hyperglycemia?

The most common symptoms of hyperglycemia are increased urination, excessive thirst or hunger, and unexplained weight loss.

What causes hyperglycemia and diabetes?

Treatment with HIV **protease inhibitors** (PIs) and infection with hepatitis C virus increase the risk of hyperglycemia and diabetes in people with HIV. The risk of developing hyperglycemia is about the same with all PIs.

People who are older, overweight, have family members with diabetes, or are from certain ethnic groups are also at greater risk for developing hyperglycemia.

Terms Used in This Fact Sheet:

Hypoglycemic medications: medications used to decrease the level of glucose in the blood. Common oral hypoglycemic medications include Amaryl, Avandia, Glucophage, and Glucotrol.

Insulin: a hormone made by the pancreas. Insulin directs cells to take up glucose from the blood.

Insulin resistance: Insulin resistance occurs when cells are unable to respond to (resist) insulin's message to take up glucose from the blood.

Protease inhibitor (PI): class of anti-HIV medication. PIs work by blocking protease, a protein that HIV needs to make copies of itself. The PIs approved by the FDA are Agenerase, Aptivus, Crixivan, Fortovase, Invirase, Kaletra, Lexiva, Norvir, Reyataz, and Viracept.

I am taking a PI and am worried about hyperglycemia. What should I do?

Tell your doctor if you have symptoms of hyperglycemia and discuss other risk factors you may have for hyperglycemia or diabetes. Do your best to maintain a healthy body weight.

A fasting blood glucose test measures the level of glucose in your blood and is used to diagnose hyperglycemia. You should have this test every 3 to 4 months during the first year you take a PI.

What happens if I develop hyperglycemia?

You and your doctor will discuss your treatment options. For most people, hyperglycemia goes away if they stop taking PIs. Don't stop taking any medication without first talking with your doctor. Together you may decide to make changes to your HIV treatment regimen.

You and your doctor may decide to continue using PIs in your treatment regimen despite your hyperglycemia. Your doctor may suggest you take **hypoglycemic medications** (by mouth) or insulin (injected under the skin) to decrease your blood glucose levels.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.

Hyperlipidemia

What is hyperlipidemia?

Hyperlipidemia is an increase in the amount of fat (such as **cholesterol** and **triglycerides**) in the blood. These increases can lead to heart disease and **pancreatitis**.

Which anti-HIV medications can cause hyperlipidemia?

Some **protease inhibitors** (PIs) can raise blood lipid (fat) levels. Some PIs, such as Norvir, are more likely to cause hyperlipidemia than other PIs. Sustiva is a non-protease inhibitor drug that can also raise blood lipid levels.

Other factors can increase your risk of developing hyperlipidemia. Risks you can control include your alcohol intake, physical activity, and diet. Other risks include hypothyroidism, diabetes, and genetic factors. Oral contraceptives (birth control pills) can also increase triglycerides and total cholesterol.

What are the symptoms of hyperlipidemia?

Hyperlipidemia has no symptoms. The only way your doctor can diagnosis it is through laboratory tests. Your doctor should order a **lipid profile** when you start anti-HIV medication. Once your baseline lipid levels are determined, your doctor should monitor your levels every 3 to 4 months, or at least once a year.

What can I do if I have hyperlipidemia?

There are several things you can do to control your cholesterol and triglyceride levels. You can switch to a low-fat diet and control your weight. Your doctor may refer you to a dietician for help with your diet. Regular aerobic exercise has been shown to lower cholesterol. Quitting smoking and avoiding or limiting alcohol can also lower your cholesterol. Keeping your blood pressure under control is critical; you may need to take medication to lower your blood pressure.

What medications are used to treat hyperlipidemia?

You and your doctor may decide that you should take a cholesterol-lowering medication. This might be a

Terms Used in This Fact Sheet:

Cholesterol: a waxy, fat-like substance present in every cell in your body. Your liver produces cholesterol from stored carbohydrates and fats. Certain foods provide additional amounts of cholesterol, which may be more than your body needs. Cholesterol levels that are too high increase your risk of heart disease.

