Managing Side Effects of HIV MEDICATIONS
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What are side effects?

HIV medications help many people with HIV infection live longer, healthier lives. Taking these medications on a regular basis lowers the amount of HIV (viral load) in your body and protects your immune system. Lowering your viral load also reduces your risk of transmitting HIV to others.

How often and how many medications you take to treat HIV infection has also been simplified. Now, many medications are combined into a single pill you take once a day, making HIV medications easier to take and treatment more manageable as a whole.

As with most medications, HIV medications can cause side effects. Side effects are symptoms or problems that may occur when you take a medication. Almost all medications can cause side effects, including HIV medications.

You may experience side effects from your HIV medications at some point, especially when you begin taking the drug. But most side effects can be managed and will NOT cause you serious problems. Many people find they can get into a routine of taking their HIV medications as prescribed while keeping side effects to a minimum. If you work with your provider to manage any side effects you experience and keep taking your HIV medications, you have a better chance of lowering the amount of HIV in your body and staying healthy longer. Once you have a handle on side effects, it will be easier to stick with your medication schedule and keep your HIV viral load down.

Most side effects you can see and feel, like headaches, upset stomach, a rash, nervousness, or trouble concentrating. But other side effects may not be so obvious, like effects on your liver or kidneys. Some side effects are very common and many people will experience them. Other side effects are very rare. Your age, body weight and size, gender and overall health can play a role in how you experience side effects.

Why do I need to know about side effects of HIV medications?

Learning how to handle side effects is an important part of taking HIV medications. Dealing with side effects will help with taking your HIV medications on schedule — if you have a plan and stick with it, you’ll have a better chance of staying healthy. Try to develop a plan for dealing with possible side effects before you begin taking a drug for the first time.

When you start taking a medication, your doctor or pharmacist will explain any possible side effects and steps for dealing with them. If those steps don’t reduce the side effects and you continue to feel ill, call your doctor. Your doctor or pharmacist will give you information on each medication telling you when you should stop taking the drug and call for help.

What questions should I ask when my doctor first prescribes an HIV medication?

Make sure you understand what the medication does and the best way to take it.

Ask your doctor:

- What is the name of the drug? Learn the drug’s brand name and its generic (scientific) name. In this booklet, the generic name is listed first and the brand name follows in parentheses.
- What is the drug supposed to do?
- When do I take it? What is the best time of day to take the drug — for example, before bed or first thing in the morning?
- Should I take it with food or without food?
- Are there any foods or liquids I should avoid when taking the drug?
- Are there any other medications I should avoid when taking the drug?
Why does the package insert list so many side effects?

The package insert is the printed information that usually comes with your medication. By law, drug companies have to list all the possible side effects, even if they are very rare. The most common side effects usually are listed first, followed by the less common ones. Package inserts list ALL possible side effects, but that does not mean you will experience them.

Are there tests that can tell if I’m going to have side effects from a certain HIV medication?

Yes. Some patients have a genetic make-up that makes them more likely to have side effects from certain HIV medications. There are genetic tests for two HIV drugs:

**Abacavir (Ziagen)** is an NRTI that is also found in the combination drugs Trizivir and Epzicom. Abacavir can cause hypersensitivity and a severe rash in some patients. A genetic test is available that may be able to predict which patients will develop this rash. The FDA recommends that all patients have this test before starting abacavir treatment.

**Atazanavir (Reyataz)** is a protease inhibitor. Hyperbilirubinaemia (or jaundice) can occur when this medication slows the liver’s ability to get rid of old red blood cells. A genetic test is available that may be able to predict this reaction for some, but not all patients.

Common side effects with all HIV medications

Some side effects can be caused by many different HIV medications. These include:

- Diarrhea
- Feeling tired (fatigue)
- Headache
- Liver problems
- Upset stomach (nausea), stomach pain, vomiting, and poor appetite.

