BioScrip isn’t the kind of pharmacy that can print your digital photos. But we’ll give you a reason to smile for them.

At BioScrip, we understand the challenges that you face with complex medical and chronic health conditions, like HIV/AIDS and Hep C. We are committed to providing you with the medications and support you need so you can focus on what matters most - your life.

Community Pharmacy Locations

San Diego, CA
877.901.9973

San Francisco, CA
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Sherman Oaks, CA
800.377.5977

West Hollywood, CA
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866.523.6005

Miami, FL
800.332.1850

Orlando, FL
866.523.5996

St. Petersburg, FL
866.523.6004

Tampa, FL
800.573.5858

West Palm Beach, FL
866.755.7697

Atlanta, GA
866.851.4396

Chicago, IL
866.798.2905

Indianapolis, IN
877.358.7828

866.656.8629

Baltimore, MD
866.218.2964

Boston, MA
877.349.7628

Minneapolis, MN
800.403.4414

Kansas City, MO
800.829.3044

St. Louis, MO
866.899.8413

Las Vegas, NV
866.282.5928

New York, NY
866.851.4395

Bronx, NY
877.827.3890

Hawthorne, NY
800.993.0006

Long Island, NY
800.724.6996

Columbus, OH
800.781.4422

Philadelphia, PA
877.277.1737

Memphis, TN
866.557.8811

Dallas, TX
866.523.6002

888.505.9048

Houston, TX
866.523.5995

Washington, DC
866.490.5046

Seattle, WA
866.793.1540

Milwaukee, WI
866.746.3799

Long Island, NY
800.724.6996

Columbus, OH
800.274.6996

Philadelphia, PA
877.277.1737

Memphis, TN
866.557.8811

Dallas, TX
866.523.6002

888.505.9048

Houston, TX
866.523.5995

Washington, DC
866.490.5046

Seattle, WA
866.793.1540

Infusion Center Locations

Burbank, CA
800.584.0265

San Francisco, CA
877.901.9971

Pompano Beach, FL
877.592.3949

Morris Plains, NJ
800.552.3462

Las Vegas, NV
702.386.9280

King of Prussia, PA
877.610.7137

Memphis, TN
866.557.8811

Seattle, WA
866.793.1540
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Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)
Dual-Class Fixed Dose Combination
Protease Inhibitor (PI)
Entry Inhibitor
Integrase Inhibitor

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The distribution of Positively Aware is supported in part through an unrestricted grant from GlaxoSmithKline.

A model, photographer, or author’s HIV status should not be assumed based on their appearance in Positively Aware.

You can view these (and other stories from previous issues) online at www.tpan.com and www.positivelyaware.com
INDICATION
ATRIPLA® (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate [DF] 300 mg) is a prescription medication used alone as a complete regimen or with other medicines to treat HIV-1 infection in adults. ATRIPLA does not cure HIV-1 and has not been shown to prevent passing HIV-1 to others. Do not stop taking ATRIPLA unless directed by your healthcare provider. See your healthcare provider regularly.

IMPORTANT SAFETY INFORMATION
Contact your healthcare provider right away if you experience any of the following serious or common side effects:
• Severe depression, strange thoughts, or angry behavior have been reported by a small number of patients. Some patients have had thoughts of suicide and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness.
• Kidney problems (including decline or failure of kidney function). If you have had kidney problems, or take other medicines that may cause kidney problems, your healthcare provider should do regular blood tests. Symptoms that may be related to kidney problems include a high volume of urine, thirst, muscle pain, and muscle weakness.
• Bone changes. Lab tests show changes in the bones of patients treated with tenofovir DF, a component of ATRIPLA. Some HIV patients treated with tenofovir DF developed thinning of the bones (osteopenia) which could lead to fractures. Also, bone pain and softening of the bone (which may lead to fractures) may occur as a consequence of kidney problems. If you have had bone problems in the past, your healthcare provider may want to check your bones.

Common side effects:
• Dizziness, headache, trouble sleeping, drowsiness, trouble concentrating, and/or unusual dreams. These side effects tend to go away after taking ATRIPLA for a few weeks. These symptoms may be more severe with the use of alcohol and/or mood-altering (street) drugs. If you are dizzy, have trouble concentrating, and/or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.
• Rash is a common side effect that usually goes away without any change in treatment, but may be serious in a small number of patients.
• Other common side effects include: tiredness, muscle pain, and muscle weakness.

Other possible side effects:
• Changes in body fat have been seen in some people taking anti-HIV-1 medicines. The cause and long-term health effects are not known.
• Skin discoloration (small spots or freckles) may also happen.
• If you notice any symptoms of infection, contact your healthcare provider right away.
• Additional side effects are inflammation of the pancreas, allergic reaction (including swelling of the face, lips, tongue, or throat), shortness of breath, pain, stomach pain, weakness and indigestion. You should take ATRIPLA once daily on an empty stomach. Taking ATRIPLA at bedtime may make some side effects less bothersome.

ATRIPLA is one of several treatment options your doctor may consider.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see Patient Information on the following pages.
“My entire HIV regimen in one pill daily. For me, that’s great.”

Phillip
on ATRIPLA for 2 years

ATRIPLA is the #1 prescribed HIV regimen.*

- Only ATRIPLA combines 3 HIV medications in 1 pill daily.
- Proven to lower viral load to undetectable† and help raise T-cell (CD4+) count to help control HIV through 3 years of a clinical study.
- ATRIPLA does not cure HIV-1 and has not been shown to prevent passing HIV-1 to others.
- Selected Important Safety Information: Some people who have taken medicine like ATRIPLA have developed the following: a serious condition of acid buildup in the blood (lactic acidosis), and serious liver problems (hepatotoxicity). For patients with both HIV-1 and hepatitis B virus (HBV), hepatitis may worsen if ATRIPLA is discontinued.

ATRIPLA®
(efavirenz 600 mg/emtricitabine 200 mg/
tenofovir disoproxil fumarate 300 mg) Tablets

Talk to your doctor to see if ATRIPLA is right for you. Your doctor may prescribe ATRIPLA alone or with other HIV medications.

To learn more, visit www.ATRIPLA.com

*Synovate Healthcare Data, US HIV Monitor, Q2 2009.  †Defined as a viral load of less than 400 copies/mL.
ATRIPLA® (efavirenz/emtricitabine/tenofovir disoproxil fumarate)

Do not take any kind of sex without protection. Always practice safer sex by using a latex or polyurethane condom or other barrier to reduce the chance of sexual contact with semen, vaginal secretions, or blood.

Who should not take ATRIPLA?

Together with your healthcare provider, you need to decide whether ATRIPLA is right for you. Do not take ATRIPLA if you are allergic to ATRIPLA or any of its ingredients. The active ingredients of ATRIPLA are efavirenz, emtricitabine, and tenofovir DF. See the end of this leaflet for a complete list of ingredients.

What should I tell my healthcare provider before taking ATRIPLA?

Tell your healthcare provider if you:

- Are pregnant or planning to become pregnant (see “What should I avoid while taking ATRIPLA?”).
- Are breast-feeding (see “What should I avoid while taking ATRIPLA?”).
- Have kidney problems or are undergoing kidney dialysis treatment.
- Have bone problems.
- Have liver problems, including hepatitis B virus infection. Your healthcare provider may want to do tests to check your liver while you take ATRIPLA.
- Have ever had mental illness or are using drugs or alcohol.
- Have ever had seizures or are taking medicine for seizures.

What important information should I know about taking other medicines with ATRIPLA?

ATRIPLA may change the effect of other medicines, including the ones for HIV-1, and may cause serious side effects. Your healthcare provider may change your other medicines or change their doses. Other medicines, including herbal products, may affect ATRIPLA. For this reason, it is very important to let all your healthcare providers and pharmacists know what medicines, herbal supplements, or vitamins you are taking.

MEDICINES YOU SHOULD NOT TAKE WITH ATRIPLA

- The following medicines may cause serious and life-threatening side effects when taken with ATRIPLA. You should not take any of these medicines while taking ATRIPLA:
  - Vacostr (tipranavir/ritonavir) should not be taken with ATRIPLA since it may cause problems with ATRIPLA.
  - ATRIPLA also should not be used with Combivir (lamivudine/zidovudine), EMTRIVA, Epivir-HBV (lamivudine), Epzicom (abacavir sulfate/lamivudine), Trizivir (abacavir sulfate/lamivudine/zidovudine), SUSTIVA, TRUVADA, or VIREAD.

- Vind (voriconazole) should not be taken with ATRIPLA since it may lose its effect or may increase the chance of having side effects from ATRIPLA.
- Do not take St. John’s wort (Hypericum perforatum), or products containing St. John’s wort with ATRIPLA. St. John’s wort is an herbal product sold as a dietary supplement. Talk with your healthcare provider if you are taking or are planning to take St. John’s wort. Taking St. John’s wort may decrease ATRIPLA levels and lead to increased viral load and possible resistance to ATRIPLA or cross-resistance to other anti-HIV-1 drugs.
- ATRIPLA should not be used with HEPRESA® (adefovir dipivoxil).

It is also important to tell your healthcare provider if you are taking any of the following:

- Fortovase, Invirase (saquinavir), Blinax (dienethromycin), or Sporanox (itraconazole); these medicines may need to be replaced with another medicine when taken with ATRIPLA.
- Calcium channel blockers such as Cardizem or Tiazac (diltiazem), Covera HS or lipten (verapamil) and others; Crizivan (indinavir); the immunosuppressant medicines cyclosporine (Gengraf, Neoral, Sandimmune, and others), Prograf (tacrolimus), or Rapamune (sirolimus); Methadone; Mycophenyl (ritubatin); Rifampin; cholesterol-lowering medicines such as Lipitor (atorvastatin), Pravachol (pravastatin sodium), or Zocor (simvastatin); or Zoloft (sertraline); these medicines may need to have their dose changed when taken with ATRIPLA.

- Viread, Vexoc EC (didanosine); tenofovir DF (a component of ATRIPLA) may increase the amount of didanosine in your blood, which could result in more side effects. You may need to be monitored more carefully if you are taking ATRIPLA and didanosine together. Also, the dose of didanosine may need to be changed.
- Reyataz (atazanavir sulfate) or Kaletra (lopinavir/ritonavir); these medicines may increase the amount of tenofovir DF (a component of ATRIPLA) in your blood, which could result in more side effects. Reyataz is not recommended with ATRIPLA. You may need to be monitored more carefully if you are taking ATRIPLA and Kaletra together. Also, the dose of Kaletra may need to be changed.
- Medicines for seizures (for example, Dilantin (phenytoin), Tegretol (carbamazepine), or phenobarbital); your healthcare provider may want to switch you to another medicine or check drug levels in your blood from time to time.

These are not all the medicines that may cause problems if you take ATRIPLA. Be sure to tell your healthcare provider about all medicines that you take.

Keep a complete list of all the prescription and nonprescription medicines as well as any herbal remedies that you are taking, how much you take, and how often you take them. Make a new list when medicines or herbal remedies are added or stopped, or if the dose changes. Give copies of this list to all of your healthcare providers and pharmacists every time you visit your healthcare provider or fill a prescription. This will give your healthcare provider a complete picture of the medicines you use. Then he or she can decide the best approach for your situation.
How should I take ATRIPLA?

- Take the exact amount of ATRIPLA your healthcare provider prescribes. Never change the dose on your own. Do not stop this medicine unless your healthcare provider tells you to stop.
- You should take ATRIPLA on an empty stomach.
- Swallow ATRIPLA with water.
- Taking ATRIPLA at bedtime may make some side effects less bothersome.
- Do not miss a dose of ATRIPLA. If you forget to take ATRIPLA, take the missed dose right away, unless it is almost time for your next dose. Do not double the next dose. Carry on with your regular dosing schedule. If you need help in planning the best times to take your medicine, ask your healthcare provider or pharmacist.
- If you believe you took more than the prescribed amount of ATRIPLA, contact your local poison control center or emergency room right away.
- Tell your healthcare provider if you start any new medicine or change how you take old ones. Your doses may need adjustment.
- When your ATRIPLA supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to ATRIPLA and become harder to treat.
- Your healthcare provider may want to do blood tests to check for certain side effects while you take ATRIPLA.

What should I avoid while taking ATRIPLA?

- Women should not become pregnant while taking ATRIPLA and for 12 weeks after taking it. They should use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control.
- Women should not rely only on hormone-based birth control, such as pills, injections, or implants that may make these contraceptives ineffective. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control. Estrogen-based contraceptives may make these contraceptives ineffective. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control.
- Women should not breast-feed if you are taking ATRIPLA. Swallow ATRIPLA with water.
- Do not breast-feed if the seal over bottle opening is broken or missing.
- Avoid doing things that can spread HIV-1 infection. For example, do not share needles or syringes, or certain other items with another person.

How should I take ATRIPLA?

- Do not use ATRIPLA if the seal over bottle opening is broken or missing.
- Keep ATRIPLA in its original container and keep the container tightly closed.
- Do not use ATRIPLA if the seal over bottle opening is broken or missing.
- Store ATRIPLA at room temperature (77 °F [25 °C]). Keep ATRIPLA in its original container and keep the container tightly closed.
- Do not use ATRIPLA if the seal over bottle opening is broken or missing.
- General information about ATRIPLA:

ATRIPLO(®) (efavirenz/ emtricitabine/tenofovir disoproxil fumarate) may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density. Additionally, bone pain and softening of the bone (which may contribute to fractures) may occur as a consequence of kidney problems.

Common side effects:

Patients may have dizziness, headache, trouble sleeping, drowsiness, trouble concentrating, and/or unusual dreams during treatment with ATRIPLA. These side effects may be reduced if you take ATRIPLA at bedtime on an empty stomach. They also tend to go away after you have taken the medicine for a few weeks. If you have these common side effects, such as dizziness, it does not mean that you will also have serious psychiatric problems, such as severe depression, strange thoughts, or angry behavior. Tell your healthcare provider right away if any of these side effects continue or if they bother you. It is possible that these symptoms may be more severe if ATRIPLA is used with alcohol or mood altering (street) drugs. If you are dizzy, have trouble concentrating, or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.

Rash may be common. Rashes usually go away without any change in treatment. In a small number of patients, rash may be serious. If you develop a rash, call your healthcare provider right away.

Other common side effects include tiredness, upset stomach, vomiting, gas, and diarrhea.

Other possible side effects with ATRIPLA:

- Changes in body fat. Changes in body fat develop in some patients taking anti-HIV-1 medicine. These changes may include an increased amount of fat in the upper back and neck (‘‘buffalo hump’’), in the breasts, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these fat changes are not known.
- Skin discoloration (small spots or freckles) may also happen with ATRIPLA.
- In some patients with advanced HIV infection (AIDS), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to an improvement in the body’s immune response, enabling the body to fight infections that may have been present with no obvious symptoms. If you notice any symptoms of infection, please inform your doctor immediately.
- Additional side effects are inflammation of the pancreas, allergic reaction (including swelling of the face, lips, tongue, or throat), shortness of breath, pain, stomach pain, weakness and indigestion.

Tell your healthcare provider or pharmacist if you notice any side effects while taking ATRIPLA. Contact your healthcare provider before stopping ATRIPLA because of side effects or for any other reason.

This is not a complete list of side effects possible with ATRIPLA. Ask your healthcare provider or pharmacist for a more complete list of side effects of ATRIPLA and all the medicines you will take.

How do I store ATRIPLA?

- Keep ATRIPLA and all other medicines out of reach of children.
- Store ATRIPLA at room temperature (77 °F [25 °C]).
- Keep ATRIPLA in its original container and keep the container tightly closed.
- Do not keep medicine that is out of date or that you no longer need. If you throw any medicines away make sure that children will not find them.

What are the possible side effects of ATRIPLA?

ATRIPLA may cause the following serious side effects:

- Lactic acidosis (buildup of an acid in the blood). Lactic acidosis can be a medical emergency, and may need to be treated in the hospital. Call your healthcare provider right away if you get signs of lactic acidosis. (See “What is the most important information I should know about ATRIPLA?”)
- Serious liver problems (hepatotoxicity), with liver enlargement (hepatomegaly) and fat in the liver (steatosis). Call your healthcare provider right away if you get any signs of liver problems. (See “What is the most important information I should know about ATRIPLA?”)
- “Flare-ups” of hepatitis B virus (HBV) infection, in which the disease suddenly returns in a worse way than before, can occur if you have HBV and you stop taking ATRIPLA. Your healthcare provider will monitor your condition for several months after stopping ATRIPLA. If you have both HIV-1 and HBV infection and may recommend treatment for your HBV. ATRIPLA is not approved for the treatment of hepatitis B virus infection. If you have advanced liver disease and stop treatment with ATRIPLA, the “flare-up” of hepatitis B may cause your liver function to decline.
- Serious psychiatric problems. A small number of patients may experience severe depression, strange thoughts, or angry behavior while taking ATRIPLA. Some patients have thoughts of suicide and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness. Contact your healthcare provider right away if you think you are having these psychiatric symptoms, so your healthcare provider can decide if you should continue to take ATRIPLA.
- Kidney problems (including decline or failure of kidney function). If you have had kidney problems in the past or take other medicines that can cause kidney problems, your healthcare provider should do regular blood tests to check your kidneys. Symptoms that may be related to kidney problems include a high volume of urine, thirst, muscle pain, and muscle weakness.
- Changes in bone mineral density (thinning bones). Laboratory tests show changes in the bones of patients treated with tenofovir DF, a component of ATRIPLA. Some HIV patients treated with tenofovir DF have developed thinning of the bones (osteopenia) which could lead to fractures. If you have had bone problems in the past, your healthcare provider
By starting HIV treatment, I went from living in shame to standing up and taking control.

If you’re HIV positive, the decision to begin taking medication can be difficult. But it can be the first step toward reclaiming your life and living longer. Talking to your doctor and getting the right information on HIV treatment can help take you from feeling ashamed to feeling in control.

Take the next step and go to hivtreatmentispower.com or call (877) Y-TREAT-HIV

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TPAN empowers people living with HIV through peer-led programming, support services, information dissemination, and advocacy.

We also provide services to the broader community to increase HIV knowledge and sensitivity, and to reduce the risk of infection.
By starting HIV treatment, I went from living in shame to standing up and taking control.

If you’re HIV positive, the decision to begin taking medication can be difficult. But it can be the first step toward reclaiming your life and living longer. Talking to your doctor and getting the right information on HIV treatment can help take you from feeling ashamed to feeling in control.

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Swarup Mehta, PharmD, MBA, AAHIVE

Swarup Mehta was born and raised in Naperville, Illinois. He earned his PharmD and MBA at Drake University in Des Moines, Iowa in 2002. After graduation, Swarup worked for Walgreens Pharmacy in many Chicagoland locations. He is currently the Clinic Pharmacy Manager for Walgreens at Northstar Medical in Chicago. There, he specializes and counsels on HIV, hepatitis, and oncology. He is also an immunizer and offers a variety of vaccinations at his clinic. He has served on the TPAN board for three years and is the co-chair of the fundraising committee. Swarup received the 2009 Outstanding Health Care Advocate of the Year award from the AIDS Legal Council of Chicago. Working at the clinic pharmacies for Walgreens has given him the ability to build relationships with his patients and make their lives easier. He is doing what he loves.

Calvin “Cal” J. Cohen, MD, MS

Dr. Cal Cohen is research director of Harvard Vanguard Medical Associates and Community Research Initiative of New England in Boston, Massachusetts. He is also a clinical instructor at Harvard Medical School. In addition, he works as an HIV clinical management consultant and internist at Harvard Pilgrim Health Care.

Dr. Cohen was co-chair of the Scientific Advisory Committee of amfAR community-based clinical trials network, and served as co-principal investigator of the Harvard/BCH AIDS Clinical Trials Unit, AIDS Clinical Trials Group. He holds appointments at Brigham and Women’s Hospital and Beth Israel Hospital, both in Boston.

In addition to caring for HIV-positive patients and directing clinical research at a large HIV community-based research site, Dr. Cohen is actively involved in evaluating new antiretroviral therapies, the durability and longevity of the benefits from such therapies, and issues regarding compliance and adherence.

Jeff Taylor

Jeff is a 25-year survivor of AIDS and cancer, and has been active in HIV research advocacy since enrolling in the AIDS Clinical Trials Group’s (ACTG) AZT trials in the late 80s. He served for five years on the ACTG’s Community Constituency Group (now CSS), where he was the community liaison to the Complications Research Agenda Committee (now OpMan), and was on the ACTG’s original metabolics focus group formed to study emerging lipodystrophy. Currently, he continues to serve on the University of California, San Diego Antiviral Research Center’s Community Advisory Board, and on the NCI’s AIDS Malignancy Consortium as a community representative. He is a vice-chair of the AIDS Treatment Activists Coalition’s Drug Development Committee, which meets regularly with pharmaceutical companies and the FDA on HIV drug development issues. Jeff resides in Palm Springs, where he produces a monthly treatment education series for area HIV patients and providers.
The Art and Science of Treating HIV

Treating HIV, it has been said, is as much an art as it is a science. There is a certain amount of deftness and skill that your doctor and you must apply in order to achieve lifelong success in combating the virus. In addition to the question of when to start treatment, and what combination of meds to start with, there are a whole host of other considerations that must be taken into account as well. Am I ready to take the medications, as prescribed, every day for the rest of my life? Which treatment is best for me? Do I have other medical conditions that affect how I can take my drugs? Will they fit into my lifestyle? Do I have other problems, such as insufficient housing, inadequate health insurance, or substance abuse issues, which need to be looked at or dealt with first, before beginning treatment? Or are these issues now affecting my ability to remain adherent?

The cover of this year’s HIV Drug Guide uses a familiar image, Leonardo da Vinci’s “Vitruvian Man”. Vitruvius was a first century Roman architect who believed that the measurements and proportions of the human body were divinely created, perfect, and correct, and symbolized the merging of both art and science together.

When we take medications to treat and suppress the virus, we not only are benefiting from the science that has gone into the years of research and development in creating those drugs, but we also gain from the lessons learned, as well as the mistakes made, by the many health care providers who have had years of experience successfully treating their HIV-positive patients. And we then use our own skills and tricks that we have developed over time to help us remember to take our meds at the prescribed time, either with or without food, and at the correct dosage.

But beware—don’t fall into the trap of letting the art trump the science. I was talking with a friend recently who told me that he was feeling so much better since he recently switched his meds. Side effects were greatly reduced, he told me, and his numbers were vastly improved—better than they had been in a long time. However, in an effort to reduce the severity of the GI upset he was still experiencing, he had cut the doses of all of his medications in half, and he felt this was a reasonable and equitable compromise.

I tried to explain to my friend that this was not a good idea—actually a really bad one—because while doing so might make him feel better in the short term, and his numbers may indeed be okay for a while, he would eventually most likely begin to develop resistance to the medications and they would no longer work, and would possibly limit his other treatment options in the future. I stressed to him the importance of talking to his physician to find out if there were perhaps other meds he could try that would be easier to take, or about ways to reduce the side effects.

And then, sadly, a lot of it ultimately boils down to just plain economics. The Wall Street Journal recently reported that many of the strides in scaling up treatment and advancing prevention efforts which have been made over the last few decades in Uganda are in danger of being lost due to cutbacks in funding from the U.S. A pregnant Ugandan woman with HIV was turned away from clinic after clinic, the article explained, because they simply did not have the capacity to accept any more patients. Other women who are lucky enough to get treatment will often share their pills with friends who aren’t as lucky, resulting in none of them taking enough medication to keep the virus suppressed. The end result, of course, is the development of resistance to the medications for all of the women.

But I never give up hope, and am continually inspired by our readers and those who I am privileged to meet through the work that I do. Recently, I was approached by a bright, attractive young man who I had never met, but who called me by name. He said, “Jeff, I just wanted to tell you that your magazine saved my life.” I was speechless, and completely caught off guard. He was truly genuine and articulate as he went on to explain that at first he was depressed and didn’t know what to do when he learned of his diagnosis, but then picked up a copy of Positively Aware and began reading it. It gave him so much hope, he said, and he realized that he was going to be okay, and would be able to get on with living the rest of his life.

And to me, that is the perfect blend of art and science, while living with HIV.

Be good to yourself, and each other.