Lipid profile: a group of tests that indicates your risk of heart disease. The lipid profile tests levels of total cholesterol, HDL-cholesterol (good cholesterol), LDL-cholesterol (bad cholesterol), and triglycerides.

Pancreatitis: inflammation of the pancreas that can produce severe pain and debilitating illness.

Protease inhibitor (PI): class of anti-HIV medication. PIs work by blocking protease, a protein that HIV needs to make copies of itself. The PIs approved by the FDA are Agenerase, Aptivus, Crixivan, Fortovase, Invirase, Kaletra, Lexiva, Norvir, Reyataz, and Viracept.

Triglycerides: a type of fat-like substance. Fats from food are digested and released as triglycerides into the bloodstream. Triglycerides help transfer energy from food into cells. However, triglyceride levels that are too high increase your risk of heart disease and have been associated with diabetes and pancreatitis.

medication from the statin group. Examples of statins are Lipitor (atorvastatin) and Pravachol (pravastatin). If statins are not effective, another medication from a group called fibrates might be added. Lopid (gemfibrozil) and Tricor (fenofibrate) are drugs from the fibrate group. All of these medications can cause serious side effects and should be taken only as directed by your doctor.

Will I need to change my HIV treatment regimen?

If your hyperlipidemia is severe or you do not respond to other treatments, you and your doctor may decide to change your anti-HIV medications. One option may be to replace your PI(s) with an anti-HIV medication from a different class; this might mean changing your entire regimen.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.

Lactic Acidosis

What is lactic acidosis?

Lactic acidosis is a life-threatening condition caused by too much lactate in the blood and low blood pH. Low blood pH means that your blood contains too much acid, which can be harmful to the cells of your body.

What is lactic acid?

Lactic acid is a chemical byproduct of energy production in cells. Cells contain mitochondria, rod-like structures that serve as a cell's powerhouse. Mitochondria help convert the food you eat into the energy you need to function.

The food you eat is broken down into a type of sugar called glucose. Mitochondria use oxygen to turn glucose into energy. If there is not enough oxygen or if the mitochondria aren't working properly, cells must make energy by an alternative method. Making energy by this alternative method produces lactic acid as a byproduct.

Lactic acid is quickly converted to lactate in the blood. Though lactic acid and lactate are not the same, the terms are often used interchangeably. Lactate is formed when lactic acid loses a hydrogen atom. The hydrogen atom lost by lactic acid stays in the blood; this decreases the blood's pH and makes it more acidic.

Your muscles produce lactic acid and lactate when you exercise. It is the lactate in your muscles that makes them feel sore after a workout. Lactate is broken down by your liver, so if your body produces too much lactate, your liver may have a hard time keeping up.

What causes too much lactate?

High levels of lactate in the blood, referred to as *hyperlactatemia*, occur either when you make too much lactate or when your liver isn't working properly and can't break it down.

Terms Used in This Fact Sheet:

Liver function tests (LFTs): tests that measure the blood levels of liver enzymes (proteins made and used by the liver) to determine if your liver is working properly.

Mitochondrial toxicity: also referred to as mitochondrial dysfunction. Damage to the mitochondria that can cause problems in the heart, nerves, muscles, pancreas, kidneys, and liver. It may also cause changes in the blood, such as thrombocytopenia (too few platelets), anemia (too few red blood cells), and neutropenia (too few neutrophils). Mitochondrial damage can lead to lactic acidosis and hepatic steatosis (fatty liver) and may also play a role in lipodystrophy (see [Lipodystrophy Fact Sheet](#)).

Nucleoside reverse transcriptase inhibitor (NRTI): class of anti-HIV medication. NRTIs are faulty versions of the building blocks (nucleosides) used by reverse transcriptase, a protein that HIV needs to make copies of itself. The NRTIs approved by the FDA are Combivir, Emtriva, Epivir, Epzicom, Hivid, Retrovir, Trizivir, Truvada, Videx, Viread, Zerit, and Ziagen.