Most people find these side effects decrease over time or go away completely. But other side effects — like liver and kidney damage — you can’t feel, so your doctor will test for them.
**Diarrhea**

If your HIV medications are causing the diarrhea, drink plenty of fluids to replace what you lose through diarrhea. Drinks like Gatorade that replace minerals and nutrients are a good choice. Over-the-counter medications such as Imodium, Kapectate, Lomitol, or Pepto-Bismol can help. Many people with HIV have controlled their diarrhea for years by eating some foods and avoiding others. Different things work for different people. Try these tips:

- The BRAT diet: Bananas, Rice (white), Applesauce, and Toast. Oatmeal and tofu can also help.
- Avoid spicy, fatty, starchy, or processed foods, caffeine, alcohol, dairy products, and foods that give you gas (beans, broccoli).
- Try soluble fiber drinks (like Metamucil, Citrocel, or psyllium) or foods like oatmeal or Cream of Wheat.
- Take calcium supplements (500 mg twice a day).
- Ask your doctor or nutritionist about digestive enzymes, acidophilus or other suggestions.

Diarrhea will often decrease or go away if you try some of these steps. If you have diarrhea for five days in a row or longer, or if you lose five pounds or more, tell your doctor.

**Feeling tired (fatigue)**

Feeling tired (fatigue) is a common side effect when you begin taking any medication. Sometimes it is difficult to tell whether the medication or the HIV itself is tiring you out. Many people feel less tired as their bodies get used to a new drug and the medications bring HIV under control.

You may feel tired due to anemia — a low level of red blood cells. Some HIV drugs, like AZT, can cause anemia. If the anemia is severe, your doctor may change your HIV medication or prescribe medication to increase your red blood cell count.

**Headache**

Headaches are a common side effect of many HIV medications, especially during the first few weeks of taking a new drug. They may become worse when you're under pressure or feel tense. Several over-the-counter medications may help. These steps may help with headaches:

- Eat regularly and drink plenty of fluids.
- Sit or lie down in a quiet, dark room; place a cold wash cloth over your forehead and eyes.
- Gently massage the base of your skull with your thumbs.
- Use aspirin, acetaminophen (Tylenol), or ibuprofen (Advil, Motrin) according to the directions on the label. Ask your doctor which pain reliever is best for you. Talk with your doctor. If your headaches are very painful and occur often, they may be migraine headaches that aren't caused by your HIV medications and need special treatment.

**Liver problems**

The liver releases enzymes — proteins that help you digest foods and process the medications you take. Some HIV medications cause the release of too many enzymes, which can damage the liver, especially in people who have both HIV and hepatitis C. If you have previous liver damage from alcohol, street drugs, viral hepatitis, HIV, or medications, this side effect can become worse. Your doctor will check your liver with blood tests on a regular schedule.
Certain herbs and alternative treatments can also harm the liver. If you are taking or planning to use herbal or alternative treatments, discuss them with your doctor to make sure which ones are safe for you.

To reduce liver side effects:
- Drink less alcohol or stop drinking alcohol completely.
- Your doctor will probably do regular tests of your liver enzyme levels.
- Get a hepatitis test. If you test positive, there are treatments that may help.

If your liver is damaged, avoiding alcohol is the best thing you can do to keep it healthy. Be sure to tell your doctor about all of the prescription drugs, over-the-counter medications, and alternative treatments you take, including herbs or vitamin supplements. Some of these treatments may be harmful to your liver.

Upset stomach (nausea), stomach pain, vomiting, poor appetite
These common side effects usually lessen or go away in a few weeks. If you vomit or have stomach pain for several days in a row, call your doctor. Prescription drugs called antiemetics can help control nausea and vomiting. Ask your doctor about taking Compazine, Marinol, Zofran, or Phenergan. Over-the-counter drugs like Pepto-Bismol may relieve nausea. To help settle an upset stomach:
- Use the Bananas, Rice (white), Applesauce, and Toast (BRAT) diet.
- Avoid hot, spicy, or greasy foods.
- Eat dry foods like crackers, toast, and dry cereal.
- Sip cold, carbonated drinks (like ginger ale) or try peppermint, chamomile, or ginger tea.

Some medications are easier on the stomach if you take them with food. But some HIV medications that you’re supposed to take with food may still be hard on your stomach. Ask your doctor or nutritionist how to time your meals and medications to avoid upsetting your stomach.