With this issue, we bid a fond farewell to our good friend Russell McGonagle, Positively Aware’s Art Director for the last 10 years. Russell’s amazing vision and artistry has been an integral part of our team, and a key to the continued success of the publication… we’ll miss you, Russell! We welcome PA’s new Art Director, Rick Guasco, into the TPAN family.
REYATAZ® (atazanavir sulfate)

**INDICATION:** REYATAZ is a prescription medicine used in combination with other medicines to treat people who are infected with the human immunodeficiency virus (HIV). REYATAZ has been studied in a 48-week trial in patients who have taken anti-HIV medicines and a 96-week trial in patients who have never taken anti-HIV medicines.

REYATAZ does not cure HIV or lower your chance of passing HIV to others.

**IMPORTANT SAFETY INFORMATION:**

Do not take REYATAZ if you are allergic to REYATAZ or to any of its ingredients.

Do not take REYATAZ if you are taking the following medicines due to potential for serious, life-threatening side effects or death: Versed® (midazolam) when taken by mouth, Halcion® (triazolam), ergot medicines (dihydroergotamine, ergonovine, ergotamine, and methylergonovine such as Cafergot®, Migralex®, D.H.E. 45®, ergotrate maleate, Metergine®, and others), Propulsid® (cisapride), or Orap® (pimozide).

Do not take REYATAZ with the following medicines due to potential for serious side effects: Camptosar® (irinotecan), Crixivan® (indinavir), Mevacor® (lovastatin), or Zocor® (simvastatin).

Do not take REYATAZ with the following medicines as they may lower the amount of REYATAZ in your blood, which may lead to increased HIV viral load and resistance to REYATAZ or other anti-HIV medicines: rifampin (also known as Rimactane®, Rifadin®, Rifater®, or Rifamate®), St. John’s wort (Hypericum perforatum)-containing products, or Viramune® (nevirapine).

Do not take Vfend® (voriconazole) if you are taking REYATAZ and Norvir® (ritonavir).

The above lists of medicines are not complete. Taking REYATAZ with some other medicines may require your therapy to be monitored more closely or may require a change in dose or dose schedule of REYATAZ or the other medicine. Discuss with your healthcare provider all prescription and non-prescription medicines, vitamin and herbal supplements, or other health preparations you are taking or plan to take.

Tell your healthcare provider if you are pregnant, breast-feeding, planning to become pregnant or breast-feed, or if you have end-stage kidney disease managed with hemodialysis or severe liver dysfunction.

Tell your healthcare provider right away if you have any side effects, symptoms, or conditions, including the following:

- **Mild rash** (redness and itching) without other symptoms sometimes occurs in patients taking REYATAZ, most often in the first few weeks after the medicine is started, and usually goes away within 2 weeks with no change in treatment.
- **Severe rash** has occurred in a small number of patients taking REYATAZ. This type of rash is associated with other symptoms that could be serious and potentially cause death.

If you develop a rash with any of the following symptoms, stop using REYATAZ and call your healthcare provider right away:

- Shortness of breath
- General ill-feeling or “flu-like” symptoms
- Fever
- Muscle or joint aches
- Yellowing of the skin and/or eyes may occur due to increases in bilirubin levels in the blood (bilirubin is made by the liver).
- A change in the way your heart beats may occur. You may feel dizzy or lightheaded. These could be symptoms of a heart problem.
- Diabetes and high blood sugar may occur in patients taking protease inhibitor medicines like REYATAZ. Some patients may need changes in their diabetes medicine.
- If you have liver disease, including hepatitis B or C, it may get worse when you take anti-HIV medicines like REYATAZ.
- Kidney stones have been reported in patients taking REYATAZ. Signs or symptoms of kidney stones include pain in your side, blood in your urine, and pain when you urinate.
- Some patients with hemophilia have increased bleeding problems with protease inhibitor medicines like REYATAZ.
- Changes in body fat have been seen in some patients taking anti-HIV medicines. The cause and long-term effects are not known at this time.
- Gallbladder disorders (including gallstones and gallbladder inflammation) have been reported in patients taking REYATAZ.

Other common side effects of REYATAZ taken with other anti-HIV medicines include: nausea; headache; stomach pain; vomiting; diarrhea; depression; fever; dizziness; trouble sleeping; numbness, tingling, or burning of hands or feet; and muscle pain.

You should take REYATAZ once daily with food (a meal or snack). Swallow the capsules whole; do not open the capsules. You should take REYATAZ and your other anti-HIV medicines exactly as instructed by your healthcare provider.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.
Once-daily REYATAZ can fit into your schedule and help fight your HIV.

REYATAZ, a protease inhibitor (PI), in HIV combination therapy:

- Can help lower your viral load and raise your T-cell (CD4+ cell) count
- Has a low chance of diarrhea (shown in clinical trials)*
- Is taken once a day with a snack or meal
- **REYATAZ** in combination therapy had a 1%-3% rate of moderate-to-severe diarrhea in adults.

REYATAZ is one of several treatment options your doctor may consider.

Ask your healthcare team about REYATAZ. [www.REYATAZ.com](http://www.REYATAZ.com)

REYATAZ does not cure HIV, a serious disease, and has not been shown to reduce the risk of passing HIV to others.
REYATAZ® (atazanavir sulfate)

(floaters) given by nose or eye. Read the section “What important information should I know about taking REYATAZ with other medicines?”

Read the Patient Information that comes with REYATAZ before you start using it and each time you get a refill. There may be new information. This leaflet provides a summary about REYATAZ and does not include everything there is to know about your medicine. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is REYATAZ?

REYATAZ is a prescription medicine used with other anti-HIV medicines to treat people who are infected with the human immunodeficiency virus (HIV). HIV is the virus that causes acquired immune deficiency syndrome (AIDS). REYATAZ is a type of anti-HIV medicine called a protease inhibitor. HIV infection destroys CD4+ (T) cells, which are important to the immune system. The immune system helps fight infection. After a large number of (T) cells are destroyed, AIDS develops. REYATAZ helps block HIV protease, an enzyme that is needed for the HIV virus to multiply. REYATAZ may lower the amount of HIV in your blood, help your body keep its supply of CD4+ (T) cells, and reduce the risk of death and illness associated with HIV.

Does REYATAZ cure HIV or AIDS?

REYATAZ does not cure HIV infection or AIDS. At present there is no cure for HIV infection. People taking REYATAZ may still get opportunistic infections or other conditions that happen with HIV infection. Opportunistic infections are infections that develop because the immune system is weak. Some of these conditions are pneumonia, herpes virus infections, and Mycobacterium avium complex (MAC) infections. It is very important that you see your healthcare provider regularly while taking REYATAZ.

REYATAZ does not lower your chance of passing HIV to other people through sexual contact, sharing needles, or being exposed to your blood. For your health and the health of others, it is important to always practice safer sex by using a latex or polyurethane condom or other barrier to lower the chance of sexual contact with semen, vaginal secretions, or blood. Never use or share dirty needles.

Who should not take REYATAZ?

Do not take REYATAZ if you:

- are taking certain medicines. (See “What important information should I know about taking REYATAZ with other medicines?”) Serious life-threatening side effects or death may happen. Before you take REYATAZ, tell your healthcare provider about all medicines you are taking or planning to take. These include other prescription and nonprescription medicines, vitamins, and herbal supplements.
- are allergic to REYATAZ or to any of its ingredients. The active ingredient is atazanavir sulfate. See the end of this leaflet for a complete list of ingredients in REYATAZ. Tell your healthcare provider if you think you have had an allergic reaction to any of these ingredients.

What should I tell my healthcare provider before I take REYATAZ?

Tell your healthcare provider:

- If you are pregnant or planning to become pregnant. It is not known if REYATAZ can harm your unborn baby. Pregnant women have experienced serious side effects when taking REYATAZ with other HIV medicines called nucleoside analogues. You and your healthcare provider will need to decide if REYATAZ is right for you. If you use REYATAZ while you are pregnant, talk to your healthcare provider about the Antiretroviral Pregnancy Registry.
- If you are breast-feeding. You should not breast-feed if you are HIV-positive because of the chance of passing HIV to your baby. Also, it is not known if REYATAZ can pass into your breast milk and if it can harm your baby. If you are a woman who has or will have a baby, talk with your healthcare provider about the best way to feed your baby.
- If you have liver problems or are infected with the hepatitis B or C virus. See “What are the possible side effects of REYATAZ?”
- If you have end stage kidney disease managed with hemodialysis.
- If you have diabetes. See “What are the possible side effects of REYATAZ?”
- If you have hemophilia. See “What are the possible side effects of REYATAZ?”

About all the medicines you take including prescription and nonprescription medicines, vitamins, and herbal supplements. Keep a list of your medicines with you to show your healthcare provider. For more information, see “What important information should I know about taking REYATAZ with other medicines?” and “Who should not take REYATAZ?” Some medicines can cause serious side effects if taken with REYATAZ.

How should I take REYATAZ?

- Take REYATAZ once every day exactly as instructed by your healthcare provider. Your healthcare provider will prescribe the amount of REYATAZ that is right for you.
- For adults who have never taken anti-HIV medicines before, the dose is 300 mg once daily with 100 mg of NORVIR® (ritonavir) once daily taken with food. For adults who are unable to tolerate ritonavir, 400 mg (two 200-mg capsules) once daily (without NORVIR®) taken with food is recommended.
- For adults who have taken anti-HIV medicines in the past, the usual dose is 300 mg plus 100 mg of NORVIR® (ritonavir) once daily taken with food.
- Your dose will depend on your liver function and on the other anti-HIV medicines that you are taking. REYATAZ is always used with other anti-HIV medicines. If you are taking REYATAZ with SUSTIVA® (efavirenz) or with VIREAD® (tenofovir disoproxil fumarate), you should also be taking NORVIR® (ritonavir).
- Always take REYATAZ with food (a meal or snack) to help it work better. Swallow the capsules whole. Do not open the capsules. Take REYATAZ at the same time each day.
- If you are taking antacids or didanosine (VIDEX® or VIDEX® EC), take REYATAZ 2 hours before or 1 hour after these medicines.
- If you are taking medicines for indigestion, heartburn, or ulcers such as AXID® (nizatidine), PEPCID AC® (famotidine), TAGAMET® (cimetidine), ZANTAC® (ranitidine), AcipHex® (rabeprazole), NEXIUM® (esomeprazole), PREVACID® (lansoprazole), PRILOSEC® (omeprazole), or PROTONIX® (pantoprazole), talk to your healthcare provider.
- Do not change your dose or stop taking REYATAZ without first talking with your healthcare provider. It is important to stay under a healthcare provider’s care while taking REYATAZ.
- When your supply of REYATAZ starts to run low, get more from your healthcare provider or pharmacy. It is important not to run out of REYATAZ. The amount of HIV in your blood may increase if the medicine is stopped for even a short time.
- If you miss a dose of REYATAZ, take it as soon as possible and then take your next scheduled dose at its regular time. If, however, it is within 6 hours of your next dose, do not take the missed dose. Wait and take the next dose at the regular time. Do not double the next dose. It is important that you do not miss any doses of REYATAZ or your other anti-HIV medicines.
- If you take more than the prescribed dose of REYATAZ, call your healthcare provider or poison control center right away.

Can children take REYATAZ?

Dosing recommendations are available for children 6 years of age and older for REYATAZ Capsules. Dosing recommendations are not available for children from 3 months to less than 6 years of age. REYATAZ should not be used in babies under the age of 3 months.

What are the possible side effects of REYATAZ?

The following list of side effects is not complete. Report any new or continuing symptoms to your healthcare provider. Ask your healthcare provider if you have questions about side effects.

- Mild rash (redness and itching) without other symptoms sometimes occurs in patients taking REYATAZ, most often in the first few weeks after the medicine is started. Rashes usually go away within 2 weeks with no change in treatment. Tell your healthcare provider if rash occurs.
- Severe rash: In a small number of patients, a rash can develop that is associated with other symptoms which could be serious and potentially cause death.

If you develop a rash with any of the following symptoms stop using REYATAZ and call your healthcare provider right away:

- Shortness of breath
- General ill feeling or “flu-like” symptoms
- Fever
- Muscle or joint aches
- Conjunctivitis (red or inflamed eyes, like “pink eye”)
- Blisters
- Mouth sores
- Swelling of your face
REYATAZ® (atazanavir sulfate)

- **yellowing of the skin or eyes.** These effects may be due to increases in bilirubin levels in the blood (bilirubin is made by the liver). Call your healthcare provider if your skin or the white part of your eyes turn yellow. Although these effects may not be damaging to your liver, skin, or eyes, it is important to tell your healthcare provider promptly if they occur.
- **a change in the way your heart beats (heart rhythm change).** Call your healthcare provider right away if you get dizzy or light-headed. These could be symptoms of a heart problem.
- **diabetes and high blood sugar (hyperglycemia)** sometimes happen in patients taking protease inhibitor medicines like REYATAZ. Some patients had diabetes before taking protease inhibitors while others did not. Some patients may need changes in their diabetes medicine.
- **If you have liver disease including hepatitis B or C,** your liver disease may get worse when you take anti-HIV medicines like REYATAZ.
- **kidney stones** have been reported in patients taking REYATAZ. If you develop signs or symptoms of kidney stones (pain in your side, blood in your urine, pain when you urinate) tell your healthcare provider promptly.
- **some patients with hemophilia** have increased bleeding problems with protease inhibitors like REYATAZ.
- **changes in body fat.** These changes may include an increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these conditions are not known at this time.

Other common side effects of REYATAZ taken with other anti-HIV medicines include nausea; headache; stomach pain; vomiting; diarrhea; depression; fever; dizziness; trouble sleeping; numbness, tingling, or burning of hands or feet; and muscle pain.

**Gallbladder disorders** (which may include gallstones and gallbladder inflammation) have been reported in patients taking REYATAZ.

**What important information should I know about taking REYATAZ with other medicines?**

Do not take REYATAZ if you take the following medicines (not all brands may be listed; tell your healthcare provider about all the medicines you take). REYATAZ may cause serious, life-threatening side effects or death when used with these medicines.

- **Ergot medicines:** dihydroergotamine, ergonovine, ergotamine, and methylergonoamine such as CAFERGOT®, MIGRANIL®, D.H.E. 45®, ergotrate maleate, METHERSINE®, and others (used for migraine headaches).
- **ORAP®** (glimazide, used for Tuottee’s disorder).
- **PROPLISDI®** (cisapride, used for certain stomach problems).
- **Trizolam,** also known as HALCION® (used for insomnia).
- **Midazolam,** also known as VERSED® (used for sedation), when taken by mouth.

Do not take the following medicines with REYATAZ because of possible serious side effects:

- **CAMPTOSAR®** (irinotecan, used for cancer).
- **CRIXIVAN®** (indinavir, used for HIV infection). Both REYATAZ and CRIXIVAN sometimes cause increased levels of bilirubin in the blood.
- **Cholesterol-lowering medicines MEVACOR® (lovastatin) or ZOCOR® (simvastatin).**

Do not take the following medicines with REYATAZ because they may lower the amount of REYATAZ in your blood. This may lead to an increased HIV viral load. Resistance to REYATAZ or cross-resistance to other HIV medicines may develop:

- Rifampin (also known as RIMACTANE®, RIFADIN®, RIFATER®, or RIFAMATE®, used for tuberculosis).
- St. John’s wort (Hypericum perforatum), an herbal product sold as a dietary supplement, or products containing St. John’s wort.
- VIRAMUNE® (nevirapine, used for HIV infection).

Do not take the following medicine if you are taking REYATAZ and NORVIR® together:

- **VFEND®** (voriconazole).

The following medicines may require your healthcare provider to monitor your therapy more closely:

- **CIALIS®** (tadalafil), **LEVITRA®** (vardenafil), or **VIAGRA®** (sildenafil). REYATAZ may increase the chances of serious side effects that can happen with CIALIS, LEVITRA, or VIAGRA. Do not use CIALIS, LEVITRA, or VIAGRA while you are taking REYATAZ unless your healthcare provider tells you it is okay.
- **LIPTOR®** (atorvastatin) or **CRESTOR®** (rosuvastatin). There is an increased chance of serious side effects if you take REYATAZ with this cholesterol-lowering medicine.
- **Medicines for abnormal heart rhythm:** CORDORANE® (amiodarone), lidocaine, quinidine (also known as CARDIOQUIN®, QUININDEX®, and others).
- **VASCOR®** (bepridil, used for chest pain).

**REYATAZ® (atazanavir sulfate)**

- **COUMADIN®** (warfarin).
- **Tricyclic antidepressants such as ELAVIL® (amitriptyline), NORTRIPTYLINE® (desipramine), SINEQUAN® (doxepin), SURMONTIL® (trimipramine), TOFRANIL® (mipramine), or Vivactil® (protriptyline).**
- **Medicines to prevent organ transplant rejection:** SANDIMMUNE® or NEORAL® (cyclosporin), RAPAMUNE® (sirolimus), or PROGRAF® (tacrolimus).
- **The antidepressant trazodone** (DESYREL® and others).
- **Fluticasone propionate** (ADVAIR®, FLONASE®, FLOVENT®), given by nose or inhaled to treat allergic symptoms or asthma. Your doctor may choose not to keep you on fluticasone, especially if you are also taking NORVIR®.

The following medicines may require a change in the dose or dose schedule of either REYATAZ or the other medicine:

- **INVIRASE® (saquinavir).**
- **NORVIR®** (ritonavir).
- **SUSTIVA®** (efavirenz).
- **Antacids or buffered medicines.**
- **VIDEX®** (didanosine).
- **VIREAD®** (tenofovir disoproxil fumarate).
- **MYCOBUTIN®** (rifabutin).
- **Calcium channel blockers such as CARDIZEM® or TIAZAC® (diltiazem), COVERA- HS® or ISOPTIN SR® (verapamil) and others.**
- **BIAXIN®** (clarithromycin).
- **Medicines for indigestion, heartburn, or ulcers such as AXID® (nizatidine), PEPCID AC® (famotidine), TAGAMET® (cimetidine), or ZANTAC® (ranitidine).**

Talk to your healthcare provider about choosing an effective method of contraception. REYATAZ may affect the safety and effectiveness of hormonal contraceptives such as birth control pills or the contraceptive patch. Hormonal contraceptives do not prevent the spread of HIV to others.

**Remember:**

1. **Know all the medicines you take.**
2. **Tell your healthcare provider about all the medicines you take.**
3. **Do not start a new medicine without talking to your healthcare provider.**

**How should I store REYATAZ?**

- **Store REYATAZ Capsules at room temperature, 59° to 86° F (15° to 30° C).** Do not store this medicine in a damp place such as a bathroom medicine cabinet or near the kitchen sink.
- **Keep your medicine in a tightly closed container.**
- **Keep all medicines out of the reach of children and pets at all times.** Do not keep medicine that is out of date or that you no longer need. Dispose of unused medicines through community take-back disposal programs when available or place REYATAZ in an unrecognizable, closed container in the household trash.

**General information about REYATAZ**

This medicine was prescribed for your particular condition. Do not use REYATAZ for another condition. Do not give REYATAZ to other people, even if they have the same symptoms you have. It may harm them. Keep REYATAZ and all medicines out of the reach of children and pets.

This summary does not include everything there is to know about REYATAZ. Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Remember no written summary can replace careful discussion with your healthcare provider. If you would like more information, talk with your healthcare provider or you can call 1-800-321-1335.

**What are the ingredients in REYATAZ?**

Active Ingredients: atazanavir sulfate

Inactive Ingredients: Crospovidone, lactose monohydrate (milk sugar), magnesium stearate, gelatin, FD&C Blue #2, and titanium dioxide.

VIDEX® and REYATA® are registered trademarks of Bristol-Myers Squibb Company. COUMADIN® and SUSTIVA® are registered trademarks of Bristol-Myers Squibb Pharma Company. DESYREL® is a registered trademark of Mead Johnson and Company. Other brands listed are the trademarks of their respective owners and are not trademarks of Bristol-Myers Squibb Company.

US Patent Nos: 5,849,911 and 6,087,383

Bristol-Myers Squibb
Princeton, NJ 08543 USA

1246226A5 F-1800018-11-09 Rev November 2009
Disgusted in SD

I recently saw a cover of your magazine [January/February] at the clinic I work at, and am thoroughly disgusted by it! On the cover are two “cowboys” with their arms around each other and the words written on the magazine are “HIV in Rural America.”

As a rodeo promoter, stock contractor, my husband a member of the Professional Rodeo Cowboy Association, and my father who has been a rancher in South Dakota for 30 years; this is a slap in the face. How dare you associate cowboys with HIV! Just because of that horrible movie “Brokeback Mountain,” you think two gay men who have on cowboy hats should be on the cover of a national magazine. And to send this magazine out to rural South Dakota, you have got to have a lot of guts. Think about the gay man who does come into the clinic and sees this magazine, what do you think they are going to think? You could have chosen to put a million different pictures on the cover of this magazine, but you chose the most distasteful picture imaginable.

I will be expecting a full apology and for these horrific magazines to be pulled. This is so disturbing, someone should be fired for this type of slander!

Ashley
South Dakota

Ashley, I am the photographer who took the image used for the cover and feature for Positively Aware magazine. There was no ridicule nor intended malice directed toward rodeos or cowboys in any regard to capturing this image. I, too, am from a fourth-generation ranching family in the mountains of western Montana, the ranch having been homesteaded by my great-grandfather before Montana was a state. I grew up on the cattle ranch and my brothers and I still own it. I am very proud of my heritage and to have grown up in such an inspirational and traditional lifestyle. I am also a card-carrying member of the Pro Rodeo Association, as well as the Pacific Northwest Gay Rodeo Association, and have photographed rodeo events for both organizations around my home state of Montana.

Don’t be fooled, there are more gay cowboys out there than you would imagine, most of them feeling isolated, lonely, and shut off from the rest of world and still engaging in unsafe or risky behaviors, many of them with wives and girlfriends, stepping out on the side, trying to hide feelings born within them. I am gay and have been gay from birth. It’s what I am. It doesn’t change my connection to the land and my family or friends that surround me.

I have been living with being HIV-positive for the past 24 years and, believe me, these are real issues that have hit all communities across the country. HIV does not discriminate whether you are straight, bi, gay, male or female, single or married. In fact, we have a fairly large group of straight, traditional women here in Montana who have been living and struggling with this virus for years, many of them with families and children. My job has been to reach out and educate people about what’s happening here. A couple of years ago, I received an award from the Governor of Montana in recognition of my efforts toward prevention and helping others within my community. I am glad it has stirred a reaction from you in South Dakota—that means it’s working. A little awareness and compassion go a long way.

Terry J. Cyr
• Drugs are color-coded by class and are listed alphabetically within each class by brand name, which is listed on the outside margin of each drug page. The brand name is listed first, and typically begins with a capital letter. The generic name, or scientific designation, along with more common names and abbreviations, is listed in parentheses. Only a few drugs have a “common” name. Example: Retrovir (zidovudine, AZT, or ZDV). Retrovir is the brand name, zidovudine is the generic name or scientific designation, AZT is the common name, and ZDV is the abbreviation.

• A fixed dose combination (FDC) is a formulation that combines two or more drugs, and is marked “Combo Drug” on the drug page. A dual-class fixed dose combination combines two or more drugs from two different classes. Currently, there is only one dual-class FDC, Atripla, which combines three drugs—two nukes and one non-nuke.

• The Average Wholesale Price (AWP) is an industry standard that pharmacies and other buyers use to negotiate the amount they pay for drugs. The AWP is included on the drug page as a way to compare drug prices. It is not what you would pay out-of-pocket.

• Drugs included in the HIV Drug Guide are only those that are FDA approved and currently on the market, or are available through an expanded access program (EAP). There are no drugs in expanded access this year.

• The side effects and drug interactions charts make it easier to quickly find some of the more common side effects and interactions associated with each drug. Always refer to the individual drug pages, the manufacturer’s package insert, or your physician or pharmacist for more information.

• Our special pull-out chart allows you to easily pinpoint dosing information and food and liquid requirements for each drug. Check with your health care provider, or refer to the drug page or package insert for more information.

• The U.S. Department of Health and Human Services (DHHS) Treatment Guidelines are periodically updated by a panel of experts; the most recent update to the Guidelines was in December of 2009. See page 55 for an abbreviated version of the guidelines. The entire document is available online as a downloadable PDF document, and includes comprehensive and detailed guidelines on treatment strategies, explanation of lab tests, when and what to start, use in special populations, co-infection, and much more. Visit www.aidsinfo.nih.gov.
**MIX AND MATCH**

With as many as six drug categories, more than ever, how to treat HIV can become a matter of strategy

by Joel Gallant, MD, MPH

Antiretroviral drugs are classified based on the stage of the HIV life cycle they target. In the end, they all do the same thing—prevent the virus from replicating—but they do it in different ways. There are now six classes of drugs from which to choose. With few exceptions, most antiretroviral regimens include drugs from at least two classes, because attacking the virus with drugs that work in different ways is thought to help prevent resistance. The traditional combinations, especially for initial therapy, have been combinations of nucleoside analog reverse transcriptase inhibitors (NRTIs) plus either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI), but integrase inhibitor-based combinations were recently added to the list of recommended starting regimens, a CCR5 antagonist was recently approved for first-line therapy, and there are ongoing studies looking at novel combinations, including regimens that don’t include NRTIs.