Nucleoside reverse transcriptase inhibitors (NRTIs) can cause hyperlactatemia by disrupting the function of the mitochondria. This is known as **mitochondrial toxicity**. When the mitochondria don't work efficiently, excess lactate is produced.

NRTIs can also cause the liver to become fatty, a condition called *hepatic steatosis* (see [Hepatotoxicity Fact Sheet](#)). A fatty liver doesn't work well and can't break down lactate efficiently.

Severe hyperlactatemia leads to lactic acidosis. Lactic acidosis is a serious but very rare complication of treatment with NRTIs. Although all NRTIs are associated with hyperlactatemia and lactic acidosis, people taking Zerit (stavudine) and Videx (didanosine) seem to be at greater risk than people taking other NRTIs.

Lactic Acidosis (continued)

Are there other risk factors for lactic acidosis?

Yes. Women and people who are overweight are at increased risk of developing hepatic steatosis and lactic acidosis. Fatal lactic acidosis has also occurred in pregnant women taking a combination of Zerit and Videx. HIV infected patients taking Rebetol (ribavirin) for hepatitis C virus infection may also be at increased risk for lactic acidosis.

What are the symptoms of hyperlactatemia and lactic acidosis?

You can have mild hyperlactatemia without experiencing any symptoms.

Signs and symptoms of severe hyperlactatemia and lactic acidosis are:

- persistent nausea, vomiting, and abdominal pain
- unexplained tiredness
- shortness of breath
- rapid breathing
- enlarged or tender liver
- cold or blue hands and feet
- abnormal heart beat
- weight loss

What should I do if I experience these symptoms?

Tell your doctor right away if you have any of the symptoms of lactic acidosis. Your doctor may then order blood tests, including:

- **liver function tests (LFTs)**
- lactate level (this test is difficult to do and is not done routinely)
- electrolyte level
- blood pH level

Your doctor should also perform a physical exam to check for an enlarged liver and may also order a CT scan or ultrasound of your liver.

What does my lactate level mean?

Lactate levels are usually reported as mmol/dL (millimoles of lactate per deciliter of blood). Lactate levels of 2 to 5 mmol/dL are elevated and should be considered with any symptoms you have. Levels greater than 5 mmol/dL are abnormal, and levels greater than 10 mmol/dL indicate a serious and possibly life-threatening situation.

Lactate levels may vary depending on how the test was performed and which lab did the testing. Your doctor can help you understand what your lactate level means.

What is the treatment for lactic acidosis?

Lactic acidosis is treated by stopping any NRTIs you are taking. You may need to be hospitalized. Some people with lactic acidosis need intravenous (IV) fluids and a machine to help them breathe. Some doctors recommend giving riboflavin (vitamin B2), thiamine (vitamin B1), coenzyme Q, L-carnitine, or vitamins C, E, and K to patients with lactic acidosis, but the effectiveness of these treatments is uncertain.

You should not stop taking any anti-HIV medications without talking with your doctor, even if you have symptoms of lactic acidosis. If you are diagnosed with lactic acidosis, you and your doctor will decide how to stop your anti-HIV medications, when to restart medications, and which ones to take when you go back to treatment.

If you have only mild hyperlactatemia and no symptoms, you may not need to change your HIV treatment regimen. At this time, people with mild hyperlactatemia do not seem to be at increased risk for lactic acidosis.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.

Lipodystrophy

What is lipodystrophy?

Lipodystrophy, also called fat redistribution, is a disturbance in the way your body produces, uses, and stores fat. There are two different kinds of lipodystrophy. In *fat wasting*, also known as *lipoatrophy*, fat is lost from particular areas of the body, especially the arms, legs, face, and buttocks. The second kind of lipodystrophy is *fat accumulation*, also known as *hyperadiposity*. In fat accumulation, fat builds up in particular parts of the body, especially the belly, breasts, and back of the neck.

What does lipodystrophy look like?