Long-term loss of appetite and weight loss
When you have HIV, long-term loss of appetite and weight loss can be a serious problem. Starting a new medication may reduce your appetite or upset your stomach so that you eat less. Try these steps to restore your appetite and avoid weight loss:
- Eat foods that appeal to you even when you are not hungry.
- Eat five or six small meals a day rather than three large ones.
- Avoid foods and drinks that fill you up but don’t provide useful calories.
- Try nutritional supplement drinks like Ensure or Boost.
- Keep track of your weight closely. Is your weight loss due to lack of appetite or vomiting? Did it begin when you started a new medication? Is it related to exercise, stress, or other factors? People with HIV need to maintain their weight. If you feel that your medications are causing you to eat less or lose weight, talk with your doctor or nutritionist.

Dietary supplements and natural therapies
Many people with HIV take over-the-counter supplements, herbs, and natural therapies to improve their health and to reduce the side effects of HIV drugs. Many natural therapies have not been scientifically studied; several have their own side effects or may not be totally safe. Here are some things to remember:
- Nutritional supplement shakes are safe to drink and can help you keep weight on.
- A basic, single multivitamin pill is safe and healthy to use. Large doses of vitamins and minerals can make you sick and may hurt your liver.
- Many herbal and natural remedies have not been scientifically studied. You can’t tell how well they work, how much you should take, or whether they are safe.
- Some herbal products can affect your HIV medications. Protease inhibitors will not work if you take St. John’s Wort; and garlic supplements can block the effect of saquinavir. Some herbs and alternative treatments may also hurt your liver. Tell your doctor about all of the medications or treatments you use, including prescription drugs, over-the-counter drugs, and alternative treatments like herbs or vitamin supplements.
Side effects from different types of HIV drugs

This section describes side effects that are common to each type, or class, of HIV medication.

**Protease inhibitors**
- Atazanavir (Reyataz)
- Darunavir (Prezista)
- Fosamprenavir (Lexiva)
- Indinavir (Crixivan)
- Nelfinavir (Viracept)
- Tipranavir (Aptivus)
- Ritonavir (Norvir)
- Saquinavir (Invirase)

**Fat problems (lipodystrophy)**
Lipodystrophy is a change in the way your body stores fat. It may develop after taking protease inhibitors for many months. If you have lipodystrophy, you may:
- Lose fat (lipoatrophy), especially in the arms, legs, buttocks, or face;
- Gain fat (lipohyperatrophy) in the waist, stomach, or breasts; or
- In rare cases, develop fat deposits at the base of the neck.

If you develop lipodystrophy, your doctor may advise you to change HIV medications, get more exercise, change your diet, or undergo other medical or surgical treatments.

**Metabolic problems**
HIV medications can affect your metabolism — the way your body stores and uses its nutrients: sugars (glucose), fats, and proteins. HIV medications and HIV itself tend to change the level of fats (triglycerides and cholesterol), sugar (glucose), and insulin, which controls glucose in your blood. These metabolic changes can lead to heart disease, heart attacks, stroke, or diabetes. Some HIV drugs cause metabolic problems more often than others. Because you probably won’t feel these side effects, your doctor will need to do blood tests and exams to keep track of these levels.

**Heart disease, heart attacks, stroke**
Higher levels of fats in your blood can raise your risk of heart attack, heart disease, diabetes, stroke, and pancreatitis. Protease inhibitors, especially ritonavir, seem to increase fat levels in many people. During treatment, your doctor should test your cholesterol and triglyceride levels regularly. If the levels get too high, these things might help:
- Quit smoking.
- Get regular exercise.
- Change to a low-fat diet that lowers cholesterol.
- Ask your doctor about medications that can help lower your cholesterol.

**Diabetes**
Diabetes is a disease where your body doesn’t produce the right amount of insulin to control your blood sugar (glucose). Too much glucose in the blood can slowly damage the eyes, kidneys, blood vessels, heart, and nerves. Having high blood pressure or high cholesterol or being overweight all raise your risk of getting diabetes. Diabetes symptoms include being thirsty often, needing to urinate often, and dry mouth.

If you have diabetes before you start taking HIV medications, or if you develop diabetes, your doctor will create a diabetes treatment and nutrition plan. If your doctor doesn’t have experience treating diabetes, ask for a referral to a specialist.

**Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**
- Abacavir (Ziagen)
- Didanosine, ddl (Videx)
- Emtricitabine (Emtriva)
- Lamuvidine, 3TC, (Epivir)
- Stavudine, d4t (Zerit)
- Tenofovir (Viread)
- Retrovir (Zidovudine)

**Blood problems**
Zidovudine and the medications containing zidovudine (Combivir, Trizivir) can slow the production of different types of blood cells. HIV itself may also be the cause. Three main blood problems are:
- Anemia: a decrease in the number of red cells in your blood, which can make you feel very tired.
- Neutropenia and leukopenia: a decrease in the number of white blood cells. These cells fight bacteria and infection and help to keep your immune system healthy.
- Thrombocytopenia: a decrease in platelets, the cells that help your blood to clot and stop bleeding.

If you have mild blood problems, you may not need to change your HIV medications at all. Other prescription drugs can help your body produce more blood cells. If you have a severe blood problem, your doctor will suggest changing HIV medications.
Sleeping problems (insomnia)

Insomnia is a common problem for people with HIV. It may be caused by the disease itself or by HIV medications, such as Sustiva, Atripla or Maraviroc. Insomnia may also be caused by other health problems, such as chronic pain, and the medications used to treat those health problems. Some lifestyle habits and activities may also need to be changed.

Try these tips for reducing insomnia:
• Avoid or reduce your use of alcohol and caffeine (including soda) in the evening.
• Keep a regular sleep schedule — go to bed and get up at the same time. Don’t spend too much time in bed if you can’t get to sleep.
• Exercise regularly.
• Eat a consistent, healthy diet. Don’t go to bed hungry. In the evenings, eat foods that increase your level of melatonin: chicken, turkey, rice, bananas, cottage cheese, ginger, soy nuts, and pumpkin seeds.
• Talk with your doctor about the benefits of using sleep supplements such as melatonin.
• Use relaxation techniques as part of a bedtime routine to reduce restlessness and anxiety and help you “wind down.”
• If you have been prescribed sleep medications, use them only when you really need them.

Lactic acidosis

Lactic acid is produced as your body uses glucose (blood sugar). Lactic acidosis is an uncommon but dangerous side effect that occurs when your lactic acid level gets too high. It is more common in women and in people who are very overweight. It can lead to liver failure and death. It occurs most often in people who are taking NRTIs. Symptoms include:
• Shortness of breath when exercising (if this has usually not happened to you before);
• Feeling extremely tired;
• Upset stomach and throwing up;
• Stomach pain; and
• Bloating

If you feel several of these symptoms at the same time, call your doctor right away. You will need a blood test to find out if you have lactic acidosis.

Nerve problems, tingling hands and feet (neuropathy)

Neuropathy is damage to your nerves that gives you tingling, numbness, or burning in the hands or feet that doesn’t go away. This side effect happens mostly with Stavudine and Didanosine and less commonly with Zidovudine. If the cause of the neuropathy is not stopped, it can get worse and become very painful. Tell your doctor if you get these symptoms in your hands and to see if the problem is due to the medication or other causes, such as diabetes.

Here are some tips for managing neuropathy:
• Avoid long walks or standing for a long time.
• Soak your feet in cool water.
• Ask a friend to give you a massage.
• Keep your feet uncovered at night.
• Avoid tight socks or shoes.

If the HIV medication is the cause, your doctor may replace the drug with a different one. Milder cases of neuropathy can be treated with over-the-counter pain relievers or creams. For more serious cases, your doctor may prescribe a certain type of antidepressant drug or a narcotic pain reliever.

Thinning bones (osteoporosis, osteopenia)

Everyone’s bones become thinner as they grow older — it’s a normal part of aging. But there is evidence that some NRTIs may make your bones become thinner more quickly than normal — so thin they might break more easily. This is called osteoporosis or osteopenia.

Doctors generally do not recommend testing for thinning bones, except for women who are past menopause. To reduce your risk of osteoporosis:
• Stop smoking;
• Get enough calcium (from supplements, dairy products, tofu);
• Get enough vitamin D (from sunlight, fortified milk, and fortified soy or rice milks); or
• Do weight-bearing exercise, like walking or weightlifting.
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- Delavirdine (Rescriptor)
- Efavirenz (Sustiva)
- Nevirapine (Viramune)
- Etravirine (Intelence)
- Rilpivirine (Edurant)

Skin-related side effects

Some HIV medications (mostly NNRTIs) can cause a rash, itchiness, or very dry skin. In rare cases of severe rash, symptoms can also include fever, throwing up, and abdominal pain.

Call your doctor right away if you get a rash, especially if it itches or looks like hives (large red bumps).