**Nucleoside Analog Reverse Transcriptase Inhibitors (NRTIs) or “Nukes”**

Nucleoside analogs, or “nukes,” work by preventing reverse transcriptase, a viral enzyme, from turning HIV RNA into DNA. The nukes mimic the normal building blocks of DNA, but when they get pulled into the growing DNA chain, they screw up the process and keep the chain from being completed. The nukes were the only drugs we had until 1996, and they’ve been components of just about every drug regimen since the approval of Retrovir (AZT) in the mid-80s. Most ART combinations today consist of at least two nucleosides (the “backbone”) plus one or more drugs from a different class. The popularity of nukes took a hit when we learned they caused lipoatrophy, which we’d been blaming on protease inhibitors. But it turned out that lipoatrophy (and other related toxicities) were caused primarily by the thymidine analogs (Zerit and Retrovir) but not by Epivir, Emtriva, Ziagen, or Viread. As a result, we’re not as afraid of nukes as we used to be. Still, even the newer agents can have their problems. Viread (a component of Truvada and Atripla) sometimes causes kidney problems, and there is some evidence suggesting that Ziagen (a component of Epzicom and Trizivir) may increase the risk of heart attacks, especially in people who already have cardiac risk factors.

**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) or “Non-Nukes”**

The NNRTIs, or “non-nukes,” are powerful, convenient drugs with little long-term toxicity. NNRTIs block reverse transcriptase by binding to a different site compared to nukes. Rather than getting incorporated into the virus’ DNA, they interfere with the function of reverse transcriptase so it can’t make DNA. Side effects occur early on, usually in the first few weeks, and include nervous system side effects with Sustiva, liver toxicity with Viramune, and rash with both. In contrast to boosted PI s, resistance to NNRTIs can occur easily and quickly if the viral load isn’t suppressed. These are great drugs for people who are good at taking meds and want a simple combination, but they’re not the best choice for those who start and stop meds frequently. The newest drug in this class, Intelence, is used for people who have developed resistance to the other NNRTIs.

**Protease Inhibitors (PIs)**

The PIs inhibit the activity of protease, an enzyme used by HIV to cleave large proteins into smaller proteins, which are then used to assemble new viral particles. The PIs are the drugs that changed everything. It was the combination of NRTIs plus PI s that first allowed us to completely suppress HIV viral load. Suddenly, we could do more than just temporarily boost the CD4 count for a year or two. HIV infection quickly went from being a progressive fatal disease to one that was chronic and manageable. Management wasn’t easy, though. The early PIs were hard drugs to take: lots of pills, lots of doses, and lots of side effects and long-term toxicity. That’s changed, in part because of ritonavir “boosting.” Almost all PIs are now taken with a low dose of ritonavir (Norvir), which boosts drug levels and simplifies dosing (see “Norvir”). New PIs and new formulations of old PIs have also expanded options and have made PIs a lot easier to take than they used to be. Still, it’s important to be aware of PI toxicity. To varying degrees, the PIs can raise lipids (cholesterol and triglycerides), can cause insulin resistance (which can lead to diabetes), and have been linked to body shape changes, especially fat accumulation. However, these problems seem to occur less frequently with the newer agents. PIs can sometimes cause diarrhea or loose stools that typically disappear with fiber supplements like Metamucil, Fibercon, or Citrucel. Don’t be put...
off by the word “laxative” on the bottle—fiber helps whether you’ve got diarrhea or constipation.

**Integrase inhibitors**

Integrase inhibitors, the newest class of drugs, block the insertion of HIV DNA into human DNA. There is one approved integrase inhibitor, Isentress, and several more in development. Isentress is now approved for both initial therapy and treatment of drug-resistant virus.

**CCR5 Antagonists**

Entry inhibitors block entry of the virus into the CD4 cell. There are several stages of viral entry. The first is attachment of the virus to the CD4 receptor. There aren’t any attachment inhibitors available yet, but this is a potential target for drug development. The next step is binding of the virus to a co-receptor (either CCR5 or CXCR4). In 2007, the first CCR5 antagonist, Selzentry, was approved by the FDA. It was initially approved for use in treatment-experienced patients, but the FDA recently expanded its indication to include initial therapy. Tropism testing is necessary before using a CCR5 antagonist, since it won’t suppress virus that can get into the cell using the CXCR4 co-receptor.

**Fusion inhibitors**

The final step of viral entry involves fusion of the envelope of the virus with the membrane of the CD4 cell, a step blocked by Fuzeon. Fuzeon requires twice-daily subcutaneous injection, so it’s not often used these days. However, it’s still a useful option for people with extensive drug resistance.

Joel Gallant, MD, MPH, is Professor of Medicine and Epidemiology at the Johns Hopkins University School of Medicine’s Division of Infectious Diseases, and Associate Director of the Johns Hopkins AIDS Service, and author of the book, 100 Questions & Answers About HIV and AIDS.

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<td>Nucleoside Reverse Transcriptase Inhibitors (also called nucleoside analogs, NRT Is, or nukes)</td>
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**NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR**

**Common Name:** zidovudine (AZT) and lamivudine (3TC)

**Brand Name:** Combinvir

**Class:** fixed dose combination—nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)

**Standard dose:** One tablet (150 mg Epivir/3TC/lamivudine, 300 mg Retrovir/AZT/zidovudine), twice a day (12 hours apart), with or without food, and no food restrictions. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.

**AWP:** $937.66 / month

**Manufacturer contact:** ViiV Healthcare, 1 (877) 844-8872

**Potential side effects and toxicity:** Also see drug pages for Epivir (lamivudine, 3TC) and Retrovir (zidovudine, AZT) for more details. Myopathy (muscle damage), flare-up of hepatitis B upon stopping (due to the withdrawal of Epivir, which is contained in Combinvir) and hematologic (blood-related) toxicity including anemia and neutropenia. May be taken with food to decrease potential nausea associated with AZT. Rare but potentially serious toxicity with all NRTIs: enlarged, fatty liver (hepatomegaly with steatosis) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis may cause persistent fatigue, abdominal pain or distension, nausea/vomiting, difficulty breathing or shortness of breath, and enlarged, fatty liver.

**Potential drug interactions:** See the drugs contained in Combinvir—Epivir (lamivudine, 3TC), and Retrovir (zidovudine, AZT). Do not take zidovudine (Retrovir), Epivir, Epivir-HBV, Epzicom, Trizivir, Emtriva, Truvada, stavudine (Zerit), or Atripla while taking Combinvir, since all or part of these medications are already in Combinvir or have equivalent medications.

**Tips:** Combinvir is the combination of lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir) into one pill; see the pages of those individual drugs for more information. Combinvir has been shown in multiple clinical trials to be a potent regimen with either a protease inhibitor or an NNRTI. The zidovudine (AZT) in Combinvir can cause fatigue and anemia. One head-to-head study against Truvada found greater toxicity with Combinvir, due to anemia (see Retrovir). The warning on the anemia drugs Procrit and Epogen has not been linked to patients with HIV, although clinical data do not rule out a possible increased risk for cardiovascular events. The zidovudine/AZT in Combinvir is associated with lipoatrophy (fat loss of the arms, legs, face, and/or buttocks—sometimes called “AZT butt”). The lipoatrophy could be irreversible or take a long time to rebuild. Please see package insert for more complete potential side effects and interactions.

**Doctor**

Combinvir (combination AZT/3TC) was the first fixed dose combination antiretroviral therapy approved (1997) for HIV infection. By simplifying taking two tablets twice a day into just one tablet twice a day, it became one of the first demonstrations of the importance and enthusiasm for “fixed combinations.” As a result, it became widely used in combination with other antivirals at the time. However, there were several limitations that also became apparent over time. One was that it could not be successfully used when taken once daily, due to the short amount of time enough AZT would stay in the cells—not enough when it was dosed just once daily. Second was that AZT was increasingly associated with both initial and longer term side effects that were not shared by other treatment options. For example, fat loss, or “lipoatrophy” is more common when taking AZT when compared to what was seen when taking either abacavir or tenofovir, though AZT was at least better than d4T (Zerit) on this side effect. In addition, some data suggest that the lipoatrophy associated with three or more years of taking AZT is difficult to reverse even after switching to other safer antivirals. Thus, the popularity of this combination has declined and it is considered an “alternative” by the DHHS guidelines panel. However, it continues to be listed as “preferred” for women who are pregnant, given the extensive data for this drug in that setting, despite its association with nausea and anemia, both undesirable side effects for anyone, including pregnant women. —Cal Cohen, MD

**Activist**

The original fixed dose combination that started the craze for combining drugs. Effective and still widely used, it’s still the sum of its parts, so suffers from the anemia, fatigue, and lipoatrophy caused by its AZT component. These days there are better options for those who don’t want to take their meds twice a day, so it’s no longer a preferred medication in the Guidelines. But the positive central nervous system (CNS) penetration profile makes it valuable for those experiencing cognitive difficulties. It’s also the recommended backbone in regimens for pregnant women. —Jeff Taylor
Emtriva (emtricitabine, also known as FTC) was approved as a stand-alone antiretroviral for once-daily treatment of HIV infection in 2003, and in the fixed dose combinations Truvada (tenofovir/emtricitabine) in 2004, and Atripla (tenofovir/emtricitabine/ efavirenz) in 2006. This antiretroviral is chemically and clinically very similar to 3TC and thus is often considered interchangeable in any regimen in which 3TC is used. There are a few differences however, including a longer half-life for FTC, and data showing that FTC is modestly more active when studied as a single drug in short term studies. The importance of these attributes is not clear, but may be one reason why Truvada has shown more virologic activity than Epzicom in one large study of patients with a high viral load at baseline. In almost all settings, FTC is only used in one of the fixed dose combinations previously listed. While its use is often associated with long term successful virus suppression, it is one of the drugs in the regimen to which resistance is commonly observed if there is less than complete virus suppression. Resistance to FTC leads to cross resistance to 3TC as well. The expected FTC resistance mutation, referred to as M184V, slightly improves the antiretroviral activity of AZT and tenofovir, which leads some clinicians to maintain the use of these combinations even after resistance occurs. Also of interest is that this mutation causes HIV to be less “fit” than wild type, meaning that despite resistance development, HIV is still partially suppressed by about one-half log due to the impact of this M184V mutation. It is also active against hepatitis B virus, but like 3TC, its use alone is associated with the development of viral resistance by the hep B virus to the drug and should therefore only be used in combination with another agent, typically tenofovir as it is also active against hep B virus. FTC is very well tolerated. Early clinical trials reported an infrequent association with discoloration of the skin and nails, but this has not been a toxicity associated with the use of the combination “Atripla” nor Truvada to any important extent. Like 3TC, FTC needs to be dose adjusted in those with significantly decreased kidney function. —Cal Cohen, MD

**ACTIVIST**

Emtriva (FTC) is Gilead’s version of 3TC for combining with Viread in their combo drugs Truvada and Atripla (Emtriva+Viread+Sustiva). It has the same favorable resistance profile as 3TC—making it part of a good nuke backbone for many regimens. Like 3TC, it has activity against the hepatitis B virus, so those with hep B should consult with their doctors before using this drug so they don’t unwittingly develop resistance to a potentially useful HBV drug. —Jeff Taylor
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: lamivudine or 3TC
Brand Name: Epivir
Class: nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)
Standard Dose: One 300 mg tablet once a day (or one 150 mg tablet twice daily), with or without food, and no food restrictions. Dose is lowered for people with kidney impairment. Dose for children 3 months to 16 years of age is 4 mg per 2.2 pounds twice daily to a maximum of 150 mg twice daily. A strawberry/banana-flavored liquid is available. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.

AWP: $432.16 / month for 300 mg tablets, $115.33/ month for 240 ml bottle

Manufacturer Contact: ViiV Healthcare, 1 (877) 844-8872

Potential Side Effects and Toxicity: This remains one of the most easily tolerated HIV medications. Side effects (rarely seen) may include headache, nausea, vomiting, diarrhea, fever, fatigue, hair loss, insomnia, malaise (general ill feeling), nasal symptoms, cough, peripheral neuropathy, low white blood cells, and anemia.

Rare but potentially serious toxicity with all NRTIs: enlarged, fatty liver (hepatomegaly with steatosis) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis may cause persistent fatigue, abdominal pain or distension, nausea/vomiting, difficulty breathing or shortness of breath, and enlarged, fatty liver.

Potential Drug Interactions: No significant drug interactions. Do not take Epzicom, CombiVir, Trizivir, Truvada, Atripla, Emtriva, or Epivir-HBV while taking Epivir, since they contain Epivir or medication equivalent to Epivir.

Tips: Exciting benefit: drug resistance that the virus develops against Epivir—the M184V mutation—makes the virus less fit to replicate and has even been shown to keep T-cells from dropping during a treatment interruption as much as they would have otherwise. It is also approved for treatment of hepatitis B virus (HBV), under the brand name Epivir-HBV. Patients co-infected with HIV/HBV should use Epivir with Viread as their nucleoside backbone to increase activity and avoid HBV resistance. If you have hepatitis B and HIV, this drug works for both diseases, but make sure you are taking Epivir at HIV doses—always ask your doctor or pharmacist.

Worsening of hepatitis B (HBV) in people co-infected with HIV/HBV has occurred when Epivir was discontinued. These patients should be closely monitored by their physician. Epivir is also available combined with Retrovir (zidovudine, AZT), called CombiVir (one tablet twice a day); in a once-daily formula with Ziagen (Epzicom, one tablet daily); and in a triple combination with both Retrovir and Ziagen (Trizivir, one tablet twice a day). Please see package insert for more complete potential side effects and interactions.

Doctor

Epivir (lamivudine, known also as 3TC) was among the first antivirals to be widely used in the regimens containing only two nucleosides that were common just before the current “HAART” or three-drug era started in the late 1990s. Lamivudine was approved by the FDA in 1995 for twice-daily dosing and again in 2002 for once-daily dosing as studies showed similar responses with once-daily use when given in combination with two other antivirals. It is a component of the fixed dose combinations CombiVir, Trizivir, and Epzicom. Epivir is also approved for hepatitis B infection, but should not be used as a single drug for that virus either, as resistance will typically occur rendering this drug and others less active as a result. Lamivudine, or a closely related antiviral emtricitabine [Emtriva], forms the nucleoside backbone for nearly all HAART regimens since the HAART era began. While its use is often associated with long term successful virus suppression, it is one of the drugs in the regimen to which resistance is commonly observed if there is less than complete virus suppression. Resistance to 3TC leads to cross resistance to FTC as well. The expected 3TC resistance mutation, referred to as M184V, slightly improves the antiretroviral activity of AZT and tenofovir, which leads some clinicians to maintain the use of these combinations even after resistance occurs. Also of interest is that this mutation causes HIV to be less “fit” than wild type, meaning that despite resistance development, HIV is still partially suppressed by about one-half log due to the impact of this M184V mutation. It is very well tolerated by nearly all who take it with only rare reports of drug toxicity. It must be dose adjusted in individuals who have reduced kidney function. Overall, the generally favorable tolerability of 3TC has historically made it a commonly used drug, though its use is typically linked to the fixed dose combinations containing either abacavir or AZT. One other issue is that this drug will be “generic” sometime in 2010, but the impact of this change on insurance coverage for HIV treatment is not yet clear. —Cal Cohen, MD

Activist

An easy to tolerate twice-daily drug, it quickly develops the M184V resistance mutation. Paradoxically, this makes HIV more susceptible to AZT which is why it’s usually used in combo drugs like CombiVir (AZT+3TC), Epzicom (abacavir+3TC), or Trizivir (AZT+abacavir+3TC). It also has activity against hepatitis B virus—so those with hep B should check with their doctors before going on Epivir to avoid potential resistance to a drug for HBV. —Jeff Taylor
difficulty breathing, and sore throat); and possible rash. Symptoms warning card with you. Hypersensitivity might be confused with flu stopped because of this serious reaction, you can never take Ziagen, are already in Epzicom or have equivalent medications. Some observational studies seemed to indicate that abacavir may during flu season, but remember that HSR worsens with every dose. If treatment is usually worsen, very slowly, with every dose. If treatment is stopped because of this serious reaction, you can never take Ziagen, Trizivir, or Epzicom again (called “re-challenging”) because of life-threatening, and, in a few instances, fatal reaction. (This does not apply to missed doses when there’s no HSR, but watch for symptoms if you’ve stopped the drug for at least a few days). Symptoms usually, but not always, include some combination of sudden fever; muscle ache; malaise (general ill feeling); severe nausea, vomiting, diarrhea, or abdominal pain; severe tiredness; respiratory symptoms (cough, difficulty breathing, and sore throat); and possible rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. Hypersensitivity might be confused with flu during flu season, but remember that HSR worsens with every dose. Some observational studies seemed to indicate that abacavir may increase the risk of cardiovascular events, including heart attacks, in people with greater risk factors (such as smoking, diabetes, high blood pressure, and drug use), and is reversible upon discontinuation. Studies looking into this possible association had mixed results (see interview with Dr. Cal Cohen on page 56). One explanation for the unexpected link was a finding that people with kidney problems were put on Ziagen in order to avoid its primary competitor, Viread, which has the potential for kidney toxicity. These individuals already have a strong risk for cardiovascular disease. The available data regarding cardiovascular risk with abacavir remains inconclusive.

Potential drug interactions: See also the drugs contained in Epzicom, Epivir and Ziagen, for more information. Do not take Combivir, Epivir, Epivir-HBV, Trizivir, Ziagen, Emtriva, Truvada, or Atripla while taking Epzicom, since all or part of these medications are already in Epzicom or have equivalent medications.

Tips: Remember, Epzicom is two drugs in one pill, so see the pages for those drugs, Epivir, Epivir-HBV and Ziagen. Currently, U.S. HIV treatment guidelines recommend Truvada over Epzicom as a preferred agent for the NRTI component of a treatment regimen. Epzicom is listed as an alternative NRTI backbone due to the aforementioned potential cardiac risks. See Ziagen for more details. Also, with publication last year of preliminary results from a study of 2,000 participants, ACTG 5202, Epzicom has lost its battle—for now—against its main competitor, Truvada. The study team reported that while both medications reduced viral load, for those people who started treatment with more than 100,000 viral load, Epzicom was “significantly less effective at controlling HIV” in the regimens tested. Moreover, time to a serious adverse event was sooner in the people taking Epzicom. These efficacy and safety findings were not confirmed in a manufacturer-sponsored study, HEAT, another large study (700 participants) comparing Epzicom and Truvada. Still, in HIV therapy, there’s always use for an alternative choice of drugs and the DHHS guidelines state, “Pending additional data, [Epzicom] should be used with caution in individuals who have plasma HIV RNA [viral load] greater than 100,000 copies/mL, as well as in persons at higher risk for cardiovascular disease. However, [Epzicom] remains a good alternative dual-NRTI option for some treatment-naïve patients.” Remember, too, that Truvada has its own side effect and drug interaction issues, although it’s famed for its tolerability. Ziagen by itself is FDA approved for either once-daily or twice-daily dosing. The once-daily formula in Epzicom was found to leave the same amount of Ziagen in the blood over 24 hours (bioequivalence) as Ziagen twice a day. The test should never be used to diagnose HSR. Do not use a skin patch test to confirm HSR. Regardless of the results, it is important to monitor the potential for this reaction. If HSR is suspected or cannot be ruled out, abacavir products should be discontinued. Check with your doctor if you have any side effects after taking this medicine—don’t just stop! The incidence of HSR was the same between Epzicom once-daily and Ziagen twice-daily (8% vs. 9%), but the incidence of severe reactions was higher with Epzicom (5% vs. 2%). Remember that the HSR cited may have been suspected, not definitely diagnosed. Please see package insert for more complete potential side effects and interactions.

Doctor

Epzicom (fixed dose 3TC/abacavir) was approved for once-daily dosing in the treatment of HIV in 2004. This fixed dose combination is usually well tolerated, and has no food restrictions. While there was initial enthusiasm and study of this drug, both for initiating treatment and for simplification for patients already on suppressive treatment, there are a few factors that have limited its use and contribute to why this combination is no longer considered “preferred” by the 2009 DHHS guidelines. It is also critical to recall that since Epzicom contains abacavir, this combination must not be given to an individual who has had an abacavir hypersensitivity reaction (HSR—see Ziagen). An HLA-B*5701 genetic test should be done prior to use of Epzicom in an individual who has never had the drug abacavir as this test does an excellent job of predicting likelihood of the HSR reaction. If an individual has significant kidney and/or liver problems, fixed dose Epzicom is not recommended for use. The most recent studies of Epzicom demonstrated a greater risk of virologic failure versus what is seen with the use of Truvada in those individuals starting treatment with viral loads of greater than 100,000 copies/mL. In addition, there were more side effects reported with this drug versus Truvada in that ACTG study. Recently, guideline panels have commented on data seen in several, but not all, studies about an increased risk of cardiovascular disease—specifically heart attacks, when using an abacavir-containing regimen as compared to what is seen when patients are on most other nucleosides. Finally, there are data raising a question about the interaction of abacavir and ribavirin, a drug that is currently essential for the treatment of hep C, and this has led to some reluctance to use abacavir-containing regimens in someone being treated for hep C. Collectively, these concerns—reduced virologic activity, additional toxicity issues, and drug interactions—have led this agent to be considered primarily for patients in whom Truvada is not considered reasonable for whatever reason. —Cal Cohen, MD

Activist

This convenient once-a-day pill was once considered a major improvement over Combivir. The abacavir in Epzicom, with its potential for hypersensitivity, and now, possible cardiac risks (see Ziagen), makes Epzicom less popular than it once was now that there are other options available. —Jeff Taylor
**NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR**

**Common Name:** zidovudine or AZT  
**Brand Name:** Retrovir

**Class:** nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)  
**Standard Dose:** One 300 mg tablet twice a day (12 hours apart); two 100 mg capsules three times a day also available, with or without food, and no food restrictions. Clear, strawberry-flavored liquid available for infants four weeks of age and up; dose is weight-based. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose. Generic is available.

**AWP:** $505.31 (generic $365.09) / month for 300 mg tablets, $67.37 (generic $56.42) for 240 ml syrup  
**Manufacturer Contact:** ViiV Healthcare, 1 (877) 844-8872

**Potential Side Effects and Toxicity:** May include headaches, fever, chills, muscle soreness, fatigue, nausea, and fingernail discoloration. Zidovudine (AZT) has been associated with alteration of various cells in the blood through bone marrow suppression, resulting in anemia (low red blood cell counts) and/or neutropenia (low white blood cell counts), particularly during the first three months of therapy in people with advanced HIV. Potential exists for severe anemia requiring blood transfusion, erythropoietin injections, or hospitalization when used on its own or in combination with hydroxyurea. Rare but potentially serious toxicity with all NRTIs: enlarged fatty liver (hepatomegaly with steatosis) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis may cause persistent fatigue, abdominal pain or distension, nausea/vomiting, difficulty breathing or shortness of breath, and enlarged, fatty liver.

**Potential Drug Interactions:** Biaxin and rifampin (under various brand names) may decrease zidovudine blood levels. Benemid (probenecid), Dilantin (phenytoin), and Depakote (valproic acid) may increase zidovudine blood levels and decrease zidovudine clearance, but no dosing adjustments are recommended. Zidovudine and Zerit should not be used together due to evidence that one limits the other’s effectiveness. Also, bone marrow suppression should be monitored with use of Cytovene (ganciclovir), Valcyte, amphotericin B, pentamidine, dapsone, flucytosine, sulfadiazine, interferon-alpha, ribavirin (Rebetol), and with cancer treatments such as hydroxyurea and doxorubicin. Ribavirin and zidovudine may cancel each other out, so this combination should be monitored closely. New Procrit or Epogen warning: if hemoglobin target is above manufacturer’s recommendation (12 g/dL), the risk for serious and life-threatening cardiovascular complications significantly increases. For zidovudine patients, measure hemoglobin once a week after starting the anemia drugs until hemoglobin has stabilized. Notify health care provider if experiencing pain and/or swelling in the legs, worsening in shortness of breath, increases in blood pressure, dizziness or loss of consciousness, extreme tiredness, or blood clots in hemodialysis vascular access ports. Do not take with Combivir or Trizivir, since zidovudine is already in these medications.