Places where fat may accumulate:

- back of the neck and upper shoulders (often described as "buffalo hump")
- abdomen (also called "protease paunch" or "Crixivan potbelly")
- breasts (in both men and women)
- lipomas (fatty growths in different parts of the body)

Places where fat may be lost:

- face (sunken cheeks, temples, and eyes)
- arms and legs (veins may become more visible; this is called "roping")
- buttocks

Are there any other disorders that occur along with lipodystrophy?

If you have lipodystrophy, you may also have other **metabolic** disorders. These disorders include *hyperlipidemia* (see [Hyperlipidemia Fact Sheet](#)), *hyperglycemia* (see [Hyperglycemia Fact Sheet](#)) or, rarely, *lactic acidosis* (see [Lactic Acidosis Fact Sheet](#)). Lipodystrophy in combination with hyperlipidemia and insulin resistance is called *lipodystrophy syndrome*.

Terms Used in This Fact Sheet:

Baseline: an initial measurement made before starting therapy and used as a reference point.

Metabolic: referring to the buildup or breakdown of the body's molecular building blocks. These building blocks provide the material and energy that your body needs to function.

Magnetic resonance imaging (MRI): a way to take pictures of the inside of the body. MRI uses magnetic fields and radio waves instead of x-rays. MRIs are particularly useful for taking pictures of the body's soft tissues and organs.

Non-nucleoside reverse transcriptase inhibitor (NNRTI): class of anti-HIV medication. NNRTIs work by blocking reverse transcriptase, a protein that HIV needs to make copies of itself. The NNRTIs approved by the FDA are Rescriptor, Sustiva, and Viramune.

Nucleoside reverse transcriptase inhibitor (NRTI): class of anti-HIV medication. NRTIs are faulty versions of the building blocks (nucleosides) used by reverse transcriptase, a protein that HIV needs to make copies of itself. The NRTIs approved by the FDA are Combivir, Emtriva, Epivir, Epzicom, Hivid, Retrovir, Trizivir, Truvada, Videx, Viread, Zerit, and Ziagen.

Protease inhibitor (PI): class of anti-HIV medication. PIs work by blocking protease, a protein that HIV needs to make copies of itself. The PIs approved by the FDA are Agenerase, Aptivus, Crixivan, Fortovase, Invirase, Kaletra, Lexiva, Norvir, Reyataz, and Viracept.

What causes lipodystrophy?

Early studies suggested that lipodystrophy was associated with the use of **protease inhibitors (PIs)**, a class of commonly prescribed anti-HIV drugs. However, other studies have shown that lipodystrophy also occurs in people who have never taken PIs. Evidence now suggests that lipodystrophy is linked to taking **nucleoside reverse transcriptase inhibitors (NRTIs)** and PIs at the same time.

Lipodystrophy (continued)

Other risk factors for lipodystrophy include:

- age—older people are at higher risk for lipodystrophy
- race—whites are at higher risk for lipodystrophy
- sex—men are more likely to experience fat loss in their arms and legs, while women tend to have an increase in abdominal and breast fat
- length and severity of HIV infection—the longer you have been infected and the more severe your infection, the higher your risk for lipodystrophy
- a **baseline** body mass index (BMI) in the obese range or significant weight changes are risk factors for lipodystrophy
- baseline immune system health and how well your immune system recovered after starting anti-HIV medications are also factors

Which anti-HIV drugs are most likely to cause lipodystrophy?

Zerit (stavudine, d4T) is one NRTI that has been specifically shown to cause fat loss. PIs may increase the risk of fat accumulation. The longer you take NRTIs and PIs, the greater your chance of developing lipodystrophy.

How will my doctor and I know if I have lipodystrophy?

A diagnosis of lipodystrophy is usually made by examining your body for fat changes. Your doctor may measure around your arms, thighs, waist, hips, and neck before you start medication and then periodically throughout your treatment. Abdominal **magnetic resonance imaging (MRI)** or CT scans can assess abdominal fat; however, there are currently no specific recommendations for routine assessment and monitoring of lipodystrophy.

How is lipodystrophy treated?