For less severe skin problems:
- Use a natural skin moisturizer, like aloe vera.
- Antihistamines like Benadryl can help clear up many mild rashes.
- Your doctor may prescribe an antihistamine or corticosteroid (like Prednisone) for a more serious rash or itching.
- Avoid using harsh soaps and perfumes.

Fixed-Dose Combination Drugs

- Efavirenz/emtricitabine/tenofovir (Atripla)
- Lamivudine/zidovudine (Combivir)
- Emtricitabine/rilpivirine/tenofovir (Complera)
- Abacavir/lamivudine (Epzicom)
- Lopinavir/ritonavir (Kaletra)
- Elvitegravir/cobicistat/emtricitabine/tenofovir (Stribild)
- Abacavir/lamivudine/zidovudine (Trizivir)
- Emtricitabine/tenofovir (Truvada)

HIV combination drugs

Some HIV medications have been combined into single pills. Combining medications in one pill means you have to take fewer pills, which can make taking HIV medications easier. But when you experience side effects from combination drugs, it’s more difficult to determine which component medication is causing the problem.

Specific side effects for combination drugs are listed in the chart at the end of this booklet.

Fusion inhibitors

Fusion inhibitors can help patients who are resistant to many other drugs from other classes of HIV medications. Fuzeon (enfuvirtide, T-20) is the only approved fusion inhibitor. Because patients inject Fuzeon twice a day, they sometimes have problems with their skin — called injection site reactions — where they place the shots. These problems can include itching, swelling, redness, pain and tenderness, hardened skin, and bumps.

To reduce these effects:
- Try showering before taking the shot to soften the skin.
- Pinch a small layer of skin and fat between your thumb and index finger and inject there so that you don’t push into muscle.
- Wear loose-fitting clothes that don’t rub against the skin where the medication was injected.

CCR5 Antagonists (Chemokine Coreceptor Antagonists)

- Maraviroc (Selzentry)

If you have liver problems — including hepatitis B or hepatitis C — kidney problems, or heart disease, tell your doctor before starting to take maraviroc. Symptoms of liver problems can include yellow (jaundiced) skin or eyes, dark urine, an itchy body rash, or stomach pain and vomiting. Because it can make you drowsy, don’t drive or operate heavy equipment while first taking maraviroc.
Integrase Inhibitors
Raltegravir (Isentress)
Dolutegravir (Tivicay)
Elvitegravir/cobicistat/emtricitabine/tenofovir (Stribild)
No serious side effects have been associated with integrase inhibitors.

Drug-specific side effects

Abacavir: Severe allergic reaction
About 5 out of every 100 people who take abacavir (ABC, Ziagen) will have an allergic reaction that can be dangerous. Abacavir is also contained in the combination drugs Trizivir and Epzicom, which can produce the same allergic reaction. You may be having this reaction if you have a type of skin rash or if you have two or more of the following sets of symptoms when taking abacavir:
- Fever;
- Nausea, vomiting, diarrhea, or stomach pain; or
- Severe tiredness, achiness, or generally feeling ill.

**If you notice these symptoms while taking abacavir, Trizivir or Epzicom, call your doctor or clinic right away.** These symptoms usually go away soon after you stop taking Abacavir. Don’t resume taking the drug unless your doctor tells you the symptoms were not part of a hypersensitivity reaction.

Tenofovir (Viread), Truvada, Atripla, Stribild, Complera: Chronic renal insufficiency (kidney failure)
HIV infection hurts the ability of the kidneys to function properly. Some HIV medications also may harm the kidneys. Tenofovir (Viread), an NRTI, has caused kidney failure in some patients. Tenofovir is also part of the combination drugs Truvada, Atripla, Stribild, and Complera.

Tipranavir (Aptivus): Hepatotoxicity (liver injury)
If you have liver illness — such as chronic hepatitis B or hepatitis C — you could get very sick from taking tipranavir. Your doctor will closely monitor your liver enzymes, a measure of your liver health.