**Tips:** The not-so-good news for people adding zidovudine: the fatigue and the potential anemia. You can start taking erythropoietin (Procrit or Epogen) for some anemias, but that’s adding an expensive weekly injectable. Some doctors would prefer switching out the zidovudine for another drug. Zidovudine/AZT is associated with lipoatrophy (fat loss of the arms, legs, face, and/or buttocks—sometimes called “AZT butt”). The lipoatrophy could be irreversible or take a long time to rebuild. Taking with food may minimize upset stomach. Please see package insert for more complete potential side effects and interactions.

**Doctor**

Retrovir (zidovudine, known to most as AZT, with a generic form available in the U.S.) was the first antiretroviral developed and has had a significant impact on the course of HIV infection. Historically, AZT development has served as an example of a highly successful government and industry partnership to combat a lethal disease. AZT is now primarily used in the fixed dose combinations Combivir or Trizivir. Since the approval of other more convenient and safer antiretrovirals, the use of AZT in HAART therapy has decreased significantly. There is one time when AZT is still considered “preferred” which is for a pregnant woman during her pregnancy—this is the recommendation of guideline panels who have reviewed all of the amount of information that is available about this drug in that setting. —Cal Cohen, MD

**Activist**

The original, and much maligned, AZT continues to be a widely used and well tolerated drug for many—though it’s no longer included in the recommended regimens on the guidelines. Despite the potential anemia, fatigue, and lipoatrophy, its penetration into the central nervous system makes it very useful for those suffering from dementia and other cognitive problems. —Jeff Taylor
Common Name: abacavir sulfate, zidovudine, and lamivudine
Brand Name: Trizivir
Class: fixed dose combination—nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)
Standard dose: One tablet (300 mg Ziden/ABC/abacavir, 150 mg Epivir/3TC/lamivudine, and 300 mg Retrovir/zidovudine/AZT), twice a day, with or without food, and no food restrictions. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.
AWP: $1,518.76 / month
Manufacturer contact: ViiV Healthcare, 1 (877) 844-8872

Potential side effects and toxicity: The most common side effects of Trizivir are the same as those of the drugs it contains—see Epivir, Retrovir, and Ziden. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir; see Ziden. A simple and inexpensive blood test for HLA-B*5701 can identify people at high risk for this reaction and virtually eliminate HSR. Symptoms worsen, very slowly, with every dose. If treatment is stopped because of this serious reaction, never take Ziden, Trizivir, or Epizomic (Epivir, Retrovir, zidovudine/AZT) again (called “re-challenging”) because of lifethreatening and, in a few instances, fatal reaction. (This does not apply to missed doses when there’s no HSR, but watch for symptoms if you’ve stopped the drug for at least a few days). Symptoms usually, but not always, include some combination of sudden fever; muscle ache; severe nausea, vomiting, diarrhea, or abdominal pain; severe tiredness; respiratory symptoms (cough, difficulty breathing, and sore throat); and possibly rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. Hypersensitivity might be confused with flu during flu season, but Hypersensitivity might be confused with flu during flu season, but

Potential drug interactions: See also the drugs contained in Trizivir—Epivir, Retrovir (zidovudine, AZT), and Ziden, for more information. Do not take Retrovir (zidovudine), Epivir, Epivir-HBV, Ziden, Epizomic, Emtriva, Truvada, or Atripla while taking Trizivir, since all or part of these medications are already in Trizivir or have equivalent medications. If you are taking one of the following medications, consult your doctor or pharmacist before starting Trizivir: Zerit, ribavirin, interferon, rifampin, probenecid, methadone, Cytoxene (ganciclovir), Valcyte (valganclovir), Biaxin (clarithromycin), Daraprim (pyrimethamine), flucytosine, Fungizone (amphotericin B), doxorubicin, and hydroxyurea.

Tips: See the drugs contained in Trizivir—Epivir, Retrovir (zidovudine, AZT), and Ziden. Trizivir is the only triple combination NRTI that has been studied in a randomized, controlled study, but this has shown it to be inferior to the standard treatment of two NRTIs plus an NNRTI. U.S. treatment guidelines recommend that Trizivir should only be used if other options are not possible due to toxicities or drug interactions associated with other HIV regimens. The zidovudine/AZT in Trizivir is associated with lipoprotein-

Pharmacy

Drug

Potential side effects and toxicity: The most common side effects of Trizivir are the same as those of the drugs it contains—see Epivir, Retrovir, and Ziden. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir; see Ziden. A simple and inexpensive blood test for HLA-B*5701 can identify people at high risk for this reaction and virtually eliminate HSR. Symptoms worsen, very slowly, with every dose. If treatment is stopped because of this serious reaction, never take Ziden, Trizivir, or Epizomic (Epivir, Retrovir, zidovudine/AZT) again (called “re-challenging”) because of lifethreatening and, in a few instances, fatal reaction. (This does not apply to missed doses when there’s no HSR, but watch for symptoms if you’ve stopped the drug for at least a few days). Symptoms usually, but not always, include some combination of sudden fever; muscle ache; severe nausea, vomiting, diarrhea, or abdominal pain; severe tiredness; respiratory symptoms (cough, difficulty breathing, and sore throat); and possibly rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. Hypersensitivity might be confused with flu during flu season, but

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Potential drug interactions: See also the drugs contained in Trizivir—Epivir, Retrovir (zidovudine, AZT), and Ziden, for more information. Do not take Retrovir (zidovudine), Epivir, Epivir-HBV, Ziden, Epizomic, Emtriva, Truvada, or Atripla while taking Trizivir, since all or part of these medications are already in Trizivir or have equivalent medications. If you are taking one of the following medications, consult your doctor or pharmacist before starting Trizivir: Zerit, ribavirin, interferon, rifampin, probenecid, methadone, Cytoxene (ganciclovir), Valcyte (valganclovir), Biaxin (clarithromycin), Daraprim (pyrimethamine), flucytosine, Fungizone (amphotericin B), doxorubicin, and hydroxyurea.

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**NUCLEOSIDE / NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITOR**

**Common Name:** emtricitabine and tenofovir DF  
**Brand Name:** Truvada  
**Class:** fixed dose combination—nucleoside/nucleotide analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)  
**Standard Dose:** One tablet (300 mg Viread and 200 mg Emtriva) once a day, with or without food, and no food restrictions. Dosing frequency needs to be adjusted for people with decreased kidney function. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.  
**AWP:** $1,118 / month  
**Manufacturer contact:** Gilead Sciences, Inc.  
www.gilead.com, 1 (800) GILEAD5 (445–3235)  

**Potential side effects and toxicity:** See the drugs contained in Truvada—Viread and Emtriva. Do not take with Emtriva, Viread, Atripla, Epivir, Epivir-HBV, Combidir, Epzicom, or Trizivir, since all or part of these medications are already in Truvada or have equivalent medications. The levels of Videx EC and Videx (didanosine, ddI) are increased by 44–60% when taken at the same time as Viread, which is in Truvada. Therefore, a dose reduction to 250 mg for Videx EC is recommended for people who weigh more than 132 pounds and 200 mg for those who weigh less than this. Higher Videx (ddI) concentrations could increase the risk of ddI-associated adverse events, including neuropathy. See tips. Viread decreases the concentration levels of Reyataz. In addition, Reyataz and Kaletra increase Viread concentrations. The reason for these interactions is unknown. The FDA suggests that patients receiving Reyataz and Truvada should be monitored for Truvada-associated adverse events. When taken with Truvada, it is recommended that Reyataz 300 mg is taken with Norvir 100 mg (all as a single daily dose with food). Reyataz without Norvir should not be taken with Truvada.  

**Potential drug interactions:** See the drugs contained in Truvada—Viread and Emtriva. Do not take with Emtriva, Viread, Atripla, Epivir, Epivir-HBV, Combidir, Epzicom, or Trizivir, since all or part of these medications are already in Truvada or have equivalent medications. The levels of Videx EC and Videx (didanosine, ddI) are increased by 44–60% when taken at the same time as Viread, which is in Truvada. Therefore, a dose reduction to 250 mg for Videx EC is recommended for people who weigh more than 132 pounds and 200 mg for those who weigh less than this. Higher Videx (ddI) concentrations could increase the risk of ddI-associated adverse events, including neuropathy. See tips. Viread decreases the concentration levels of Reyataz. In addition, Reyataz and Kaletra increase Viread concentrations. The reason for these interactions is unknown. The FDA suggests that patients receiving Reyataz and Truvada should be monitored for Truvada-associated adverse events. When taken with Truvada, it is recommended that Reyataz 300 mg is taken with Norvir 100 mg (all as a single daily dose with food). Reyataz without Norvir should not be taken with Truvada.  

**Tips:** Remember, Truvada is two medicines in one pill, so see the pages for those medications, Emtriva and Viread. Currently, U.S. DHHS HIV treatment guidelines recommend Truvada over Epzicom as the only preferred medication for the NRTI component of an HIV regimen. With publication last year of results from study of 2,000 participants, ACTG 5202, Truvada has won the battle against its main competitor, Epzicom. The study team reported that while both medications reduced viral load, for those people who started treatment with a viral load of more than 100,000, Epzicom was “significantly less effective at controlling HIV” in the regimens tested. Moreover, time to a serious adverse event was sooner in the people taking Epzicom. Remember, however, that Truvada has its own side effect and drug interaction issues, although it’s famed for its tolerability. Kidney function must be monitored before and during treatment with Truvada and it may not be a good option for patients with underlying kidney problems. Truvada combines with Sustiva to form Atripla, a very popular HIV regimen. Now there’s another triple regimen in one pill in the works. Last year Gilead announced an agreement to combine Truvada with another non-nucleoside (the same drug class as Sustiva), the experimental TMC 278 (rilpivirine) from Tibotec Therapeutics, maker of Prezista and Intellence. Please see package insert for more complete potential side effects and interactions.

**Activist**

The most popular fixed dose combination in use now, this combination of Viread and Emtriva has proven durable and long-lasting—earning it a place on the treatment guidelines preferred regimen backbones. And like the other combos, combining the drugs extends their patent life for the company—an added incentive beyond the convenience of single-pill dosing for patients. The same caveats about possible kidney toxicities and hepatitis B apply because of its Viread component. —Jeff Taylor
Also, ganciclovir substantially increases Videx levels, and is generally recommended not to be taken together. If there is no alternative to ganciclovir, use it with caution and monitor for Videx toxicity. Videx oral solution should be taken on an empty stomach one hour before or two hours after protease inhibitors, Tagamet (cimetidine), ketoconazole, itraconazole, and dapsone, and one hour apart from Rescriptor, while Videx EC can be taken with them, but still on an empty stomach. With Viread, it may be taken with a light snack (low-fat, 375 calories). Methadone decreases Videx powder concentrations significantly and should not be used together, but if necessary, the Videx EC formulation should be used.
NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITOR

**Common Name:** tenofovir disoproxil fumarate  
**Brand Name:** Viread  
**Class:** nucleotide analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)  
**Standard Dose:** One 300 mg tablet once a day, with or without food. No food restrictions. Dosing frequency needs to be adjusted for people with decreased kidney function. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.  
**AWP:** $771.54 / month  
**Manufacturer Contact:** Gilead Sciences, Inc., www.viread.com, 1 (800) GILEAD5 (445–3235)

**Potential side effects and toxicity:** Overall, fairly well tolerated; however, individuals may experience diarrhea, nausea, vomiting, and gas as the most common side effects of Viread. Decreases in bone mineral density (BMD) have been observed with the use of Viread in HIV-positive people. BMD monitoring should be considered in people who have a history of pathologic bone fracture or are at risk for osteopenia. Creatinine clearance (CrCl) should be assessed before initiating treatment with Viread. CrCl and serum phosphorus should be monitored in patients at risk. Less common side effects of Viread, occurring with undetermined incidence, include kidney toxicities and low blood phosphate. Rare but potentially serious toxicity with all NRTIs: enlarged, fatty liver (hepatomegaly with steatosis) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis may cause persistent fatigue, abdominal pain or distension, nausea/vomiting, difficulty breathing or shortness of breath, and enlarged, fatty liver.  

The effect of Viread on children and individuals with severe liver impairment was not studied during drug development. However, since Viread is not metabolized by the liver (and appears to have less toxicity in the liver than the majority of the NRTIs), it is believed the impact on individuals with liver disease should be minimal.  

**Potential drug interactions:** Videx levels are increased with Viread (a drug also found in Truvada and Atripla); therefore, use with caution and monitor closely when taking Viread, Truvada, or Atripla with Videx or Videx EC to avoid Videx-related toxicity, including neuropathy. See tips. Viread decreases the concentration of Reyataz. In addition, both Reyataz and Kaletra increase Viread concentrations. Higher Viread concentrations could increase the risk of Viread-associated adverse events, including kidney disorders. Patients receiving Reyataz and Viread should be monitored for Viread-associated adverse events. When taken with Viread, it is recommended that Reyataz 300 mg is given with Norvir 100 mg (all as a single daily dose with food). Unboosted Reyataz (without Norvir) should not be taken with Viread. No dosage adjustment is needed when used with Kaletra. Do not take with Truvada or Atripla, since Viread is in these medications. You should not take Viread with Hepsera, a Hepatitis B treatment.  

**Tips:** Viread combined with Emtriva (also available as Truvada) is considered the preferred NRTI combination by U.S. HIV treatment guidelines. Viread is also combined with Emtriva and Sustiva (NNRTI) to make up Atripla, the first single-tablet HIV regimen. The body clears most of Viread through the kidneys and dosing adjustment is recommended for those with impaired kidney function. Serious kidney problems have been rare and most have been in those with pre-existing kidney disease or receiving kidney-toxic drugs. However, the characteristics of kidney toxicity are still being defined. The manufacturer recommends that individuals with impaired kidney function be monitored closely, especially people with advanced HIV disease, even in those who did not start out with kidney disease. There have been reports of individuals who experienced severe kidney disorder, including some taking Kaletra with Viread. Since Kaletra increases blood levels of Viread, it may increase the likelihood of Viread side effects.

According to the DHHS guidelines, the combination of Viread and Videx is not recommended as initial therapy due to high rates of early virologic failure, rapid selection of resistant mutations (K65R), and potential for immunologic non-response (CD4 decline).

Like Epivir and Emtriva, Viread has activity against hepatitis B, which may flare up when Viread is discontinued. These patients should be closely monitored by their physician. Patients co-infected with HIV/HBV should use Epivir or Emtriva with Viread as their nucleoside backbone to increase activity and avoid HBV resistance. Viread may have prolonged activity against hepatitis B even when resistant to Epivir. Please see package insert for more complete potential side effects and interactions.

**Doctor**

Viread (tenofovir, also known as TDF) was approved (with once-daily dosing) by the FDA in 2001 for the treatment of HIV and in 2008 for the treatment of chronic hepatitis B. Also available are once-daily fixed dose combinations of emtricitabine and tenofovir (Truvada) and tenofovir, emtricitabine, and efavirenz (Atripla). In studies comparing tenofovir to other choices, there are many factors which have led tenofovir (in combination with FTC) to be listed as preferred versus all other choices by the DHHS 2009 guidelines, including better virologic response rates, and fewer side effects issues versus other antivirals. However, as with any drug, there are a few factors to be aware of when tenofovir is used. As tenofovir is cleared by the kidneys, it is important when starting on this drug to have regular monitoring of kidney function with standard lab tests—about 1 or 2% of people starting tenofovir experience important declines in kidney function that are reversed when promptly stopping this drug. Also, in someone with markedly reduced renal function, Truvada must be dose reduced. In addition, when tenofovir is used with Reyataz, Norvir must be added to the HAART regimen to compensate for the effect that tenofovir has on lowering blood levels of reyataz. Finally, there is a 1% difference of more bone loss in some, but not all, measures during the first year on tenofovir versus what’s seen with some other antivirals—after one year this difference stabilizes. The clinical relevance of this 1% difference is still not clear. —Cal Cohen, MD

**Activist**

The preferred backbone of many regimens, Viread has much to recommend it with its once-daily dosing and few side effects. But given the potential for kidney toxicity, and that this is the kind of drug people may stay on for decades, patients and their doctors should be vigilant about kidney problems and concomitant meds that may cause them. The only side effect most patients might notice is stomach gas. Viread, like Epivir, has some activity against hepatitis B, so those with hep B should consult with their doctors before starting this drug. —Jeff Taylor
**NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR**

**Common Name:** stavudine or d4T  
**Brand Name:** Zerit  
**Class:** nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)  
**Standard dose:** One 40 mg capsule twice a day for people weighing 132 pounds or more, or one 30 mg capsule twice a day for people weighing less; with or without food, and no food restrictions. Zerit is also available in 15 mg, 20 mg, 30 mg and 40 mg capsules and a powder for oral solution; check for food restrictions. Dose reduction needed in people with kidney problems. Generic now available. Take missed dose as soon as possible, unless it is almost time for your next dose.

**AWP:** $456.16 (generic $411.16) / month for 40 mg capsules  
**Manufacturer Contact:** Bristol-Myers Squibb, www.bmsvirology.com, 1 (800) 272–4878

**Potential side effects and toxicity:** Peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet) may go away once Zerit is stopped, but can be painful and permanently debilitating if not treated in time. Caregivers of young children should be instructed regarding noticing and reporting peripheral neuropathy. Additive lipoatrophy (facial wasting) and mitochondrial toxicities can occur when combined with Videx. Adverse reactions and serious laboratory abnormalities in children were similar in type and frequency to those seen in adults. Other side effects may include headache, chills/fever, malaise (general ill feeling), insomnia, anxiety, depression, rash, upset stomach (nausea and vomiting), diarrhea, and abdominal pain. Rare but potentially serious toxicity with all NRTIs: enlarged, fatty liver (hepatomegaly with steatosis) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis may cause persistent fatigue, abdominal pain or distension, nausea/vomiting, difficulty breathing or shortness of breath, and enlarged, fatty liver. Pancreatitis (inflammation of the pancreas) can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting, and blood in the urine. Risks for pancreatitis include higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Stop all HIV medications and see a health care provider right away. Your physician will check for pancreatitis by doing blood tests. People with a history of peripheral neuropathy, pancreatitis, or heavy alcohol use should avoid Zerit. Lipoatrophy, fat loss in the face and limbs (arms and legs) and, to a lesser degree, lipo hypertrophy (such as “buffalo hump” and increase in abdominal girth) has been associated with Zerit. Zerit and Retrovir (zidovudine, AZT) are the HIV drugs most implicated by studies as causing lipoatrophy. Zerit also seems to be implicated in blood lipid (fat) increases, particularly triglycerides.

**Potential drug interactions:** When used in combination with Zerit, drugs such as Fungizone (amphotericin B), Foscavir (foscarnet), dapsone, and some drugs used to treat HIV may increase the risk of developing peripheral neuropathy. Cytovene (ganciclovir), valganciclovir (Valcyte), intravenous Pentam (pentamidine), and Videx (ddI) may increase the risk of pancreatitis. Should be used with caution by people with pre-existing bone marrow suppression, kidney problems, or peripheral neuropathy. Retrovir (zidovudine, AZT) and Zerit should not be used together due to evidence that one limits the other’s effectiveness. Because of additive neurotoxicity, if possible, Zerit should not be combined with Videx.

**Tips:** Zerit is rarely used in the U.S., due to its toxicity and the availability of newer medications. Contact your health care provider right away if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your health care provider. Studies show that Zerit crosses the blood-brain barrier to a useful degree, which may be beneficial for patients at risk for neurological damage (such as dementia) from HIV. Zerit is associated with facial wasting, peripheral neuropathy, and pancreatitis, and many leading HIV advocates are adamant that it should be avoided because of these serious, and relatively common, toxicities. Please see package insert for more complete potential side effects and interactions.

**DOCTOR**

Zerit (stavudine, known to most as d4T) was the fourth antiretroviral developed and was approved for use in HIV treatment in 1994. This drug was a very effective antiretroviral, but after years of use, the adverse events associated with the drug virtually stopped the prescription of d4T as part of HAART therapy. These side effects are mainly the cause for the worst rate of fat loss called “lipoatrophy,” most often noted in the face, arms, and legs. There is ongoing concern about the use of this agent in international resource-poor settings due to the low cost availability of this drug. Nevertheless, the side effect profile has led to a widespread avoidance of this drug when affordable alternatives exist. —Cal Cohen, MD

**ACTIVIST**

Once a backbone of many successful regimens, the crippling neuropathy, followed by lipoatrophy (fat loss—especially in the face and buttocks) have knocked this drug off the preferred list for good reasons. It is truly shameful that this drug continues to be one of the most widely used drugs in resource-poor settings outside of the U.S.—exporting preventable drug toxicities to the poor, when better drugs are available but cost more. —Jeff Taylor
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: abacavir sulfate
Brand Name: Ziagen
Class: nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs, or nukes)

Standard dose: Two 300 mg tablets once a day (or one 300 mg tablet twice a day), with or without food, and no food restrictions; new scored tablets available for children. A strawberry/banana flavored liquid is available (20mg/ml).

Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.

AWP: $581.10 / month, $152.77 for 240 ml bottle

Potential side effects and toxicity: Approximately 5–8% of people taking abacavir experienced hypersensitivity reaction (HSR, an allergic-like reaction). A simple and inexpensive blood test for HLA-B*5701 can identify patients at high risk for this reaction and virtually eliminate HSR. About 90% of HSR occurs within the first six weeks of treatment. Symptoms of HSR usually worsen, very slowly, with every dose. People who think they are experiencing HSR must be evaluated by an experienced HIV provider right away before they stop taking abacavir. Symptoms resolve quickly (24–48 hours) after permanent discontinuation. If treatment is stopped because of this serious reaction, you can never take Ziagen, Epzicom, or Trizivir again (called “re-challenging”) because of life-threatening and, in a few instances, fatal reaction. (This does not apply to missed doses when there’s no HSR, but watch for symptoms if you’ve stopped the drug for at least a few days). Symptoms usually, but not always, include some combination of sudden fever; muscle ache; malaise (general ill feeling); severe nausea, vomiting, diarrhea, or abdominal pain; severe tiredness; respiratory symptoms (cough, difficulty breathing, and sore throat); and possible rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. HSR might be confused with flu during flu season, but remember that HSR worsens with every dose. See your doctor if you have them, until a clearer picture emerges on possible cardiac risks of this drug. —Jeff Taylor

Potential drug interactions: Excessive alcohol increases Ziagen levels and may increase side effects. Do not take with Epzicom or Trizivir, since Ziagen is already in these medications.

Tips: The U.S. HIV treatment guidelines now state, “Pending additional data, [Epzicom] should be used with caution in individuals who have plasma HIV RNA [viral load] greater than 100,000 copies/mL, as well as in persons at higher risk for cardiovascular disease.” The manufacturer recommends that people with symptoms of acute respiratory disease consider HSR even if another diagnosis such as pneumonia, bronchitis, or flu is possible. Do not use a skin patch test to confirm HSR. Check with your doctor if you have any side effects after taking this medicine—don’t just stop! Dose adjustment needed in people with moderate liver disease. Avoid Ziagen in people with severe liver disease. Please see package insert for more complete potential side effects and interactions.