At this time, there are no clearly effective treatments for lipodystrophy. However, if you have lipodystrophy, you may benefit from:

- *Changes to your anti-HIV medications*—People with lipodystrophy may benefit from changes to their HIV treatment regimens. If you are taking Zerit, switching to Ziagen (abacavir, ABC) may help reduce lipodystrophy. PIs may be replaced with **non-nucleoside reverse transcriptase inhibitors (NNRTIs)**, which do not appear to cause lipodystrophy. However, the results of switching drugs are uncertain; you and your doctor may decide that changing medications is not right for you. Be sure to talk with your doctor before stopping or switching any medications.
- *Diet and exercise*—Changes to your diet and exercise regimen may help build muscle and reduce fat accumulation.
- *Medications*—If you have insulin resistance and are hyperglycemic (see [Hyperglycemia Fact Sheet](#)), the drug Glucophage (metformin) may help decrease abdominal fat.
- *Injections, implants, and surgery*—If you have fat wasting, you may benefit from injections of human growth hormone (hGH) to boost muscle size in your arms and legs. Injections of fat or synthetic fat substitutes like Sculptra can fill out sunken cheeks, as can cosmetic cheek implants. However, most of these treatments, along with surgery to remove fat accumulation, are still being studied and do not yet have FDA approval for the treatment of HIV-related lipodystrophy. Sculptra is the only treatment that is currently approved; it received FDA approval in August 2004.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.

Osteonecrosis, Osteopenia, and Osteoporosis

What is osteonecrosis, and what are its symptoms?

Osteonecrosis means "bone death." Bone can die if its blood supply is cut off and it can't get nutrients; this is called *avascular necrosis*. Osteonecrosis occurs in the hip bones of some people with HIV, but doctors aren't sure why. It is not clear if osteonecrosis occurs because of HIV infection itself or as a side effect of the medications used to treat HIV.

Symptoms of osteonecrosis include:

- pain in the affected area of the body
- limited range of motion, joint stiffness, or limping
- muscle spasms
- progressive bone damage leading to bone collapse

How is osteonecrosis diagnosed?

If you have symptoms of osteonecrosis, early diagnosis is best made by **magnetic resonance imaging (MRI)** of the bone. MRI is able to detect osteonecrosis before bone is significantly damaged and before abnormalities can be seen on an x-ray. X-rays and CT scans may also be used to look for osteonecrotic bone damage.

What is the treatment for osteonecrosis?

While some treatments may provide relief from the pain associated with osteonecrosis, surgical removal of the dead bone and joint replacement are the only effective treatments for people who have serious osteonecrosis. If you have osteonecrosis, you may benefit from:

- *Surgery* – options range from minor outpatient procedures to reinforce bone to major surgeries such as partial or total hip replacement.

Terms Used in This Fact Sheet:

Dual energy x-ray absorptiometry (DEXA) scan: a test that uses low energy x-rays to measure the mineral content of bones. A DEXA scan uses less radiation than a standard chest x-ray.

Magnetic resonance imaging (MRI): a way to take pictures of the inside of the body. MRI uses magnetic fields and radio waves instead of x-rays. MRIs are particularly useful for taking pictures of the body's soft tissues and organs.

Protease inhibitor (PI): class of anti-HIV medication. PIs work by blocking protease, a protein that HIV needs to make copies of itself. The PIs approved by the FDA are Agenerase, Aptivus, Crixivan, Fortovase, Invirase, Kaletra, Lexiva, Norvir, Reyataz, and Viracept.

- *Medications* – **non-steroidal anti-inflammatory drugs (NSAIDs)** such as aspirin or ibuprofen may decrease the pain of osteonecrosis.
- *Assistive devices* – canes, crutches, or a walker may lessen the pain of bone disorders and may reduce the risk of falls.

What are osteopenia and osteoporosis, and what are their symptoms?

Bones are made of minerals like calcium and phosphate. *Osteopenia* is a condition in which the bones lose these minerals and become less dense. This makes the bones weaker. When bone loss becomes more severe, the condition is referred to as *osteoporosis*.