Efavirenz (Sustiva) and Atripla: Dizziness, confusion, sleeping problems
About half the people who take these medications have one of these early side-effects: dizziness, confusion, trouble concentrating, sleeping problems, depression, or anxiety. These nervous system side effects usually lessen or go away in two to four weeks. Many people find that taking efavirenz or Atripla at bedtime reduces these side effects. Your doctor also may adjust the dosage. Here are some tips for first starting out with these drugs:
- Consider taking a few days off from work while you adjust to this medication.
- Don’t drive.
- Avoid alcohol.
- Don’t use recreational drugs, including marijuana.
- If you take efavirenz or Atripla before bedtime, don’t drink or eat anything with caffeine or sugar for at least five hours beforehand.

Pancreatitis: didanosine (Videx), stavudine (Zerit); in children, lamivudine (Epivir)
The pancreas produces fluids that help the body digest and store food. HIV medications can cause problems with your pancreas (pancreatitis). Protease inhibitors can increase amounts of fat in your blood, which can also cause pancreatitis.

**Symptoms include:**
- Stomach pain;
- Upset stomach (nausea);
- Throwing up;
- Yellow skin and/or yellowing of the whites of the eyes (jaundice).

Drinking less alcohol or no alcohol at all is the best way to reduce your risk of pancreatitis. Mild pancreatitis can be treated with special medications; your doctor may stop prescribing any NRTIs.
Conclusion: Keeping your quality of life

We know that drugs that fight HIV improve the health of people with HIV. How you feel when you take those drugs — your quality of life — is important, too. Most of the side effects you have from HIV medications will decrease over time. But if you have side effects that don’t go away, talk with your doctor, case manager, nurse, nutritionist, pharmacist, or caregiver about what you can do. They may have tips to help you reduce the symptoms and make the drug easier for you to take. Because there are many different medications that fight HIV, your doctor will probably be able to find medications that work if you need to switch.
### Side Effects of HIV Medications

* Many people taking HIV medications have no side effects at all.
* Be sure to talk to your doctor about any side effects you experience.
* In most cases, side effects are short term and your doctor can help you manage them until they disappear.

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<th>Bone thinning</th>
<th>Depression, euphoria, hallucinations</th>
<th>Increased cholesterol, fats</th>
<th>Lactic acidosis</th>
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<th>Insomnia (sleeping problems)</th>
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<td>Chronic renal insufficiency</td>
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<td>Liver illness (hepatotoxicity)</td>
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**Protease Inhibitors**
- Fosamprenavir (Lexiva)
- Atazanavir (Reyataz)
- Darunavir (Prezista)
- Lopinavir/Ritonavir (Kaletra)
- Nelfinavir (Viracept)
- Ritonavir (Norvir)
- Tipranavir (Aptivus)
- Invirase (Saquinivir)

**Nucleoside Reverse Transcriptase Inhibitors**
- Abacavir (Ziagen)
- Didanosine, ddl (Videx, Videx EC)
- Emtricitabine (Emtriva)
- Lamivudine (Epivir)
- Stavudine, d4T (Zerit, Zerit XR)
- Tenofuvir (Viread)
- Zidovudine, AZT (Retrovir)

**Non-Nucleoside Reverse Transcriptase Inhibitors**
- Delavirdine, DLV (Rescriptor)
- Efavirenz (Sustiva)
- Etravirine, ETR (Intecelence)
- Rilpivirine (Edurant)
- Rilpivirine/emtricitabine/tenofovir (Complera)
- Nevirapine, NVP (Viramune, XR)

**Fixed-Dose Combinations**
- Abacavir/lamivudine (Epzicom)
- Abacavir/zidovudine/lamivudine (Trizivir)
- Lamivudine/zidovudine (Combivir)
- Rilpivirine/emtricitabine/tenofovir (Complera)
- Tenofovir/emtricitabine (Truvada)
- Tenofovir/emtricitabine/elvitegravir (Stribal)

**Fusion Inhibitors**
- Enfuvirtide (Fuzeon)

**Entry Inhibitors**
- Maraviroc (Selzentry)

**Integrase Inhibitors**
- Dolutegravir (Tivicay)
- Raltegravir (Isentress)

Headache, diarrhea, and nausea are possible side effects of any HIV medication, so they are not included in this chart. For a complete description of side effects, please go to [www.health.ny.gov/publications/9408.pdf](http://www.health.ny.gov/publications/9408.pdf).

**Symbol key:**
- $\Delta =$ hepatitis B infection may worsen if patient stops use; $X^* =$ in children; $X^{**} =$ if patient has chronic hepatitis C or history of kidney illness; $X =$ most likely cause.