Doctor

Ziagen (abacavir), first developed as a twice-daily drug, was later approved as a once-daily agent (2004) and in the fixed dose combinations Trizivir (3TC/AZT/abacavir in 2000) and Epzicom (3TC/abacavir in 2004). Abacavir rapidly became an easy to take and popular component of HAART therapy. It had also achieved favorable use due to studies showing rates of lipoatrophy that were similar to tenofovir, and lower than either AZT or d4T. However, there are a few factors which have to be considered for this drug. One is that abacavir must not be given to an individual who has a positive HLA-B*5701 test, as this test predicts who is likely to experience a “hypersensitivity reaction.” Moreover, restarting abacavir in someone who had the HSR reaction can be fatal, leading to the importance of understanding this syndrome when considering this drug. If an individual has significant liver problems, abacavir is not recommended for use. The most recent studies of Epzicom demonstrate a greater risk of virologic failure versus what is seen with the use of Truvada in those individuals starting treatment with viral loads of greater than 100,000 copies/ml. In addition, there were more side effects reported with this drug versus Truvada in that ACTG study. Recent guideline panels have uniformly commented on the data seen in several, though not all, large studies about an increased risk of cardiovascular disease (heart attacks or an MI) when using an abacavir-containing regimen versus what is seen with most of drugs in this class. Finally, there are data raising a question about the interaction of abacavir and ribavirin, a drug that is currently essential for the treatment of hep C and this has led to some reluctance to use abacavir-containing regimens in someone being treated for hep C. Thus, these concerns—reduced virologic activity as well as additional toxicity issues—have collectively led this agent to be considered primarily for patients in whom Truvada is not considered a better choice. —Cal Cohen, MD

Activist

This once-a-day drug has a couple of strikes against it. The potentially fatal hypersensitivity reaction can now be avoided with a genetic test to screen out those predisposed to have it. However, patients should be vigilant about any possible reactions (like rash) when starting this drug and let their doctor know immediately. The second strike is a little murkier—the potential for higher rates of cardiac disease that have emerged in several large trials. Subsequent research shows conflicting evidence on this, so the jury is still out on whether this drug contributes to heart disease risk or not. Nonetheless, those who already have heart disease, or are at greater risk (those who smoke, have a family history of heart disease, high blood pressure, etc.) might look into other options, if they have them, until a clearer picture emerges on possible cardiac risks of this drug. —Jeff Taylor
**Non-Nucleoside Reverse Transcriptase Inhibitor**

**Common Name:** etravirine  
**Brand Name:** Intelence  
**Class:** non-nucleoside analogs (also called non-nucleoside reverse transcriptase inhibitors, NNRTIs, or non-nukes)  
**Standard Dose:** Two 100 mg tablets twice daily, with food. Take missed doses as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.  
**AWP:** $876.82 / month  
**Manufacturer Contact:** Tibotec Therapeutics, 1 (877) REACH-TT (732-2488), www.tibotectherapeutics.com

**Potential Side Effects and Toxicity:** The most common side effects seen in Phase 3 studies were rash (19%), diarrhea (18%), nausea (15%), headache (11%), and nasopharyngitis (symptoms similar to a cold) (11%). Last year, the warning on the drug label was strengthened to include reports of hypersensitivity (allergic-like) reactions, which sometimes occur with hepatic (liver) failure, and fatality due to Stevens-Johnson Syndrome, erythema multiforme, and toxic epidermal necrolysis (TEN), all skin disorders. These are very rare side effects. The FDA reported, “Discontinue Intelence immediately if signs or symptoms of severe skin reactions or hypersensitivity reactions develop (including, but not limited to, severe rash or rash accompanied by fever, malaise [general ill feeling], fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial edema [swelling], hepatitis, and eosinophilia [increased levels of the white blood cell eosinophil, a sign of an allergic reaction]).”  
In addition, levels of liver enzymes called transaminases should be monitored. Rash is associated with all of the current non-nukes.  

**Potential Drug Interactions:** Do not take Intelence with Biaxin, Dilantin (phenytoin), phenobarbital, rifampin, St. John’s wort, or Tegetrol (carbamazepine). Intelence should not be used with unboosted (without Norvir) PIs (Intelence may cause a significant alteration in the levels of the PI), or with Sustiva, Viramune, Rescriptor, or full-dose (600 mg twice daily) Norvir (Intelence levels are lowered with each of these). Should also not be taken with Apluvia/Norvir (Intelence level is lowered 76% with Apluvia), Reyataz/Norvir, or Lexiva/Norvir. Intelence has been studied and can be used without dose adjustment with the boosted protease inhibitors Prezista/Norvir and Invirase/Norvir. Since Kaletra increases Intelence blood levels, use together with caution. Intelence may be taken without dose adjustment with Isentress and the experimental integrase inhibitor elvitegravir (when it becomes available), but Selzentry does require dose adjustment to 600 mg twice a day with Intelence when used without a boosted PI, or 150 mg twice a day if given with both Intelence and Prezista 600 mg twice a day. In people who’ve failed therapy with other NNRTIs, Intelence should not be taken only with NNRTIs (including Viracept). Use caution with anticonvulsants: Tegetrol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Monitor the effectiveness of Coumadin (warfarin) and adjust dose as needed. Do not take Intelence with Mycobutin if you’re on a Norvir-boosted PI. If you’re not, Mycobutin dose should be 300 mg once daily. No interaction was found between Intelence and the acid suppressants ranitidine (Zantac and others) or Prilosec (omeprazole). Intelence can also be safely combined with methadone and Viagra.  

**Tips:** Intelence is a badly needed drug in the NNRTI class. The older NNRTIs can develop resistance quickly, and with only one mutation in the virus. In fact, an estimated 7% of newly infected individuals in the U.S. are infected with an NNRTI-resistant virus. The second-generation NNRTI Intelence was developed to have a higher genetic barrier to drug resistance. It has shown significant viral load reduction in people with drug resistance to Sustiva or Viramune, although it may work better in Sustiva failures (where the HIV mutation K103N is more likely present, and which does not affect Intelence activity). Intelence is generally tolerable. Diarrhea is a commonly reported side effect in studies, but the incidence is no higher than with a placebo. Intelence showed a nearly 2 log drop in viral load (99% reduction in circulating virus) in a 7-day monotherapy study with people taking HIV meds for the first time, evidence of tremendous potency. Benefits in this group, however, have not been established. The FDA granted traditional approval for Intelence in November 2009, based on 48-week data from two Ph. 3 studies, DUET-1 and DUET-2. Tibotec is also developing another NNRTI, rilpivirine (TMC278), for treatment-naive people (first time on HIV therapy), which may have pharmacologic advantages over Intelence, including the ability to dose once a day. Last year, the company reached an agreement with Gilead, maker of Emtriva and Viread, to combine rilpivirine with those two drugs into a regimen in one pill. Woo-hoo! Some physicians are prescribing Intelence as 4 tablets once daily to increase adherence. Some patients complain of hard-to-swallow large chalky pills. Those unable to swallow the tablets can stir them in a glass of water until there’s a milky appearance and drink the solution. Rinse the glass with water a few more times and swallow the rinse each time to make sure you get the full dose. Please see package insert for more complete potential side effects and interactions.  

**Doctor**  
Intelence (etravirine) is the newest non-nucleoside and was approved in 2008 for use in combination with other antiretroviral drugs for therapy-experienced individuals (two tablets twice daily, following a meal). It is not approved for those individuals who are naive to HIV therapy, though there are some small studies exploring this issue. There is extensive cross-resistance among the first three drugs approved in the NNRTI class. This means that virologic breakthrough when taking one NNRTI would lead to resistance to the other two “first generation NNRTIs.” However, etravirine is a “second generation” NNRTI, which means that, unlike the previously available agents in the class, resistance to other NNRTIs usually does not confer resistance to etravirine. Resistance testing should be performed for appropriate use of this drug, however, as there are some patterns of resistance more associated with the use of nevirapine that can cause some degree of cross-resistance to this drug. Etravirine is well tolerated in our patient population with the main side effect being a rash which occurs in no more than 10% of those who take it—rarely is the rash severe enough that someone must discontinue taking the drug but it does occur. There are some drug-drug interactions with this drug and some protease inhibitors, though most of the trials used this agent with darunavir and that combination is an important and effective option for patients whose HIV is resistant to “first generation” agents. —Cal Cohen, MD

**Activist**  
The first non-nuke that is effective against typical non-nuke resistance. This drug met an enormous need for those with traditional non-nuke resistance and, along with the integrase inhibitor Isentress (which became available at about the same time), has saved many lives of those who were resistant to practically everything. It needs to be taken twice a day with food. If you’re taking a PI, it must be boosted with Norvir because Intelence lowers PI levels. And, like most older non-nukes, it can cause rash. This is nonetheless a very important drug for salvage patients. This will never become the next Sustiva, but it has proven a lifesaving drug for many who had run out of options. —Jeff Taylor
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: delavirdine  
Brand Name: Rescriptor  
Class: non-nucleoside analogs (also called non-nucleoside reverse transcriptase inhibitors, NNRTIs, or non-nukes)  
Standard dose: Two 200 mg tablets or four 100 mg tablets three times a day (every 8 hours). Only the 100 mg tablets can be dissolved in liquid; however, avoid grapefruit juice. Can be taken with or without food, with no food restrictions. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.

AWP: $331.03 / month for 200 mg tablets  
Manufacturer Contact: ViiV Healthcare, 1 (877) 844-8872

Potential side effects and toxicity: Most common side effects include headache, nausea, vomiting, diarrhea, fatigue, elevated liver enzymes, and itchy skin or rash. A serious side effect of the NNRTI class is rash, which can be life-threatening. Most rashes occur within the first 1–3 weeks after starting Rescriptor. If you experience blistering, mouth lesions, conjunctivitis (redness or inflammation of the eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or malaise (general ill feeling), you should stop the medication, and seek medical attention right away. Body fat accumulation or redistribution may occur.

Potential drug interactions: You should not take Rescriptor with Versed (midazolam), Halcion (triazolam), Xanax (alprazolam), Orap (pimozide), ergotalkoids used for migraine headaches (such as Wigraine, Methergine, and Cafergot) in any form, or the herb St. John’s wort. Do not use Zocor (simvastatin), Vytorin, or Mevacor (lovastatin) cholesterol (lipid) lowering meds; suggested alternatives are Lipitor (atorvastatin) and Lescol (fluvastatin). Liver enzymes should be checked regularly if you are on these cholesterol meds, as they can increase risk for liver toxicity with Rescriptor. Certain amphetamines and antiarrhythmic drugs should not be used with Rescriptor, therefore, inform your health care provider if you have a history of heart or blood pressure problems. Dose adjustment may be needed when taken with Biaxin (clarithromycin). Rescriptor should be used with caution with Procardia or Adalat (nifedipine), Norvasc (amlodipine), Plendil (felodipine), Coumadin (warfarin), and quinidine. Use caution with anti-convulsants: Tegetrol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Mycobutin (rifabutin) and Rifadin (rifampin), used to treat tuberculosis, are drugs that decrease Rescriptor levels. Rescriptor is not recommended with either rifampin or Mycobutin. Rescriptor increases levels of protease inhibitors Crixivan, Lexiva, Invirase, Kaletra, Norvir, and Viracept, as well as immunosuppressants, birth control pills (ethyl estradiol), and methadone, so caution is advised if using together. Cialis, Levitra, and sildenafil (Viagra) levels are increased by Rescriptor; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Also, increased levels of trazodone can occur with Rescriptor and therefore should be used with caution. Increased levels of the inhaled and nasal sprays that contain fluticasone, a steroid for asthma or allergies (found in Advair, Flonase, and Flovent) can occur with Rescriptor and therefore should be used with caution or an alternative should be considered.

Tips: Research demonstrates that smaller doses of Rescriptor increase blood levels of some protease inhibitors, making it unique among the NNRTIs. Some people who cannot tolerate Norvir (ritonavir) are successfully using Rescriptor instead to boost their protease inhibitor. Studies of this use, however, have not been published. Antacids (like Tagamet, Zantac, Prilosec, and Tums) and gastric achlorhydria (low stomach acid) decrease absorption of Rescriptor, so take at least one hour apart from these drugs and take with acidic beverages such as orange or cranberry juice to increase stomach acidity. Please see package insert for more complete potential side effects and interactions.

Doctor

Rescriptor (delavirdine) was approved for the treatment of HIV infection in 1997. The dosing regimen of this antiretroviral is a good example of the large number of pills that had to be taken multiple times per day in the past. The original dosing schedule was 4 tablets three times daily (thankfully, no dietary restrictions). When the pill size changed, it came down to 2 pills three times per day. In general, this antiretroviral is not used to any great extent in current HAART therapy as there are better choices in almost all cases where this drug is being considered. Data are available suggesting delavirdine could be used (like Norvir) to boost levels of protease inhibitors (such as saquinavir), but the booster effect was not as strong as the Norvir effect and few studies were done to validate this approach. In fact, there have been virtually no studies using this drug in the past decade, one indication of its fall out of favor. —Cal Cohen, MD

Activist

With its heavy pill burden and thrice-daily dosing, Rescriptor has largely been replaced by Sustiva and Viramune. Like others in its class, it can cause rash, and takes just one mutation to develop resistance. It does, however, have the intriguing capability to boost some protease inhibitors just like Norvir can—giving patients who can’t tolerate Norvir another option. —Jeff Taylor
Simvastatin, and diltiazem. Dose adjustment may be needed when concentrations of Sporanox (itraconazole), Zoloft, Lipitor, pravastatin, Vfend should be increased to 400 mg every 12 hours and the Sustiva dose should be decreased to 300 mg once daily using the capsule form and monitor. Rifabutin levels are decreased, so daily dose of rifabutin should be higher and also boosted with Norvir (Reyataz 400 mg/100 mg once daily) when taken with Sustiva, but treatment should be considered. Can affect birth control pill levels, so a second barrier contraceptive method is advised. Sustiva can lower the concentrations of Sporanox (itraconazole), Zoloft, Lipitor, pravastatin, simvastatin, and diiltiazem. Dose adjustment may be needed when co-administering these drugs with Sustiva. The maintenance dose of Vfend should be increased to 400 mg every 12 hours and the Sustiva dose should be decreased to 300 mg once daily using the capsule form.

Potential side effects and toxicity: Because Sustiva penetrates so readily into the brain, up to 50% of patients experience some kind of central nervous system (CNS) or psychiatric symptoms (dizziness, headache, memory loss, somnolence or hypnotic trance, confusion, insomnia, hallucinations, vivid or abnormal dreams or nightmares, depression, euphoria or mania, and agitation). These symptoms typically diminish within four weeks. If you can’t sleep (which more commonly develops later), ask about switching the timing of your dose little by little until you’re taking it in the daytime. Some people in recovery from substance use will experience flashbacks. Other side effects may include rash, nausea, vomiting, diarrhea, fever, and increased liver enzymes. These symptoms occur early and generally resolve within two to four weeks. A serious side effect of the NNRTI class is rash, which can be life-threatening. Rash is more common, and more severe, in children, as is diarrhea, fever, and low levels of some blood cells. May raise levels of triglycerides and the good cholesterol (HDL). May lead to false positive tests for use of marijuana. Women taking Sustiva should not become pregnant or breast-feed because of the risk of birth defects. Increases in liver enzymes in people with hepatitis B and/or C can occur and should be monitored.

Potential drug interactions: Do not take with Atripla, since Sustiva is already in Atripla. You cannot take the following medications with Sustiva: midazolam, triazolam, ergot medications (Wigraine, Methergine, and Cafergot), Vfend, St. John’s wort, Gingko biloba, or bepridil. Do not use with Biaxin. May affect Coumadin (warfarin) therapy. Sustiva decreases methadone levels; dosing adjustment may be necessary to avoid withdrawal symptoms. Increase Kaletra to three tablets twice daily with food (recommended) when taken with Sustiva in people who previously took HIV drugs, especially protease inhibitors. Kaletra cannot be taken once daily with Sustiva. Monitor liver enzymes closely if Sustiva and Norvir are used together due to potential risk of liver damage. Reyataz dose should be higher and also boosted with Norvir (Reyataz 400 mg/ Norvir 100 mg once daily) when taken with Sustiva, but treatment-experienced people should not use this drug combination at all. With once-daily Lexiva, boost with 300 mg Norvir. Rifampin decreases Sustiva concentrations, so maintain 600 mg once-daily dose and monitor. Rifabutin levels are decreased, so daily dose of rifabutin should be increased by 50%. When taken with anticonvulsants Dilantin (phenytoin), phenobarbital, or Tegretol (carbamazepine), periodic monitoring of blood levels of anticonvulsants and Sustiva should be performed or alternative anti-seizure medications should be considered. Can affect birth control pill levels, so a second barrier contraceptive method is advised. Sustiva can lower the concentrations of Sporanox (itraconazole), Zoloft, Lipitor, pravastatin, simvastatin, and diiltiazem. Dose adjustment may be needed when co-administering these drugs with Sustiva. The maintenance dose of Vfend should be increased to 400 mg every 12 hours and the Sustiva dose should be decreased to 300 mg once daily using the capsule form.

Drug levels of bupropion are lowered; titrate dose based on clinical response.

Tips: According to current U.S. guidelines, when choosing an NNRTI-based regimen, Sustiva is the preferred drug. Avoid driving or operating heavy machinery for a few hours after dose. Some people adjust to Sustiva by taking Ativan or Ambien to sleep for the first few weeks. However, either may make you even more groggy the next morning. Be careful when stopping Sustiva, so that you avoid the rapid development of HIV resistance to it—check with your doctor or pharmacist first. It is usually recommended that you continue your other HIV medications for several days after stopping Sustiva. A reduction in CNS side effects was found last year in a small study using stepped-up dosing in first-time users (200 mg for six days, 400 mg for seven days, then the full dose), and drug resistance was not seen. Please see package insert for more complete potential side effects and interactions.

Doctor

Sustiva (efavirenz) dosed once daily was approved for HIV infection in 2002. This antiretroviral can be used in several combinations, but its main use is when it is taken in combination with Truvada in the fixed dose combination called Atripla (tenofovir/emtricitabine/efavirenz). This combination is currently preferred by DHHS guidelines and is among the most frequently chosen regimens when starting treatment because this three-drug combination is just one tablet, once daily—and the convenience and enthusiasm for this degree of simplicity has been very important for many patients. In addition, studies have consistently shown that these three drugs are at least as potent and successful as any other three-drug regimen—there is no study that has ever shown a superior outcome versus these three drugs. However, there are some side effects associated with Sustiva. CNS side effects (dizziness, headache, vivid dreams, concentration difficulty, worsening depression, etc.) are a common issue for patients when starting this drug. Typically, up to a half of those who start it will report at least one of these side effects in the first few days of taking it. However, the majority of people find that as they stay on it, these side effects fade away leading to a consistent finding that about 1 in 20 who start this drug eventually stop it, at least in clinical trial settings. In addition, there is a risk of a rash when starting this drug, though most patients find that this rash will fade with continued dosing. Since taking the drug with food increases its concentration in the bloodstream (possibly leading to more CNS side effects), efavirenz is generally dosed at night (you are asleep and don’t perceive the problems) and on an empty stomach. Efavirenz is a category D medication in pregnancy. Its potential effects on the fetus are well documented, and it shouldn’t be given to women who are planning pregnancy. If there is incomplete virus suppression, resistance is often observed first to efavirenz in various regimens. Fortunately the most common initial mutation to this drug—K103N—does not lead to cross-resistance to etravirine. —Cal Cohen, MD

Activist

The most popular of the non-nukes, Sustiva does offer convenient once-a-day dosing. The major downsides are the sleep disturbances, vivid dreams, and nightmares that never go away for some patients. Taking the drug at bedtime, and not taking it with high fat foods can lessen those effects for some. Sustiva can also raise blood lipids (cholesterol, etc.), so patients should be sure to get fasting lipid levels, and consider switching if it causes lipid problems. The long half-life that makes Sustiva such a good once-a-day drug also means that if you have to stop it for any reason, you should consult your doctor and stop several days before your other drugs to avoid developing resistance. —Jeff Taylor
Common Name: nevirapine
Brand Name: Viramune
Class: non-nucleoside analogs (also called non-nucleoside reverse transcriptase inhibitors, NNRTIs, or non-nukes)

**Standard dose:** One 200 mg tablet daily for two weeks, then full dose of one 200 mg tablet twice daily. Can be taken with or without food, with no food restrictions. Frequently prescribed as two 200 mg tablets once a day, although once-daily dosing is not FDA approved. Dose for children 15 days or older is 150 mg once daily for 14 days, then 150 mg twice daily thereafter. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose. For dialysis patients, an additional dose of 200 mg is required after each dialysis. A 50 mg/5 ml oral suspension is also available.

**AWP:** $547.20 / month

**Manufacturer contact:** Boehringer-Ingelheim, www.viramune.com, 1 (800) 274–8651

**Potential side effects and toxicity:** Most common side effects include headache, nausea, vomiting, fever, and rash. 14-day lead-in dosing reduces the frequency of rash. Severe rash, including Stevens-Johnson syndrome, while rare, can be life-threatening; notify your health care provider immediately. Seek medical attention right away if you experience blistering, mouth sores, conjunctivitis (redness or inflammation of the eye, or pink eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or malaise (general ill feeling). Do not increase dose if rash develops during dose escalation or if you develop any rash accompanied by the above listed conditions. Once-daily lead-in dose should not exceed 28 days. An alternative drug should be considered at this time. An increase in liver enzyme levels has been observed and in rare instances, hepatitis has developed. In such cases, it may be necessary to stop taking Viramune until liver function returns to normal. Permanently discontinue it if abnormalities return. Rarely, severe and life-threatening hepatotoxicity (liver damage), including three fatal cases, have occurred. Women with CD4 counts greater than 250 T-cells, including pregnant women, and men with more than 400 T-cells have a higher risk of serious hepatotoxicity (liver damage), with women being at greater risk, though liver damage can happen to anybody. The package insert says Viramune should not be started in these groups unless the benefit outweighs the risk. The highest risk period is within the first six weeks of treatment, but patients should be monitored closely for the first 18 weeks.

**Potential drug interactions:** Viramune should not be taken with Reytataz or St. John’s wort. Rifampin should not be used with Viramune; rifabutin (Mycobutin) is the recommended alternative for the treatment of tuberculosis. Caution should be used with midazolam, triazolam, fluconazole, or ergot medications used for migraine headaches (Wigraine, Methergine, and Calergot), Cordarone, lidocaine or disopyramide, carbamazepine, ethosuximide, or clonazepam, calcium channel blockers (Procardia, diltiazem, verapamil), immunosuppressants, or the blood thinner Coumadin (warfarin). Do not use with Biaxin (clarithromycin) or Zilex (ketoconazole). Viramune decreases methadone levels; dosage adjustment may be necessary to avoid withdrawal symptoms. Viramune can reduce levels of protease inhibitors; dose adjustment may be needed if they are taken at the same time. Kafera should be increased to three tablets twice a day in people who previously took HIV drugs. Use caution with anti-convulsants: Dilantin (phenytoin), phenobarbital, and Te-gretol (carbamazepine). The effectiveness of birth control pills may be decreased; alternative contraception methods with barrier should be used. During the first six weeks of therapy, prednisone should be avoided; it can cause increased severity and incidence of rash.

**Tips:** Monitor liver function tests and signs of rash during first six months. The increased period of risk for liver injury is primarily in the first 18 weeks of taking Viramune. Do not ignore yellowing of your eyes or skin, as this may be a sign of a severe liver effect. Studies show that Viramune crosses the blood-brain barrier to a useful degree, which may be beneficial for patients at risk for neurological damage (such as dementia) from HIV. Lead-in dosing has been shown to lessen the risk of rash. If at any time of treatment you stop Viramune for more than seven days, you will need to start at the lower dose for two weeks and then increase back up to twice-daily dosing. Be careful when stopping Viramune, so that you avoid the rapid development of HIV resistance to it—check with your doctor or pharmacist first. It is usually recommended that you continue your other HIV medications for several days after stopping Viramune. Viramune has also been shown to have a positive impact on triglycerides and cholesterol levels. When given around the time of labor, Viramune has demonstrated effectiveness in preventing the transmission of HIV from mother to child, but there was an increase in HIV drug resistance when given alone. The use of at least one other HIV drug helped to cut down the incidence of resistance, and women have been shown to experience effectiveness with the drug six months after giving birth. Viramune was updated from Pregnancy Class C to Class B in 2007, meaning that it was found to be even safer. Single- or two-dose Viramune may be used for babies born to HIV-positive mothers. Mothers should not breastfeed their infants while taking Viramune. Please see package insert for more complete potential side effects and interactions.