There are no obvious symptoms in the early stages of osteopenia and osteoporosis. However, fractures may occur if bone loss continues. The most common fractures involve the spine, wrists, or hips. Fractures may cause:

- neck or low back pain
- bone pain or tenderness
- loss of height
- stooped posture

Osteonecrosis, Osteopenia, and Osteoporosis (continued)

Who is at risk of developing osteopenia and osteoporosis?

Anyone can develop osteopenia and osteoporosis. You may be at increased risk if you take HIV **protease inhibitors (PIs)**. You may also be at increased risk if you:

- are female
- take steroids or certain other medications
- smoke
- drink excessive amounts of alcohol
- have low body weight

Anti-HIV medications can cause negative side effects that may increase your risk of osteopenia and osteoporosis. These side effects include:

- *Lipodystrophy* (also known as fat maldistribution) – a disturbance in the way the body produces, uses, and distributes fat (see [Lipodystrophy Fact Sheet](#))
- *Hyperlipidemia* – high levels of cholesterol and triglycerides in the blood (see [Hyperlipidemia Fact Sheet](#))

How are osteopenia and osteoporosis diagnosed?

A **dual energy x-ray absorptiometry (DEXA)** scan is used to diagnose osteopenia and osteoporosis. A DEXA scan is a painless, noninvasive procedure to determine your bone mineral density. Your bone density is then compared to people of your age and health to determine if your bones are weaker than they should be.

Although there are currently no specific guidelines for how often HIV positive people should have a DEXA scan, you should talk with your doctor about your risk factors for osteopenia and osteoporosis.

What are the treatments for osteopenia and osteoporosis?

If you have osteopenia or osteoporosis, you may benefit from:

- *Dietary supplements* – Calcium and vitamin D supplements are often recommended for people with osteopenia and osteoporosis.
- *Medications* – Bisphosphonates (Fosamax and Actonel) and raloxifene (Evista) are prescription drugs used to prevent and treat osteoporosis. Calcitonin (Miacalcin and Calcimar) and hormone replacement therapy for post-menopausal women may also be prescribed to slow bone loss and reduce the risk of fractures.
- *Assistive devices* – Canes, crutches, or a walker may lessen the pain of osteoporosis and reduce the risk of falls.

How can I prevent bone disorders from occurring?

Some things you can do to lower your risk of bone problems:

- *Consume adequate calcium and vitamin D in your diet* – High-calcium foods include low-fat milk, yogurt, and leafy green vegetables. Calcium supplements with vitamin D are another source of calcium. Adults should consume 1,000 to 1,500 mg of calcium each day.
- *Get weight-bearing exercise* – Walking, jogging, playing tennis, dancing, and other physical activities strengthen bone.
- *Don't drink excessive alcohol or smoke* – These behaviors accelerate bone loss.
- *Prevent falls* – Bone breaks or fractures increase your risk of osteonecrosis.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.

Skin Rash

What kinds of skin rash can anti-HIV medications cause?

Anti-HIV medications can cause mild skin rashes as well as serious, even life-threatening rashes. The vast majority of skin rashes are mild to moderate. They usually appear within a few weeks of starting a new medication, and often go away with continued use of the medication. However, because some rashes can be serious, you should contact your doctor if you notice a skin rash. He or she will advise you about how best to manage the rash.

Which anti-HIV medications cause skin rash?

Skin rash may occur with medications from any of the three main HIV drug classes: **NNRTIs**, **NRTIs**, and **PIs**.

NNRTIs cause the majority of skin rashes, with Viramune (nevirapine) causing the most severe rashes. If you and your doctor decide to use Viramune in your HIV treatment regimen, you will likely be instructed to take only one pill a day for the first 14 days, then to increase to two pills a day. This dosing schedule may decrease your risk of developing a severe skin rash. Women appear to be at higher risk for developing Viramune-associated skin rashes than men.