**DOCTOR**

Viramune (nevirapine) was approved for twice-daily dosing in 1996. It was the first drug approved in the NNRTI class. This drug is currently considered an alternative to Sustiva for a number of reasons. One is that its use is associated with a risk of a rash. To minimize this risk, the drug is taken as one pill per day for two weeks before going to the full dose of one pill twice daily. Furthermore, this drug must be given only to patients whose CD4 counts are below certain thresholds in order to minimize side effects—these thresholds differ for men versus women and differ again if the person is viremic versus having a suppressed viral load when nevirapine is started. Finally, a small percentage of people have liver function test abnormalities when starting this agent—more than what is observed with other choices—thus, this drug requires careful monitoring when starting on it. It does have one attractive feature in those who do tolerate it in that it may have the most beneficial impact on lipid profiles with an increase in the HDL (“good”) cholesterol fraction. It is not yet clear if this impact decreases the rate of heart attacks over time versus what is seen with the use of other agents. Finally, resistance to this drug is usually associated with the Y181C mutation which has a risk of conferring resistance to etravirine. Therefore, careful monitoring is necessary to ensure that this drug is carefully reconsidered if someone has developed viremia while taking a nevirapine-containing regimen. —Cal Cohen, MD

**ACTIVIST**

A good twice-daily alternative for those who can’t tolerate Sustiva’s sleep and lipid problems, Viramune needs to be started carefully. In addition to women with over 250 T-cells and men with over 400 T-cells, everybody should be closely watched for liver toxicity for the first six months. After that, it should be smooth sailing, and Viramune may even be beneficial for cholesterol and triglyceride levels. Like Sustiva, Viramune has a very long half-life—which means if you’re stopping meds for any reason you should stop the Viramune several days before your other drugs to avoid developing resistance —Jeff Taylor
Atripla (tenofovir/emtricitabine/efavirenz) was approved for once-daily dosing for HIV infection in 2006. This was the first two-class, three-drug, complete HAART regimen in one pill and dosed once daily. Since this fixed dose combination became available, there has been great enthusiasm for these three drugs due to the combination of simplicity as a single tablet, plus the effectiveness that has never been “beat” in any randomized comparative drug study. One reason why this combination may be as effective as it is could be due to the long “half-lives” of all three drugs—meaning that while this drug is taken once daily, the drug levels last longer than 24 hours and there is a “cushion” in case someone is late in taking a dose. The relevance of this observation was demonstrated in a study called FOTO—Five days On, and Two days Off. This study included only people who had long-term virologic suppression while taking Atripla. After a year of taking this combination just five days per week with weekends off, the viral load remained suppressed in all of them. As these studies are small, this approach is not recommended outside of a clinical study, but it demonstrates one of the potential benefits of taking antivirals that last a long time in the cells. While this is a very successful combination, there are some limitations and considerations with the use of this drug and the sections on tenofovir and Sustiva highlight these concerns in detail. —Cal Cohen, MD

**ACTIVIST**

The ultimate convenience—this three-in-one pill taken once a day has made HIV treatment easy and tolerable for huge numbers of patients, not to mention cut co-pays from three to one for those who have to pay them. Doctors love to prescribe this combination because of its simplicity and the assumption that it will solve all adherence problems. The downside, of course, comes from the Sustiva in—it—with its potential for sleep disturbances and lipid problems. Once again, the sum is no greater than its parts. It is notable in that this is the first time two different companies collaborated to create a single-pill combo drug—setting an important precedent for other companies now following suit with other fixed dose combos in the pipeline. —Jeff Taylor
**PROTEASE INHIBITOR**

**Common Name:** tipranavir  
**Brand Name:** Aptivus  
**Class:** HIV protease inhibitors (PIs)  
**Standard Dose:** Two 250 mg capsules with two 100 mg capsules of Norvir, both twice daily. Must be taken with Norvir. Oral solution available; both formulas available for children and adults. Can be taken with or without food, with no food restrictions, but preferably with food to improve Norvir tolerability. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.  
**AWP:** $1,187.27 / month for Aptivus only  
**Manufacturer Contact:** Boehringer-Ingelheim, www.aptivus.com, 1 (800) 542–6257

**Potential side effects and toxicity:** Mostly gastrointestinal-related; mild diarrhea, nausea, vomiting, abdominal pain, and fatigue. In clinical trials, symptoms have been managed by having a light snack with the drug. Rash, including sensitivity to the sun, has occurred with Aptivus. Rash was more common in children. Also, women taking birth control pills may be at higher risk for rash. If a severe rash occurs, Aptivus should be discontinued. Stop using Aptivus if rash appears with joint pain or stiffness, throat tightness, generalized itching, muscle aches, fever, redness, blisters, or peeling of the skin, and call your health care provider right away. Other side effects may include headache, fever, dry mouth, and dizziness. Caution should be used in people with mild liver impairment, since Aptivus concentrations may be increased. Should not be taken by patients with sulfa allergies. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; patients with sulfa allergies. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts, and upper back), onset of new cases or worsening of diabetes (see your doctor promptly), and increased bleeding in hemophiliacs.

**Potential drug interactions:** Aptivus/Norvir interacts with many other drugs, so it is important to tell your health care professional of the medications you are taking. See the package insert. Aptivus lowers Intelen levels, and the two should not be combined. Do not take with Tambocor, Rythmol, quinidine, Versed (midazolam), Halcion, pimozide, ergot alkaloids (such as Cafergot, Wigraine, Methergent, and D.H.E. 45), or the herb St. John’s wort. Do not use Advicor, Altoprev, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor and Pravacol (pravastatin), but should be used with caution. Increased levels of the inhaled and nasal sprays with fluticasone (found in Advair, Flonase, Flonvent), can occur with Aptivus/Norvir and therefore should be used with caution. Aptivus can lower blood levels of Ziagen, Videx, and Retrovir (zidovudine, AZT). Take Videx and Aptivus 2 hours apart. The clinical significance of this interaction is not known. No significant changes were seen when combining Aptivus with Sustiva or Viramune. Should not be taken with other protease inhibitors because it greatly lowers their blood levels. Trough concentration (lowest level) of Aptivus is increased 45% with Fuzeon, but dose adjustments are not recommended. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Methadone doses may need to be increased. Blood levels of Aptivus decrease 40% with Suboxone, but dose adjustments are not recommended, and the effectiveness of Suboxone is not affected. Trazodone concentrations may increase; a lower dose of trazodone is recommended. Calcium channel blockers should be used with caution and monitored for side effects. Monitoring may be required when taking Coumadin or immunosuppressants. Carbamazepine, Dilantin (phenytoin), or phenobarbital may decrease Aptivus levels, so alternate seizure medications should be used and monitoring of Aptivus drug levels is recommended. Caution should be used with valproic acid, which may be less effective due to decreased concentrations when used with Aptivus. Caution must be exercised when using itraconazole or fluconazole. Rifampin should not be used; rifabutin (Mycobutin) is the recommended alternative for the treatment of TB. It requires a reduced dose and frequency. Norvir and Aptivus capsules contain alcohol (but should not be enough to trigger relapse), so be cautious with Antabuse or Flagyl. Oral solution contains vitamin E; do not take with additional vitamin E beyond that found in a standard multivitamin. Antacids can decrease levels of Aptivus. Aptivus should be taken 2 hours before or one hour after antacids. Drug levels of bupropion are lowered; titrate dose based on clinical response.

**Tips:** Due to its resistance profile and its drug interactions, Aptivus is not as popular as other PIs. Aptivus is only for treatment-experienced patients. Take with food to minimize stomach problems. Do not take at the same time as antacids. Aptivus is expected to do less well for people with combinations of certain protease-related mutations. See package insert. Although Aptivus has to be taken with 200 mg twice daily of Norvir, it actually lowers the blood levels of Norvir, so you may not see as many of the GI side effects as you might expect. The capsules should be refrigerated prior to opening. Aptivus can be stored at room temperature (up to 77°F), but must be used within 60 days Please see package insert for more complete potential side effects and interactions.

**DOCTOR**

Aptivus (tipranavir) was approved in 2005 for combination antiretroviral treatment only in those individuals with HIV infection who have evidence of viral replication, are highly treatment-experienced, and/or have HIV strains resistant to multiple protease inhibitors. While Aptivus gives us an active drug choice in those who have resistance to multiple PIs, there are several reasons why this drug is minimally used currently. The main issue is that there are several possible side effects when using it, and side effects are considered to be more likely with this PI versus other options, primarily darunavir, given its activity against similarly resistant virus. Studies of this PI as a first regimen also demonstrated limitations to this drug, as it was not as successful as boosted lopinavir (Kaletra) in either how well it would establish control of HIV, or by its safety profile, as there were more side effects. —Cal Cohen, MD

**ACTIVIST**

A lifesaving drug for patients with protease resistance when first released, Aptivus has been supplanted by newer PIs with improved resistance profiles, but without the debilitating GI problems—mostly diarrhea. A host of drug interactions—including other protease inhibitors—makes this a tricky drug to balance in a regimen, especially for salvage patients already on a host of other meds. —Jeff Taylor
**AWP**

**Class:** HIV protease inhibitors (PIs)

**Standard dose:** Rarely used by itself (two 400 mg capsules every eight hours with no food or a low-fat snack). Almost always boosted with Norvir, both twice daily: 400 mg Crixivan + 400 mg Norvir; 800 mg + 100 mg; or 800 mg + 200 mg (all doses taken with food, and with plenty of water to avoid kidney sludge or stones). Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose. Also available in 100 mg, 200 mg, and 333 mg capsules.

**AWP:** $548.12 / month for 400 mg, 180 capsules

**Manufacturer contact:** Merck and Co.,
www.crixivan.com, 1 (800) 850–3430

**Potential side effects and toxicity:** Headache, fatigue or weakness, malaise (general ill feeling), nausea, diarrhea, stomach pain, loss of appetite, yellowing of skin/eyes, changed skin color, dry mouth/throat, taste changes, painful urination, indigestion, joint pain, hives, and liver toxicity. Itchy/dry skin, indigestion, joint pain, hives, and liver toxicity. Itchy/dry skin, indigestion, joint pain, hives, and liver toxicity. Itchy/dry skin, indigestion, joint pain, hives, and liver toxicity. Itchy/dry skin, indigestion, joint pain, hives, and liver toxicity. Itchy/dry skin, indigestion, joint pain, hives, and liver toxicity.

**Potential drug interactions:**
- Do not take with Tambo
cor (flecainide), Rythmol (propafenone), Cordarone (amiodarone), midazolam, triazolam, rifampin, pimozide, ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), garlic supplements, or the herb St. John’s wort. Do not use Advicor, Altoprev, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution.

Not recommended in combination with Reyataz. Reduce Crixivan to 600 mg every eight hours when taken with Rescriptor, itraconazole (200 mg twice a day), or ketoconazole (200 mg once a day). The dose of Mycobutin should be reduced to 150 mg daily or 300 mg three times a week and Crixivan dose increased to 1,000 mg every eight hours or use Norvir-boosted dose when taken together.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception. Additional monitoring may be required when taking Coumadin (warfarin), immunosuppressants, or calcium channel blockers (such as Norvasc, Procardia, and others). Use caution with anti-convulsants: Tegetrol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Crixivan may decrease levels of methadone, but withdrawal rarely occurs. Methadone doses may need to be increased. Also, increased levels of trazadone can occur with Crixivan. Increased levels of the inhaled and nasal sprays with fluticasone, a steroid for asthma or allergies (found in Advair, Flonase, and Flovent) can occur with Crixivan and therefore should be used with caution.

**Tips:** Drink at least 48 oz. of fluids daily, preferably water or clear liquids (soda pop doesn’t count!) to decrease the chances of kidney stones. Don’t forget to drink more water in summer or with increased sweating. Large amounts of coffee or alcohol can increase risk of stones due to increased dehydration. Stones may continue after stopping Crixivan. Grapefruit juice and vitamin C (more than one gram a day) decreases Crixivan blood levels. Store in original container and keep dry. Please see package insert for more complete potential side effects and interactions.

**Doctor**

Crixivan (indinavir) was approved for use with other antiretroviral drugs for HIV infection in 1996. While this drug did provide a high degree of virologic suppression when used in several combinations, there are several reasons why its use is rare at the present time. The first issue that was evident was its complex dosing as well as dietary restrictions—two capsules had to be ingested every eight hours on an empty stomach or at least adequately separate from food. That issue was addressed by the addition of the booster drug ritonavir, allowing indinavir to be taken twice daily instead. However, other concerns remained, including a risk of kidney stones comprised of the drug. Finally, this drug seemed to be associated more with increased abdominal fat (in the area surrounding the intestines, behind the abdominal muscle) versus any other PI, and that was the beginning of the widespread concern for a condition later called “lipodystrophy.” As there are better, safer choices in the PI class, this drug is rarely used at this time. —Cal Cohen, MD

**Activist**

The drug that ushered in the Protease Revolution, its every-eight-hour dosing on an empty stomach—with enough water to float a boat—saved lives even as those lives came to revolve around the drugs that made life possible. Now boosted with Norvir, like most other PIs, for more convenient dosing with food, the risk of kidney stones, lipid problems and fat redistribution (remember “Crix belly”?) mean that it can’t compete with the newer and improved PIs. So it has become a footnote in HIV history—remembered with mixed emotions by those whose lives it saved. —Jeff Taylor
PROTEASE INHIBITOR

Common Name: saquinavir
Brand Name: Invirase
Class: HIV protease inhibitors (PIs)

Standard Dose: Two 500 mg film-coated tablets with 100 mg Norvir two times a day with food, or within two hours after a meal. Must be taken with Norvir. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.

AWP: $996.44 / month for 500 mg tablets
Manufacturer Contact: Roche Pharmaceuticals, www.rocheusa.com, 1 (800) 526-6367

Potential Side Effects and Toxicity: Most common are diarrhea, abdominal discomfort, vomiting, and nausea. As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts, and upper back), onset of new cases or worsening of diabetes (see your doctor promptly) and increased bleeding in hemophiliacs. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

Potential Drug Interactions: Viramune, Sustiva, and Mycobutin (rifabutin) decrease Invirase levels. Not recommended to be used with Atriplus/Norvir or Prezista. Should be used with caution and may require dose adjustment with Reyataz. Rescriptor, Crixivan, Norvir, Viracept, and Kaletra all significantly increase Invirase’s concentrations. No dosage change when taken with Kaletra.

Do not take with Tampocor (ilecainide), Rythmol (propafenone), Biaxin (clarithromycin), dexamethasone, Cordarone (amiodarone), Versed (midazolam), Halcion (triazolam), Rifadin (rifampin), Orap (pimozide), Lanoxin (digoxin), ergot derivatives (such as Cafergot, D.H.E. 45, Methergine, and Wigraine), quindine, the herb St. John’s wort. Do not use Advicor, Altoprev, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution. Data show that when rifampin is taken with Invirase/Norvir, there is significant liver toxicity in 40% of patients. The combination should be avoided. Methadone doses may need to be increased. Invirase increases levels of fluticasone (active component of Advair, Flonase, Flovent). Trazadone concentrations may increase; a lower dose of trazodone is recommended. Use calcium channel blockers with caution. Monitor digoxin levels; digoxin dose may need to be decreased. Use caution with anti-convulsants: Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytion).

Invirase may increase dapsone levels. Do not take with birth control pills; Invirase reduces level of ethinyl estradiol. Prescriber may need to adjust doses accordingly.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Tips: The GEMINI study compared Invirase to Kaletra, both twice daily. Similar viral suppression and increase in CD4 count were seen. Invirase/Norvir has demonstrated safety, and is listed in the U.S. DHHS HIV treatment guidelines as an alternative choice when starting HIV therapy. The higher pill burden and increase in Norvir (greater than 100 mg per day) is the reason for its alternative listing. Must be taken with food. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Invirase (saquinavir) was the first protease inhibitor approved (in 1995) for combination therapy in the treatment of HIV infection. The drug was initially taken unboosted, but studies in later years showed that its use was more reliable when taken twice daily with ritonavir. In addition, a few smaller studies showed reasonable activity when saquinavir was taken just once daily, also with ritonavir. This drug is usually well tolerated with few expected side effects. Larger studies were done in the past five years which did show that the twice-daily dose is similarly effective to lopinavir, and some international guidelines have included this PI in the choice of preferred options. However, current guidelines usually do not include saquinavir on the preferred list of PIs to start on, as there are other choices in the PI class that have enough advantages over saquinavir. This drug has minimal use at present. There is interest in what will happen when this PI becomes “generic,” which usually means it may be far less expensive versus the current “name brand.” As this drug did do fairly well compared to other choices, there may be times when financial circumstances lead to a reconsideration of the value of this drug. —Cal Cohen, MD

ACTIVIST

A drug that has come full circle—Invirase was one of the first protease inhibitors and was not well absorbed and had to be taken with a high fat meal. Even then, drug uptake was uneven, and the company switched to a gel capsule they called Fortovase. Fortovase caused lots of stomach upset and diarrhea, and quickly fell out of favor. Then studies showed that the original Invirase boosted with Norvir had fewer side effects and better absorption, so it’s back among the recommended alternative regimens. But its twice-daily dosing with food means that it’s losing ground to newer PIs such as Reyataz and Prezista. —Jeff Taylor

Common Name: saquinavir
Brand Name: Invirase

POSITIVELY AWARE
**Potential side effects and toxicity:** Diarrhea is the most common and can be very severe. Rash, nausea, vomiting, stomach pain, headache, muscle weakness, and elevated liver enzymes, a sign of liver damage—this may be more common in people with hepatitis B or C. As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts, and upper back), onset of new cases or worsening of diabetes (see your doctor promptly) and increased bleeding in hemophiliacs. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as information from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

**Potential drug interactions:** Interacts with many—tell your provider all the drugs you are taking. Do not take with Tamdocor, Rythmol, Cordarone, Versed (midazolam), Halocin, Uroxatral, rifampin, pimozone, ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), garlic supplements, or the herb St. John’s wort. Do not use Advicor, Altoprev, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution. Oral solution contains alcohol, so do not use with Antabuse or Flagyl (metronidazole). Use calcium channel blockers (such as Norvasc, Procardia, and others) with caution. Dosage of methadone may need to be increased when taken with Kaletra. Current guidelines state the Kaletra dose should total 500 mg lopinavir and 125 mg ritonavir twice daily when used with Sustiva or Viramune. That would mean 5 tablets of low-dose Kaletra twice daily. Because of high pill burden, physicians usually prescribe three tablets twice a day with food of the 200/50 mg dose when using with Sustiva or Viramune. Not recommended to be taken with Lexiva. Kaletra may lower levels of Retrovir (zidovudine, AZT) and Ziagen. Videx and Kaletra can be taken together, but without food. If Kaletra is taken with food, Videx should be taken an hour before or two hours after Kaletra. Mycobutin (rifabutin) dosage should be reduced to 150 mg every other day (or 150 mg three times per week) when used with Kaletra. Phenobarbital, phentoin or carbamazepine may lower blood levels of Kaletra. Reduces effectiveness of birth control pills; use alternative contraceptive methods. Mepron levels may be reduced with Kaletra. Avoid Sporanox (itraconazole) or Nizoral (ketoconazole) doses greater than 200 mg per day with Kaletra. Decreases V Erdogan (voriconazole) levels. People with kidney impairment may require lower Biaxin doses with Kaletra. Blood levels of immunosuppressants (cyclosporine, tacrolimus, and rapamycin) should be monitored, because their blood levels may increase when taken with Kaletra. Kaletra may alter Coumadin levels. Steroids, especially Decadron, may decrease levels of Kaletra. Increases levels of fluocasone (active component of Advair, Flonase, Flovent) and trazodone. Use caution with anti-convulsants: Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Drug levels of bupropion are lowered; titrate dose based on clinical response. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

**Tips:** In December 2009, Kaletra was downgraded from “preferred” to “alternative” therapy in U.S. HIV treatment guidelines for treatment-naïve people, but is preferred for pregnant women. For people doing well on Kaletra, this should not be an issue. According to the guidelines, the need for 200 mg a day of Norvir (contained in Kaletra) and the higher rate of gastrointestinal side effects compared with boosted PIs using 100 mg Norvir make Kaletra an alternative for treatment-naive people. Four tablets once daily can increase side effects, especially diarrhea. Taking with food and anti-diarrheal medicine helps lessen diarrhea. Kaletra should not be taken only once a day by children under 18. Please see package insert for more complete potential side effects and interactions.

**DOCTOR**

Kaletra (lopinavir/ritonavir) was approved as a capsule for use in combination with other antiretrovirals in 2000. In 2005, Kaletra tablets were approved. A liquid preparation is available and the tablet does not have to be refrigerated—both of these provide certain advantages. For some, it is the fact that Kaletra is also the only coformulated protease inhibitor (lopinavir and ritonavir in the same tablet) that leads to choosing this over other options. This was the boosted PI that taught the field about the important advantages of using a ritonavir-boosted PI versus unboosted PIs, including seeing minimal, if any, drug resistance in PI-naive patients who did not maintain virologic suppression—this “high genetic barrier” minimizing the risk of virologic resistance is an important reason why PIs are considered in some circumstances. The most common clinical adverse effect with Kaletra is diarrhea—it is this “tolerability” issue that contributes to why Kaletra was deemed a less successful choice compared to Reyataz in a recent large study in people starting treatment. There are some lipid differences, as well, that are less favorable compared to Reyataz. In addition, a study comparing Kaletra to Prezista showed that while these two antivirals are similarly successful in patients who adhere to treatment, Kaletra was less successful than Prezista in maintaining suppression in those who miss doses over time. While it is ideal to take each dose each day, it is clear that this is not necessarily something everyone can do, and that has led to a second reason to reconsider the use of Kaletra. Finally, a few studies have shown that using Kaletra increases the risk of having a heart attack and this impact is not fully explained by the cholesterol changes which occur with the use of this drug. However, in pregnant women, Kaletra is still considered the treatment of choice in combination with two NRTIs. —Cal Cohen, MD

**ACTIVIST**

Once the gold standard of protease-based regimens, Kaletra’s GI and lipid problems have knocked it off the list of preferred regimens for new HIV patients. With its Norvir boost combined with the Kaletra in one pill that doesn’t need to be refrigerated, it has an advantage over all the other PIs that need to be boosted with stand-alone Norvir (can we say marketshare insurance?) and can save on co-pays for patients who need a boosted protease inhibitor. But newer PIs, like Reyataz and Prezista, have replaced it as the preferred first line PI-based regimens. However, it still remains the preferred PI for pregnant women. —Jeff Taylor
**PROTEASE INHIBITOR**

**Common Name:** fos-amprenavir calcium  
**Brand name:** Lexiva  
**Class:** HIV protease inhibitors (PIs)  
**Standard Dose:** For people on a PI for the first time: two 700 mg tablets with either one 100 mg or two 100 mg Norvir, both once daily; or two 700 mg tablets (without Norvir), twice daily; or one 700 mg tablet with 100 mg Norvir, twice daily. For PI-experienced patients, one 700 mg tablet of Lexiva with 100 mg Norvir, twice daily. A grape/bubblegum/peppermint-flavored oral suspension is also available. Can be taken with or without food, with no food restrictions, at any dose. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.

**AWP:** $820.99 / month for 60 tablets and $125.78 for 225 ml oral suspension (50 mg/mL)  
**Manufacturer Contact:** ViV Healthcare, 1 (877) 844-8872

**Potential Side Effects and Toxicity:** Because Lexiva has a sulfa component, it should be used with caution in patients with allergies to sulfa drugs. The most common moderate to severe side effects may include nausea, rash, diarrhea, headache, vomiting, fatigue, and abdominal pain. Rash occurred in about 19% of patients, but severe rashes were uncommon. If you experience a rash, notify your doctor. For mild or moderate rashes, your doctor may choose to continue Lexiva, with close monitoring. Patients with hepatitis B or C should be monitored closely for the possibility of elevated liver enzyme levels. Dose adjustment is recommended for people with liver impairment. Side effects and laboratory abnormalities were similar when Lexiva was taken once or twice daily, with or without Norvir.  

As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts, and upper back), onset of new cases or worsening of diabetes (see your doctor promptly) and increased bleeding in hemophiliacs. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

**Potential Drug Interactions:** Not recommended to be taken with Kaletra. When taken with Sustiva, boost a once-daily dose of Lexiva with 300 mg of Norvir. Do not take with Tamobocor, Rythmol, Versed (midazolam), Halcion (triazolam), rifampin, Orap (pimozide), ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), or the herb St. John’s wort. Do not use Advicor, Altoprev, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution. Calcium channel blockers (such as Norvasc, Procardia, and others) should be used with caution and careful monitoring. Lexiva can lower methadone concentrations. A dose adjustment of Mycobutin (rifabutin) will be needed when used in combination with Lexiva. Steroids, such as Decadron, may decrease levels of Lexiva. Increased levels of the inhaled and nasal sprays with fluticasone, a steroid for asthma or allergies (found in Advair, Flonase, and Flovent) can occur with Lexiva and therefore should be used with caution. Trazodone concentrations may increase; a lower dose of trazodone is recommended. Use caution with Paxil. Use caution with anti-consualts: Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Drug levels of Paxil are lowered; titrate dose based on clinical response. The effectiveness of birth control pills may be decreased when taking Lexiva; alternative or additional contraception methods with barrier should be used. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

**Tips:** Last year, as with Kaletra, U.S. HIV treatment guidelines dropped Lexiva/Norvir as “preferred” for first-time therapy and listed it as an alternative. According to the guidelines, the change was made because regimens of once-daily dosing and no more than 100 mg of Norvir are now favored. Lexiva 1,400 mg with Norvir 100 mg once daily was shown, in one study, to have similar virological and CD4 T-cell benefit when compared to once-daily boosted Reyataz. However, this dose was precluded from the preferred list due to the small study size. It can be taken once daily in treatment-naïve patients. The lower dose of Norvir may cause less of an increase in cholesterol and triglycerides, but there is limited clinical data with this dose. Studies have demonstrated that protease inhibitor-experienced patients should take Lexiva 700 mg with Norvir 100 mg, both twice daily. The once-daily dosing is not recommended for treatment-experienced patients for whom a PI therapy has previously failed. It is important to take Lexiva exactly as your doctor instructs, and not to change dosing without discussing it with your doctor. The FDA points out that the study comparing Lexiva/Norvir against Kaletra in protease inhibitor-experienced patients was not large enough to show that the combination was clinically equivalent to Kaletra. A liquid formula of Lexiva is available. Please see package insert for more complete potential side effects and interactions. Another analysis from a French cohort showed Lexiva was associated with an increased risk of heart attacks and heart disease.

**Doctor**

Lexiva (fos-amprenavir) was approved (two tablets twice daily) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2003. A related drug called amprenavir (Agenerase) was approved by the FDA in 1997, but amprenavir was discontinued when Lexiva came to market, as it was a better version. In 2007, fos-amprenavir was approved for once-daily dosing (two tablets) with low-dose ritonavir. The DHHS Guidelines Panel previously listed ritonavir-boosted Lexiva as one of the four preferred PI options, but in the past year, this drug was listed instead as an alternative to other preferred options. Overall this drug has a very similar profile in terms of efficacy and safety to Kaletra, except it is not co-formulated as is the case for Kaletra. As it offers no particular advantage over Kaletra, it is unclear when someone should be on Lexiva versus Kaletra. —Cal Cohen, MD

**Activist**

Replacing the original Agenerase with easier dosing, it provides the option of being unboosted in those without prior PI experience. Everyone else will need the Norvir boost. Side effects are similar to most other PIs—diarrhea, increased blood lipids, lipodystrophy, etc. Add to that the possibility of rash—especially for those with a sulfa allergy (like a Bactrim allergy), and it’s no wonder this drug has fallen out of favor compared to the newer protease inhibitors. —Jeff Taylor
**Common Name:** ritonavir  
**Brand Name:** Norvir  
**Class:** HIV protease inhibitors (PIs)  
**Standard Dose:** New 100 mg tablets that don't require refrigeration became available as PA went to press (photo not available); must be taken with a meal. Almost never used at its approved dose (a lead-in dosing, then six 100 mg tablets twice daily). Norvir is primarily used as a boosting agent for other PIs, at smaller doses of 100 to 400 mg, either once or twice a day. See drug label of the other PI. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose. Approved for children ages one month and older. Liquid formula available, but tastes unbelievably horrific.  
**AWP:** $308.60 / for 30 capsules, $1,728.24 for 240 ml oral solution (80 mg/ml). Pricing for tablets unavailable at press time.  
**Manufacturer Contact:** Abbott Laboratories, www.norvir.com, 1 (800) 222–6885

**Potential side effects and toxicity:** Most common side effects include weakness, stomach pain, upset stomach (nausea, vomiting), tingling/numbness around the mouth, hands or feet, loss of appetite, taste disturbance, weight loss, headache, dizziness, pancreatitis (see NRTIs), and alcohol intolerance.

As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, breasts, and upper back), onset of new cases or worsening of diabetes (see your doctor promptly) and increased bleeding in hemophiliacs. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

Other potential side effects are liver problems, such as an increase in liver enzymes (AST, ALT, and GGT), hepatitis, or jaundice (yellowing of skin), and increased muscle enzyme (CPK) and uric acid. People with hepatitis B or C may be at increased risk.

**Potential drug interactions:** Norvir interacts with many other drugs. See the manufacturer package insert for the most complete list. Tell your provider of all drugs you are taking, prescribed or non-prescribed. Do not take with Tambocor, Rythmol, Cordarone, Versed (midazolam), Halcion (triazolam), Uroxatral, Rifadin (rifampin reduces Norvir levels by 35%), Orap (pimozide), ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), Vfend (voriconazole), garlic supplements, or the herb St. John's wort. Do not use Advicor, Altопre, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution. Norvir increases levels of fluticasone (active component of Advair, Flonase, Flovent). Trazodone concentrations may increase; a lower dose of trazodone is recommended. Norvir and Aptivus may decrease levels of methadone, but withdrawal rarely occurs. Methadone doses may need to be increased. Use caution with anti-convulsants: Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Use calcium channel blockers (such as Norvasc, Procardia, and others) with caution. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. The effectiveness of birth control pills may be decreased when taking Norvir; alternative or additional contraception methods with barrier should be used.

Levels of the street drug Ecstasy are greatly increased by Norvir, and at least one death has been attributed to the combination. GHB is also dangerous with Norvir. Tobacco and alcohol may lower blood levels of Norvir. Increases seen in Biaxin (clarithromycin) levels by 80%. Contains alcohol (but should not be enough to trigger relapse), so be cautious with Antabuse (disulfiram) or Flagyl (metronidazole)—greatly hastens intoxication.

**Tips:** There is great excitement for the new tablet formulation (which became available at press time) that doesn't require refrigeration and high hopes for a co-pay assistance card. The real strength of Norvir is in combination with other PIs (used as a boosting agent), allowing for a lower dose of both (decreased pill burden) and, in many cases, a decrease in the frequency of doses. Abbott Laboratories increased the price of Norvir 400% in 2003 and has been on the hit list of medical providers and advocates since. Promising alternatives to Norvir boosting are in research. Stomach side effects are reduced by taking Norvir with high fats foods (such as peanut butter or avocado)—however, be careful because some other HIV medicines should not be taken with high fats foods. You can mix liquid solution in ice cream, milk (especially chocolate), or pudding to hide the taste. Label says mix one hour before taking. Blood concentration increases in people with hepatic (liver) impairment. Please see package insert for more complete potential side effects and interactions.

**Doctor**

Norvir (ritonavir) was originally approved in 1996 for use as an extraordinarily bitter liquid taken twice daily in combination with other antiretroviral drugs in the treatment of HIV infection. In 1999, a soft-gel capsule formulation of the drug was approved and the original formulation was used far less often. The nearly only use of this drug is due to an important drug interaction it has with other PIs—it blocks the enzyme that breaks down other protease inhibitors, which then provides higher and more effective blood levels of that PI. Most all use of protease inhibitor drugs is when they are “boosted” with low-dose ritonavir, as boosted PIs are more successful than their unboosted versions. However, it also blocks the metabolism of several other drugs, not just protease inhibitors, and that leads to an important consideration when prescribing other medications to people on boosted PIs. While the current capsule does not require refrigeration, it is sensitive to heat and must be kept at “room temperature,” not in a warm place or else the capsule can melt. [A reformulated tablet version was approved as PA went to press.] The search is ongoing for an alternative booster drug; however, there are several expected side effects such as diarrhea with even low-dose ritonavir, and some patients just do not feel well when taking it. However, low-dose ritonavir has made a profoundly important impact by improving the efficacy and durability of PI-based HAART. —Cal Cohen, MD

**Activist**

A necessary evil—without Norvir, many PIs would be useless or have a much less convenient dosing schedule. But the GI side effects (diarrhea, gassiness, stomach cramping, and did I mention diarrhea?) can destroy quality of life for many. With a list of drug interactions longer than some phone books, it’s a daunting drug to add to the multiple meds many HIVers have to take. Even though the Norvir contained in Abbott’s PI Kaletra has long been available in a non-refrigerated Meltrex formulation, it took years for them to do the same thing for the just-approved Meltrex version of Norvir. Can we say “preserve Kaletra’s marketshare”? Additionally, Abbott’s egregious pricing history has made this a justly maligned drug—with many hoping for a new booster to replace it altogether so they can celebrate its demise. —Jeff Taylor
**PROTEASE INHIBITOR**

**Common Name:** darunavir (formerly TMC114)

**Brand Name:** Prezista

**Class:** HIV protease inhibitors (PIs)

**Standard dose:** 800 mg (two 400 mg tablets) once daily for first-time therapy or 600 mg (one 600 mg tablet) twice a day for treatment-experienced adults. All doses must be taken with 100 mg Norvir and food. 75 mg and 150 mg tablets available for children over six, dose based on weight. Missed dose as soon as possible, but not if more than 12 hours late on the once-daily dose (or six hours late on the twice-daily dose). Do not double up on your next dose; take the next dose on schedule.

**AWP:** $1,102.20 / month

**Manufacturer contact:** Tibotec Therapeutics, www.prezista.com, 1 (877) REACH-TT (732-2488)

**Potential side effects and toxicity:** Prezista may cause mild to moderate rash, but the most common side effects may include diarrhea, nausea, headache, and abdominal pain. Laboratory testing for liver function should be done before starting therapy and patients should be monitored. Increased monitoring should be considered for people with underlying chronic hepatitis, cirrhosis, or elevated levels of AST/ALT (lab measures of liver function), especially during the first several months of therapy. No dose adjustment is necessary for those with mild to moderate liver disease, but Prezista/Norvir is not recommended for people with severe liver impairment. Severe rash, while very rare, can be life-threatening. Seek medical attention immediately. You may need to stop all medications. Prezista contains a sulfa component and should be used cautiously by people with sulfa allergies.

As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides, although cholesterol changes were similar to those seen with Reyataz in a study of uninfected participants, and better than those seen with Kaletra in two head-to-head studies. Increased cholesterol and triglycerides may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts, and upper back), onset of new cases or worsening of diabetes (see your doctor promptly) and increased bleeding in hemophiliacs. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

**Potential drug interactions:** Do not take with oral midazolam, triazolam (Halcion), ergot derivatives (D.H.E. 45, Migrale, Cafergot, Ergomar, ergonovine, methylergonoine), or the herb St. John’s wort, Cisapride, pimozide (Orap), and rifampin. Prezista may cause decrease in the levels of phenytoin (Dilantin) and phenobarbital (seizure medications); blood levels of these anticonvulsants should be monitored. A similar recommendation applies to the anticonvulsant carbamazepine (Tegetrol). A reduced dose of rifabutin is recommended. Do not use Advicor, Altoprev, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution. The antifungal drugs such asitraconazole and ketoconazole may increase levels of Prezista, and Prezista may increase theirs, so caution must be exercised when used together (maximum dose is 200 mg a day for the antifungals). Blood levels of voriconazole (Vfend) may decrease. Voriconazole should not be administered unless benefit/risk justifies its use.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Prezista may increase levels of blood pressure medications called calcium channel blockers, such as Norvasc and others, and clinical monitoring of patients is recommended. A lower dose of trazodone and desimprimine is recommended. Monitoring may be required when using Coumadin (warfarin), or immunosuppressants. Increased levels of the inhaled and nasal sprays with fluticasone (found in Advair, Floanse, and Flovent) can occur and therefore alternatives should be considered, particularly for long-term use. Effectiveness of birth control pills may decrease. Alternative or additional methods contraception with barrier should be used. No dosing adjustment required with Subutex or Suboxone, but monitoring is recommended.

**Tips:** Prezista is one of two recommended PI for initial therapy in treatment-naive patients in the U.S. DHHS HIV guidelines. Tibotec received community kudos for not pricing Prezista higher than other new PIs. Please see package insert for more complete potential side effects and interactions.

**DOCTOR**

Prezista (darunavir) co-administered with ritonavir was approved in 2006 for treatment of HIV infection in antiretroviral treatment-experienced adults whose HIV had developed resistance to the PI class. At that time, there was considerable importance to this property, as a large number of people were in care whose HIV could not be fully suppressed with the PIs that were available. When this new PI became available, a much larger number of people could re-establish virologic suppression—particularly when it was taken with two other newer antivirals that became available soon after. The contribution of this drug to prolonging many people’s lives was also notable in that, in general, people had few side effects on it. As a result of this safety profile, as well as high degree of activity, in 2008 Prezista was also approved for once-daily dosing in those individuals just starting HIV therapy. The 2009 DHHS Guidelines Panel elevated once-daily ritonavir-boosted darunavir to one of the four preferred PI combinations for treatment of HIV infection, which was done at the same time that lopinavir/ritonavir was listed instead as an alternative rather than preferred choice. This was justified in part by a study comparing Kaletra to Prezista which showed that while these two antivirals are similarly successful in patients who adhere to treatment, Kaletra was less successful than Prezista in maintaining suppression in those who miss doses over time. While it is ideal to take each dose each day, it is clear that this is not necessarily something everyone can do, and that has led to consider the use of Prezista given its better “forgiveness” for missed doses. It must be taken with food once daily, but as most people eat at least once daily, this is a small factor to consider. Overall, many people taking it feel well on it, and there are few expected lab toxicities noted. It is important to note, however, that a small number of people can have a severe rash when starting it, and a small number have been reported to have liver function test changes, making it important to monitor this drug soon after starting it. In all, Prezista has become an increasingly popular choice in people selecting their first PI. —Cal Cohen, MD

**ACTIVIST**

Versatile Prezista is a preferred regimen for both treatment-naive patients as well as those who have PI resistance (albeit at different dosages). With fewer pills and less Norvir boosting than Aprotivus, it is much better tolerated for those with PI resistance. For treatment-naives, it is fast replacing Kaletra as a durable and well tolerated PI-based regimen. Its maker, Tibotec, has earned praise from the community for bucking the trend of pricing new protease inhibitors ever higher, and for its groundbreaking trial of Prezista called GRACE that included primarily women and people of color, setting the bar for other companies to follow. —Jeff Taylor
you must take them with the 400 mg Reyataz/100 mg Norvir dose for er. If taking with Viread or Truvada than 20 mg twice a day if treatment-experienced or 40 mg twice a day Norvir. H2-receptor antagonists like Pepcid may be taken (no more D.H.E. 45), pimozide, Crixivan, or St. John’s wort. Do not use Advi-nor with the acid reflux) (see your doctor promptly), and increased bleeding in hemophilics. Immune potential side effects and interactions.

Potential drug interactions: Treatment-experienced people cannot take with proton pump inhibitors (PPIs—long-acting medicine for acid reflux). Treatment-naive people can take a PPI with a dose comparable to Prilosec OTC 12 hours before their Reyataz/Norvir. H2-receptor antagonists like Pepcid may be taken (no more than 20 mg twice a day if treatment-experienced or 40 mg twice a day if treatment-naive, or equivalent doses) at the same time as Reyataz/Norvir (before the antacid has started to work) or at least 10 hours lat-er. If taking with Viread or Truvada and an H2-receptor antagonist, you must take them with the 400 mg Reyataz/100 mg Norvir dose for treatment-experienced people. When taking Reyataz without Norvir, dose can be taken at least two hours before and at least 10 hours after Pepcid, Zantac, or Axid. Reyataz should be taken two hours before or one hour after antacids (Rolaid, Tums, and Mylanta). Do not take with rifampin, Camptosar (irinotecan), Versed (midazolam), Hal-cion, ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), pimozone, Crixivan, or St. John’s wort. Do not use Advic-or, Altopen, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution.

Must be taken two hours apart from Videx, due to Videx’s buf-soluble medicines. Increased levels of the inhaled and nasal sprays with fluticasone (found in Advair, Flonase, and Flovent) can occur and should be used with caution. Effectiveness of birth control pills may be decreased, alternative or addition-al contraception with barer should be used. Oral contraceptive should contain no more than 30 mcg of ethinyl estradiol if taking Reyataz without Norvir and at least 30 mcg if taken with Norvir. Use caution when using itraconazole or ketoconazole. Viend is not recommended. Reducing dose and frequency of rifabu-tin to 150 mg every other day or three times a week is recommended. Use caution with anti-convulsants: Tegretol (carbamazepine), pheno-barbital, and Dilantin (phenytoin). Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Calcium channel blockers should be monitored. A lower dose of trazodone is recommended.

Tips: Boosted Reyataz is one of two protease inhibitors recom-mended by the U.S. HIV treatment guidelines for people on antiviral therapy for the first time. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Reyataz (atazanavir) was approved for use in combination with other antiretrovirals in 2003, and was the first protease inhibitor to be approved for once-daily dosing. While it could be taken without the ritonavir boost, atazanavir boosted and unboosted were com-pared head to head in a study done a few years ago, and it was ob-served that boosted atazanavir had enough advantages both in terms of an increased likelihood of suppression, as well as minimizing the risk of resistance in those whose viral load was not fully suppressed. Since then, studies have pursued ways in which treatment could be started with boosted atazanavir and, after achieving virologic suppression, the ritonavir could be removed and the people would re-main on unboosted atazanavir instead. This approach is still under-going exploration. However, the combination of boosted atazanavir plus Truvada once daily is among the more commonly selected first regimens in the U.S. Atazanavir is often well tolerated with low rates of GI side effects such as diarrhea, but there are two issues of note: one is that yellow discoloration of the skin and eyes can occur in perhaps one out of 10 who take the drug. It is important to note that this coloration is a “cosmetic” concern, since the reason it occurs is an increase in the blood levels of a normal substance called indirect bilirubin and such increases are not known to be harmful. Second, this drug requires stomach acid for absorption and there are dosing recommendations for those who require the use of acid-reducing medications to minimize their impact on atazanavir levels. There are advantages to this PI versus most of the others in having less of an impact on lipid (cholesterol) levels, and it has several favorable at-tributes which contribute to why it is now considered by the 2009 DHHS guidelines to be one of the two preferred PIs to consider for initial use. —Cal Cohen, MD

ACTIVIST

The first once-a-day protease inhibitor, Reyataz remains—with Prezista—one of the two most popular PIs. It can also be taken without a Norvir boost—though it should be taken with food if un-boosted. This can help avoid many of the Norvir-associated prob-lems—diarrhea, raised cholesterol and triglyceride levels, and fat accumulation (aka PI belly). The yellowing of the skin and/or eyes can be disconcerting, but isn’t dangerous, and will go away when you stop the drug, if it doesn’t improve over time on therapy. Another drawback for some is that it can’t be taken with the proton-pump inhibitors popular for controlling acid reflux, although there are op-tions, like Pepcid, to which you can switch. —Jeff Taylor
**PROTEASE INHIBITOR**

Common Name: nelfinavir  
Brand Name: Viracept  
Class: HIV protease inhibitors (PIs)  
Standard Dose: 1,250 mg taken as either two 625 mg tablets or five 250 mg tablets twice daily with food. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose. Viracept Oral Powder also available for children and individuals unable to swallow tablets.

AWP: $796.99 / month for 250 and 625 mg tablets  
Manufacturer Contact: ViiV Healthcare, 1 (877) 844-8872

**Potential Side Effects and Toxicity:** Most common include diarrhea (15–20% of patients), stomach discomfort, nausea, gas, weakness, and rash. People with phenylketonuria should be aware that the powder contains phenylalanine. As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts, and upper back), onset of new cases or worsening of diabetes (see your doctor promptly), and increased bleeding in hemophiliacs. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

**Potential Drug Interactions:** Viracept increases levels of Invirase and Crixivan (see Crixivan for potential drug interactions), so dose adjustments may be needed. Do not take with Versed (midazolam), Cordarone (amiodarone), Halcion (triazolam), Rifadin (rifampin), Prilosec-OTC (omeprazole), ergot derivatives (such as Cafergot, D.H.E. 45, Methergine, Wigraine), garlic supplements, or the herb St. John’s wort. Do not use Advicor, Altoprev, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high lipids. Lipid-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution. Viracept may decrease methadone levels but withdrawal rarely occurs; methadone doses may need to be increased. Use calcium channel blockers with caution.

Blood levels of Viracept are reduced by rifampin and may be reduced by phenobarbital, phenytoin, and carbamazepine (Tegretol and others), so it is important to inform your doctor if you are taking any of these medications. Mycobutin (rifabutin) dose must be decreased when used with Viracept. Prescriber may need to adjust doses of any of these drugs accordingly.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Increased levels of the inhaled and nasal sprays with fluticasone, a steroid for asthma or allergies (found in Advair, Flonase, and Flovent), can occur and therefore should be used with caution. The effectiveness of birth control pills may be decreased; alternative or additional methods of contraception with barrier should be used. Also, increased levels of trazodone can occur and this combination should be used with caution. A lower dose of trazodone is recommended.

**Tips:** This is the only protease inhibitor that is never used with Norvir. Do not leave the pharmacy without anti-diarrhea meds such as Imodium, or Tums or other calcium products. Taking a 500 mg calcium supplement with doses hugely decreases diarrhea. Also try Solgar oat bran tablets, psyllium husk fiber bars, and pancreatic enzymes (all with meals). As an extra precaution, take a change of clothes with you everyday for the first several weeks—stick it out, most often, symptoms improve after two or three weeks. The oral powder tastes horrible and requires a large amount for mixing into food.

People using Viracept can crush adult tablets or dissolve tablets in a small amount of water. Mixing Viracept with acidic food or juice (e.g. orange/apple juice or apple sauce) is not recommended, due to resulting bitter taste. To get the full benefit of Viracept by increasing its level in the body, it must be taken with a meal. Please see package insert for more complete potential side effects and interactions.

**Doctor**

Viracept (nelfinavir) was approved for use in combination with other antiretroviral drugs in the treatment of HIV infection in 1997. In 2003, the dosage formulation of nelfinavir was simplified to two tablets twice daily. The level of drug in the bloodstream was adequate only when it was taken with food and this was one factor leading to the results of studies showing lower rates of virologic suppression versus other choices that were not as reliant on food to be adequately absorbed. It was initially a very popular drug when first released, as it was better tolerated than the other choices that were available at that time. However, when the boosted PI Kaletra demonstrated a better rate of achieving virologic suppression, there was less enthusiasm in relying on this unboosted PI. Diarrhea is its most prominent problem occurring in many, though not all, who take it. With the availability of other protease inhibitors that have both more reliable efficacy in virologic suppression, plus better tolerability and fewer pills to take, nelfinavir use has significantly decreased. —Cal Cohen, MD

**Activist**

The best thing you can say about Viracept is that it’s a good protease inhibitor to fail, as you can still be rescued by another boosted PI. Other than that, given the explosive blue diarrhea, there’s little left to recommend this drug anymore. The one exception is for women trying to conceive, as it’s one alternative PI recommended to prevent mother-to-child HIV transmission. (Although the aforementioned diarrhea might prove a disincentive to conception, let alone nine months of pregnancy.) —Jeff Taylor
**Common Name:** enfuvirtide or T-20  
**Brand Name:** Fuzeon  
**Class:** HIV fusion inhibitor (a type of entry inhibitor)  
**Standard dose:** One subcutaneous (under the skin) injection of 90 mg (1 ml) twice daily (every 12 hours) into the upper arm, thigh or abdomen. This can be taken with or without food, with no food restrictions. Take missed doses as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.  
**AWP:** $2,973.04 / month for 90 mg kit  

**Potential side effects and toxicity:** The most common are Injection Site Reactions (ISRs), which occur in virtually all patients. The severity of reaction is variable, and for most is mild to moderate. Symptoms could include itching, swelling, redness, pain or tenderness, hardened skin or bumps. Bumps termed “nodules” seem to occur more frequently and severely in areas of high muscle mass (most notably the center of the stomach—the abs—and the legs). They will hurt with movement. Other side effects may include diarrhea, nausea, and fatigue. Hypersensitivity (allergic-like) reactions are possible. In studies, pneumonia happened more often in the patients on Fuzeon. It is unclear if this was related to the use of Fuzeon, so report cough, fever, or trouble breathing to your health care provider immediately. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

**Potential drug interactions:** To date, none that are clinically significant have been found.

**Tips:** With other powerful, newer drugs on the market, the twice-daily injectable Fuzeon has truly become a medicine of last resort. In fact, some specialists have been taking patients off Fuzeon and putting them on newer drugs, like Isentress. Several studies have shown good results with this strategy. Fuzeon is intended for treatment of HIV in patients who are treatment-experienced. Store it at room temperature. Preparing and injecting the Fuzeon can be complicated, so ask your health care provider how to do it. First, the drug needs to be dissolved with sterile water (provided in the kit), which may take up to 45 minutes. Never shake the vial with the Fuzeon, it will foam. Instead, roll it gently in your hands. You can store your second dose in the refrigerator, but it must be used within 24 hours (allow it to warm to room temperature before using). Before injecting, it is important to make sure that the Fuzeon powder is completely dissolved. To minimize injection site reactions, inject where you can pinch an inch (upper arm, stomach, or thigh). If not, then be sure to use half the length of the needle. Inject slowly and apply a gentle massage after injection. Try using vibrating devices after injections. Follow proper hygiene instructions to avoid infection. ISR may worsen when injection is repeated in the same spot or given deeper than intended, for example, into the muscle. Always rotate injection sites frequently. Never inject into moles, scars, bruises, nodules, or the navel. Switching to smaller needles, like insulin syringes, may also help with ISRs. Fuzeon can be taken at the same time as other anti-HIV drugs.