NRTIs may also cause skin rashes. Ziagen (abacavir) may cause a rash that is a symptom of a severe drug hypersensitivity (allergic) reaction. If you develop a rash while taking Ziagen, notify your doctor right away. If you and your doctor decide that you need to stop taking the drug, you should never again take Ziagen; any exposure to the drug could result in an even more severe hypersensitivity reaction.

Agenerase (amprenavir) and Aptivus (tipranavir) are the PIs most likely to cause skin rash. Women taking birth

Terms Used in This Fact Sheet:

Eosinophilia: an increased number of eosinophils, a type of white blood cell. Eosinophils are a part of the body's immune system that can damage healthy tissue if they malfunction.

Non-nucleoside reverse transcriptase inhibitor (NNRTI): class of anti-HIV medication. NNRTIs work by blocking reverse transcriptase, a protein that HIV needs to make copies of itself. The NNRTIs approved by the FDA are Rescriptor, Sustiva, and Viramune.

Nucleoside reverse transcriptase inhibitor (NRTI): class of anti-HIV medication. NRTIs are faulty versions of the building blocks (nucleosides) used by reverse transcriptase, a protein that HIV needs to make copies of itself. The NRTIs approved by the FDA are Combivir, Emtriva, Efavirenz, Epivir, Epzicom, Hivid, Retrovir, Trizivir, Truvada, Videx, Viread, Zerit, and Ziagen.

Protease inhibitor (PI): class of anti-HIV medication. PIs work by blocking protease, a protein that HIV needs to make copies of itself. The PIs approved by the FDA are Agenerase, Aptivus, Crixivan, Fortovase, Invirase, Kaletra, Lexiva, Norvir, Reyataz, and Viracept.

control pills that contain estrogen may be more likely to develop a rash when taking Aptivus. If you are allergic to sulfa drugs, your doctor should monitor you carefully if you start taking Agenerase or Aptivus as part of your HIV treatment regimen.

What characterizes a severe skin rash?

Severe skin rashes cause significant damage to the skin and can result in serious complications, even death. The severe skin rashes that may occur with the use of anti-HIV medications are *Stevens-Johnson syndrome* (SJS) and *toxic epidermal necrolysis* (TEN), which are two different forms of the same kind of skin rash. TEN differs from SJS in the extent of skin damage—TEN involves at least 30% of the total body skin area. Both SJS and TEN are severe conditions that must be treated by a doctor.

Skin Rash (continued)

What are the symptoms of SJS and TEN?

The symptoms of SJS and TEN include:

- flat or raised red spots on the skin that develop blisters in the center
- blisters in the mouth, eyes, genitals, or other moist areas of the body
- peeling skin that results in painful sores
- fever
- headache
- general ill feeling

Are there any other drug-associated skin rashes I should know about?

Another rare but life-threatening rash occurs as part of the *DRESS syndrome* (drug rash with eosinophilia and systemic symptoms). DRESS is characterized by a drug-related rash with **eosinophilia** and whole-body symptoms, such as fever, blood abnormalities, and organ inflammation.

How are skin rashes treated?

If you have a mild or moderate skin rash, you and your doctor may decide to change the medications in your HIV treatment regimen. Alternatively, your doctor may treat you with an antihistamine drug while you continue on the same HIV treatment regimen. Be sure to talk with your doctor before stopping or making any changes to your medications.

In cases of severe rash (SJS, TEN, or DRESS), your doctor will stop your anti-HIV medication and may admit you to the hospital. While in the hospital, you may be treated with intravenous (IV) fluids and medications such as anti-inflammatories and antibiotics. Patients with TEN and significant skin loss may need to be in a hospital's burn unit for specialized care.

If you have a severe rash while taking anti-HIV medications, you and your doctor must identify which medication caused the rash, and you should never take that medication again, even as part of a future HIV treatment regimen. Exposure to the problem medication could result in an even more severe, and perhaps fatal, drug reaction. Be aware that if you experienced a reaction to a drug in a particular class (for example, an NNRTI), you may be at risk of a serious reaction to another drug in that class. This is referred to as *cross-hypersensitivity*.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.