Fuzeon is the first and only anti-HIV compound on the market called a fusion inhibitor. Fusion inhibitors block fusion of HIV with a cell before the virus enters the cell and begins its replication process. Fusion inhibitors are a type of entry inhibitor, another one of which is in the pharmacy (Selzentry, taken orally). Because of injections, Fuzeon will most likely be used in the heavily treatment-experienced and salvage therapy options. U.S. HIV treatment guidelines support the use of Fuzeon with an active boosted protease inhibitor in patients who are heavily treatment-experienced. The guidelines supported the approach as it resulted in better and more prolonged virologic suppression than other regimens. Evidence included several studies of new boosted protease inhibitors in treatment-experienced patients which found an enhanced virologic response when used in conjunction with Fuzeon. This reinforces the principle of using two or more active drugs, if possible, when changing therapy, to make it more effective. Please see package insert for more complete potential side effects and interactions.

**DOCTOR**

Fuzeon (enfuvirtide, also known as T-20) was approved as a twice-daily injection for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2003. Fuzeon was the first drug approved in the class of antiretrovirals called “entry inhibitors.” Since this class of drugs stops the virus from entering the CD4 cell, they were a significant step forward for HIV therapy, especially for those whose HIV was no longer fully susceptible to the drugs in the other classes. Studies done with this drug clearly and consistently demonstrated that when it was added to a new combination of one or two other newer drugs, the rate of re-establishing virologic suppression was enhanced. Nevertheless, the need to take this drug as a (self-administered) injection twice daily led to a rapid fall off in its use as soon as there were enough medications that were similarly active and taken in the usual way (by mouth). Even though there was exploration of novel “needleless” injection devices, there is very little current enthusiasm to use this drug as long as enough active “oral” medications are available. —Cal Cohen, MD

**ACTIVIST**

The first entry inhibitor, Fuzeon has become the drug of last resort for patients with multiple drug resistance who have run out of options. Being in a new class, it’s guaranteed to be effective for salvage patients who need to construct a new regimen—and the recent approval of both Isentress and Integrelin means that many have been able to construct an effective regimen and reach undetectable for the first time. The drawback, of course, is the twice-daily injections—which can result in painful injection site reactions that can take so long to heal that some patients literally run out of available skin to inject. But the drug is literally a lifesaver, and even when added to a failing regimen, Fuzeon seems to help boost T-cell counts—buying time until more new drugs become available. —Jeff Taylor
**ENTRY INHIBITOR**

**Common Name:** maraviroc (formerly UK-427,857)

**Brand Name:** Selzentry

**Class:** CCR5 antagonist (a type of entry inhibitor)

**Standard Dose:** Available in 150 mg and 300 mg tablets. Can be taken with or without food, with no food restrictions. The recommended dose varies depending on other medications the patient is taking: 150 mg twice daily if taken with a protease inhibitor (except for Aloe) and Rescriptor; 300 mg twice daily if taken with Aloe and Viramune, Fuzon, and all of the NRTIs; 600 mg twice daily if taken with Sustiva, Intelect, rifampin, and some anti-convulsant medications such as phenobarbital, phenytoin, and carbamazepine.

Default to Selzentry 150 mg twice daily when combined with a CYP3A inhibitor dose (the PI group) if using medications from multiple classes (such as a PI with a NNRTI). Concurrent use of Selzentry and other medications that can either inhibit or induce liver metabolism will affect the dose of Selzentry. Your doctor or pharmacist can determine which medications will affect Selzentry.

**AWP:** $1,101.42 / month for 150 mg or 300 mg tablets

**Manufacturer Contact:** ViiV Healthcare, 1 (877) 844-8872

**Potential Side Effects and Toxicity:** Most common include cough, fever, cold, rash, muscle and joint pain, stomach pain, and dizziness. Other potential side effects may include liver toxicity; an allergic reaction may happen before the liver problems. It is recommended Selzentry be stopped and your doctor contacted right away if you develop a rash, yellowing of your eyes or skin, and/or dark urine, vomiting, and upper stomach pain. Other rare side effects may include low blood pressure when standing up that could lead to dizziness or fainting. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider. While no increased risk of infections or cancer was seen in clinical trials, Selzentry affects other immune system cells and could possibly increase the risk of infections and cancer.

**Potential Drug Interactions:** Not recommended with rifampin or St. John's wort. Dose adjustment needed for Biaxin, Dilantin (phenytoin), HIV NNRTIs and PIs, itraconazole, Mycobutin, Nizoral (ketoconazole), oral contraceptives, phenobarbital, rifampin, Tegretol (carbamazepine), Versed (midazolam), and Viend.

**Tips:** Maraviroc is the first oral entry inhibitor available on the market. It is indicated for the treatment-experienced patient infected only with CCR5-tropic virus. Complex dosing, the need for an expensive tropism test, and competition from recently, or soon to be, approved drugs however, have dimmed some of the initial enthusiasm for this drug.

**Viral Tropism** refers to the types of HIV that a person can have: CCR5-tropic (R5) virus and CXCR4-tropic (X4) virus. (Tropism is pronounced with a long “o,” as in “okay.”) HIV latches on to the CD4 receptor on the surface of some human T-cells (hence, CD4+ T-cells), and then it latches on to one of the two co-receptors on the surface of the cells, CCR5 (R5) or CXCR4 (X4). These two chemokine co-receptors basically invite HIV to come inside. As the name “CCR5 inhibitor” suggests, Selzentry inhibits (blocks) CCR5, shutting down this point of entry for the virus. (The co-receptor inhibitors are also called “antagonists,” as in “CCR5 antagonist.”) X4 virus is associated with advanced HIV disease. HIV infection may involve viruses that infect only CCR5 cells, only CXCR4, both of these types of cells (dual tropic), or a mix (mixed tropic). Most people are infected with CCR5 virus, and then over time more CXCR4 and mixed viruses accumulate. In results from various studies, Pfizer did not find that blocking R5 with maraviroc caused virus to shift to X4 or show negative effect on disease progression or CD4 count in so-called “dual tropic” people (their virus can use either R5 or X4). In 2007, the company reported that a switch to X4- or dual-tropic virus was transient and reversible when people went off maraviroc. In studies with treatment-experienced people, a large number of patients were excluded because they did not have exclusive CCR5-tropic virus, limiting the number of patients who could truly benefit from this drug. A sub-analysis reported that Selzentry seems to have minimal impact on lipid levels. Selzentry has been studied in treatment-naive patients (first time on therapy) in the MERIT clinical trial. Although the initial analysis suggested that Selzentry was unable to match Sustiva at viral loads less than 50 copies, a re-analysis of the data using the enhanced Trofile test (Trofile ES) showed the regimens to be comparable (59% for Selzentry vs. 63% for Sustiva in less than 50 copies at 96 weeks). The follow-up results of 96-week data led to it’s FDA approval for this population. Other CCR5 inhibitors are in the works. Please see package insert for more complete potential side effects and interactions.

**Doctor**

Selzentry (maraviroc) was approved (one tablet twice daily without any food restriction) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2007. This antiretroviral is the first oral entry inhibitor produced. The mechanism of how it works is unique among other approved antivirals—it blocks a cell surface receptor called CCR5—which is one of two pathways that HIV uses on cell surfaces to attach to and subsequently enter cells. In someone who has a test showing their virus population uses CCR5, this drug is likely to be fully active. However, as with resistance testing, tests can miss very small amounts of virus populations that use the other cell receptor (CXCR4), and this drug shows no activity in blocking those virus populations. While it was initially approved only for those who were already treatment-experienced, as it improves the rate of virologic suppression, re-analyses of the study done using maraviroc as part of a first regimen recently led to FDA approval for its use as part of the first combination. Nevertheless, there is ongoing ambiguity about the degree of enthusiasm for this drug as part of a first regimen. The 2009 DHHS guidelines state that there was insufficient data available at the time of writing their most recent update to decide what recommendation to offer for this drug for initial treatment. However, to date, it has been shown to be a safe drug with few side effect concerns. Maraviroc also interacts with a number of PIs and ritonavir and thus must be dose adjusted depending on the other antiretrovirals. —Cal Cohen, MD

**Activist**

The second comer to the entry inhibitor class, Selzentry is technically a CCR5-antagonist—meaning it only works against HIV that binds to the CCR5 receptor on T-cells. Finding out if you have this type of virus requires an expensive “tropism test” that may or may not be covered by your insurance. Add to that a complicated dosing depending on what other HIV meds you’re taking, and this becomes a drug that neither doctors nor patients want to bother with unless they have to. Unfortunately, the sickest patients who could benefit the most from this new drug are less likely to have the pure CCR5 virus that Selzentry would work against. —Jeff Taylor
**Common Name:** raltegravir (formerly MK-0518)  
**Brand Name:** Isentress  
**Class:** HIV integrase inhibitor (also called integrase strand transfer inhibitor or INSTI)  
**Standard dose:** One 400 mg film-coated tablet twice a day. Can be taken with or without food, with no food restrictions. Take missed dose as soon as possible, unless it is almost time for your next dose. Do not double up on your next dose.  
**AWP:** $1,074.64 / month  
**Manufacturer Contact:** Merck and Co., www.isentress.com, 1 (800) 622–4477

**Potential side effects and toxicity:** Very tolerable, but most common were diarrhea, nausea, headache, and fever. Less common were abdominal pain, vomiting, fatigue, weakness, dizziness, and lipodyrophy. Other observations with unclear relationship to Isentress include cancer (new and recurrent, though most patients had other risk factors for cancer), low white blood cell count (neutropenia), low platelets, and elevated liver enzyme levels. May cause elevated levels of a muscle enzyme (creatinine kinase) on blood tests. Contact your health care provider if you experience unexplained muscle pain, tenderness, or weakness. May cause hypersensitivity (allergic reaction), anemia, neutropenia, and gastritis. Increases in ALT, AST, and total bilirubin, all signs of liver toxicity, seen in around 8% of people taking Isentress. Increases were more likely in people also infected with hepatitis B or C. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.  

**Potential drug interactions:** Aptivus/Norvir can also decrease the concentrations of Isentress, but no clinically significant interaction was observed from the clinical studies in patients receiving both drugs. Dose adjustment is not required. Reyataz and Reyataz/Norvir increase blood levels of Isentress, but no dose adjustment is recommended. Use caution with rifampin, which reduces plasma concentrations of Isentress. Prilosec (omeprazole) can increase concentrations of Isentress, but no dose adjustment is recommended. There is no interaction with methadone.  

**Tips:** This star continues to shine bright. In July, Isentress became indicated for treatment in naive patients (those who have never been on HIV therapy). In December 2009, U.S. HIV guidelines added Isentress along with a Truvada backbone as a preferred regimen for treatment-naive patients. The guidelines noted drawbacks: twice-a-day dosing, lack of long-term data, and a lower barrier to drug resistance than seen with boosted PIs. Greater tolerability, however, may help overcome those issues. Also, it’s only one tablet per dose, and does not have to be taken with the dreaded Norvir, the way PIs are. The lack of long-term data is due to the relative newness of Isentress. Moreover, it is from a new drug class. Still, Isentress was on the market in 2007, and there has been no word from the community about toxicity, which came about much earlier with other drugs and drug classes. Last year, Isentress did something no other HIV drug ever did: it dropped viral load to undetectable in more than a whopping 90% of treatment-experienced people, out to one full year. Undetectable viral load is more difficult to achieve in this population than in people on HIV therapy for the first time. The results were exciting, but from a small study of only 103 individuals in the French ANRS 139 TRIO trial. Isentress was taken with Prezista and Intelence, a novel, nuke-sparing combination. The data is in accord with the advocate view that advanced patients are having dramatic results and almost no side effects. Many people on long-time therapy became undetectable for the first time. One doctor reported that patients at his clinic could not believe they had received Isentress instead of placebo during studies. Isentress is exciting for several reasons. This is one of the truly new drugs that advanced patients are in such desperate need of. A big plus: 48-week results show cholesterol and triglyceride blood levels have not been a problem with Isentress. Moreover, it has no drug interactions with lipid-lowering medications the way PIs do.

**ACTIVIST**

The first in its class, and fast becoming the fair-haired darling of new HIV drugs, Isentress has been accorded preferred status for both treatment-experienced and treatment–naive patients. This drug has been a lifesaver for many who had run out of options, and with virtually no side effects, it is fast becoming a favorite for patients who want to switch to a more tolerable regimen without the CNS, GI, or lipid problems of the more common HIV meds. The only minor drawback is the fact that it must be taken twice daily. Other integrase inhibitors in the pipeline will offer once-daily dosing, but require Norvir or another booster. —Jeff Taylor

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**DOCTOR**

Isentress (raltegravir) was approved (one tablet twice daily without food restrictions) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2007. It is approved for use both as part of a first combination as well as for those who are treatment-experienced. It has shown great success in both settings. Raltegravir is the first drug approved in a new class of antiretrovirals called integrase inhibitors. There was a significant impact of this drug for those whose HIV had developed resistance to other drugs, since the use of raltegravir in various combinations of two other active drugs led to re-establishing virologic suppression in nearly everyone who took it. Furthermore, the studies of this agent in starting treatment showed that it was as successful as a combination based on efavirenz—and this is one reason why the current DHHS guidelines list the combination of Truvada and raltegravir as one of four preferred initial combinations when starting treatment. While the long-term adverse effects of raltegravir are not yet fully known, given this is among the newer drugs in the field, there are several years of experience with this drug and all of the current data clearly supports that this is very well tolerated by most, though not all, people who take it. The current focus of research for this drug is to assess how well it works when taken once daily instead of twice daily—early reports are encouraging, but large studies are underway to be more confident about this simpler dosing schedule. —Cal Cohen, MD
A quick guide to HIV drug interactions

Please see the drug’s page for details, or refer to the manufacturer’s package insert for a full comprehensive list of potential drug interactions. Also, make your pharmacist and health care providers aware of any drug that you add. Some interactions are more serious than others; some drugs may only require a dose adjustment, while others may either render the drug completely ineffective, or worse, lead to a potentially fatal reaction. Discuss any changes, however minor, with your health care providers, including your pharmacist, since small reactions may become serious. Look up your drugs with “Check my meds” at www.aidsmeds.com, which lists the effect of food as well as interactions for medications. The University of Liverpool also has an interactive database that allows you to look up antiretroviral drug interactions and has PDF charts of interactions between antiretrovirals and other drugs. Remember, brand names are usually capitalized, while generic names are not. Visit www.hiv-druginteractions.org.

### Nucleoside Reverse Transcriptase Inhibitors (also called nucleoside analogs, NRTIs, or nukes)

<table>
<thead>
<tr>
<th>Potential drug class interactions</th>
<th>None.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combivir (Retrovir and Epivir)</td>
<td>See Epivir and zidovudine (Retrovir). Do not take zidovudine (Retrovir), Epivir, Epivir-HBV, Epzicom, Trizivir, Emtriva, Truvada, or Atripla while taking Combivir, since all or part of these medications are already in Combivir or have equivalent medications.</td>
</tr>
<tr>
<td>Emtriva (emtricitabine, or FTC)</td>
<td>No significant drug interactions. Do not take Truvada, Atripla, Epivir, Epivir-HBV, Epzicom, Combivir, or Trizivir while taking Emtriva, since they contain Emtriva or medication equivalent to it.</td>
</tr>
<tr>
<td>Epivir (lamivudine, or 3TC)</td>
<td>No significant drug interactions. Do not take Epivir-HBV, Epzicom, Combivir, Trizivir, Truvada, Emtriva, or Atripla while taking Epivir, since they contain Epivir or medication equivalent to it.</td>
</tr>
<tr>
<td>Epzicom (Epivir and Zidovudine)</td>
<td>See Epivir and Zidovudine. Do not take Combivir, Epivir, Epivir-HBV, Trizivir, Emtriva, Truvada, or Atripla while taking Epivir, since all or part of these medications are already in Epzicom or have equivalent medications.</td>
</tr>
<tr>
<td>Retrovir (zidovudine, or AZT)</td>
<td>Do not take with Combivir or Trizivir, since zidovudine is already in these medications. Amphotericin B, Benemid, Biaxin, dapsone, Depakote, doxorubicin, flucytosine, ganciclovir, hydroxyurea, interferon-alpha, methadone, Mycobutin, pentamidine, phenytoin (Dilantin), ribavirin, rifampin, sulfadiazine, Valcyte, and Zerit.</td>
</tr>
<tr>
<td>Trizivir (Epivir, Retrovir, and Zidovudine)</td>
<td>See Epivir, Retrovir, and Zidovudine. Do not take zidovudine (Retrovir), Epivir, Epivir-HBV, Epzicom, Zidovudine, Emtriva, Truvada, or Atripla while taking Trizivir, since all or part of these medications are already in Trizivir or have equivalent medications.</td>
</tr>
<tr>
<td>Truvada (Viread and Emtriva)</td>
<td>See Emtriva and Viread. Do not take with Emtriva, Viread, Atripla, Epivir, Epivir-HBV, Combivir, Epzicom, or Trizivir, since all or part of these medications are already in Truvada or have equivalent medications.</td>
</tr>
<tr>
<td>Videx &amp; Videx EC (didanosine, or ddl)</td>
<td>Alcohol, allopurinol, cimetidine, dapsone, ganciclovir, HIV protease inhibitors, hydroxyurea, itraconazole, ketoconazole, methadone, pentamidine, Rescriptor, Retrovir, ribavirin, valganciclovir, Viread, and Zerit.</td>
</tr>
<tr>
<td>Viread (Tenofovir)</td>
<td>Do not take with Truvada or Atripla, since Viread is in these medications. Hepsera, Kaletra, Norvir, Reyataz, Videx and Videx-EC.</td>
</tr>
</tbody>
</table>
| **Zerit**  
(stavudine, or d4T) | Amphotericin B, dapsone, foscarnet, ganciclovir, pentamidine, Valcyte, Videx and Videx-EC, and zidovudine (AZT, Retrovir). |
| **Ziagen**  
(abacavir sulfate) | Do not take with Epzicom or Trizivir, since Ziagen is already in these medications. Alcohol and methadone. |

### Non-Nucleoside Reverse Transcriptase Inhibitors  
(Also called non-nucleoside analogs, NNRTIs, or non-nukes)

| Potential drug class interactions | Anti-convulsants; HIV protease inhibitors; methadone. |
| **Intelegence**  
(etravirine, or TMC-125) | Aptivus/Norvir, Biaxin, diazepam, Dilantin (phenytoin), Kaletra, Lexiva/Norvir, Mycobutin, Norvir, phenobarbital, Rescriptor, Reyataz/Norvir, rifampin, Selzentry, St. John’s wort, Sustiva, Tegetrol (carbamazepine), Viramune, warfarin, and unboosted (without Norvir) PIs. |
| **Rescriptor**  
(delavirdine) | Agenerase, amlopidine, certain amphetamines and antiarrhythmic drugs, Biaxin, birth control pills, Cialis, Crixivan, dapsone, Dilantin (phenytoin), ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), felodipine, fluticasone (Advair, Flonase, Flovent), immunosuppressants, Intelegence, Invirase, Kaletra, Levitra, Lexiva, methadone, lovastatin, midazolam, Mycobutin, nifedipine, Norvir, phenobarbital, pimozone, Propulsid, quinidine, Reyataz, rifampin, simvastatin, St. John’s wort, Tegetrol (carbamazepine), trazodone, triazolam, Viagra, Viracept, Vytorin, warfarin, and Xanax (alprazolam). |
| **Sustiva**  
(efavirenz) | Do not take with Atripla, since Sustiva is already in Atripla. Bepridil, Biaxin, birth control pills, bropionon, Crixivan, Dilantin (phenytoin), diltiazem, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), Gingko biloba, Invirase, itraconazole, Kaletra, Lexiva, Lipitor, methadone, midazolam, Mycobutin, Norvir, pravastatin, Reyataz, rifampin, phenobarbital, pravastatin, simvastatin, St. John’s wort, Tegetrol (carbamazepine), triazolam, VIend, warfarin, and Zoloft. |
| **Viramune**  
(nevirapine) | Biaxin, birth control pills, calcium channel blockers (Adalat, Norvasc, Procardia, and others), clonazepam, Cordarone, Dilantin (phenytoin), disopyramide, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), ethosuximide, flucanozole, HIV protease inhibitors, immunosuppressants, Kaletra, ketoconazole, lidocaine, methadone, midazolam, Mycobutin, phenobarbital, prednisone, Reyataz, rifampin, St. John’s wort, Tegetrol (carbamazepine), triazolam, and warfarin. |

### Dual-class Fixed Dose Combination

| **Atripla**  
(Sustiva/Truvada) | See Sustiva and Truvada (Emtriva/Viread). Do not take Sustiva, Emtriva, Truvada, Viread, Epivir, Epivir-HBV, Epzicom, Combivir, or Trizivir, while taking Atripla, since all or part of these medications are already in Atripla or have equivalent medications. |

### Protease inhibitors (PIs)

| Potential drug class interactions | Cardiac medications, cholesterol medication, dexamethasone, migraine medications, erectile dysfunction drugs, sedatives, and tuberculosis drugs. |
| **Aptivus**  
(tipranavir)  
(must be taken with Norvir) | Aptivus/Norvir interacts with many other drugs, so it is important to tell your health care professional all the medications you are taking. See the manufacturer package insert for the most complete list. Advicor, Altoprev, antacids, birth control pills, bropionon, calcium channel blockers (Adalat, Norvasc, Procardia, and others), Cialis, Crestor, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), disulfiram (Antabuse), Flagyl, flucanozole, fluticasone (Advair, Flonase, Flovent), Fuzeon, other HIV protease inhibitors, immunosuppressants, Intelegence, itraconazole, ketoconazole, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam, Mycobutin, Paxil, phenobarbital, phenytoin (Dilantin and others), pimozone, pravastatin, quinidine, rifabutin, rifampin, Rythmol, simvastatin, St. John’s wort, Suboxone, Tambocor, Tegetrol (carbamazepine), trazodone, triazolam, valproic acid, Viagra, vitamin E, Videx, Vytorin, warfarin, Ziazen, zidovudine (Retrovir), and Zoloft. |
<table>
<thead>
<tr>
<th><strong>Protease inhibitors (PIs) continued</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crixivan</strong> (indinavir sulfate)</td>
</tr>
<tr>
<td><strong>Invirase</strong> (saquinavir) (must be taken with Norvir)</td>
</tr>
<tr>
<td><strong>Kaletra</strong> (lopinavir/ritonavir)</td>
</tr>
<tr>
<td><strong>Lexiva</strong> (fos-amprenavir calcium)</td>
</tr>
<tr>
<td><strong>Norvir</strong> (ritonavir)</td>
</tr>
</tbody>
</table>
### Protease inhibitors (PIs) continued

| **Prezista** (darunavir) | Advicor, Altoprev, Biaxin, birth control pills, calcium channel blockers (Norvasc, Procardia, and others), Cialis, Cisapride, Crestor, desimpramine, Dilantin (phenytoin), ergot alkaloids (Cafergot, D.H.E. 45, Ergomar, ergonovine, methylergonovine, Migranal), fluticasone (Advair, Flonase, and Flovent), immunosuppressants, Invirase, itraconazole, Kaletra, ketoconazole, Levitra, Lipitor, lovastatin, methadone, Mevacor, midazolam, nifedipine, Paxil, pimozone, phenobarbital, pravastatin, rifabutin, rifampin, Simcor, simvastatin, St. John’s wort, Suboxone, Subutex, Tegretol (carbamazepine), triazolam, Vfend, Viagra, Vytorin, warfarin, and Zoloft. |
| **Reyataz** (atazanavir sulfate) | Advicor, Altoprev, antacids (including Axid, Rolaids, Tums, Mylanta, Pepsid, and Zantac), bepridil, birth control pills, calcium channel blockers (Adalat, Norvasc, Procardia, and others), Cialis, Crixivan, Camptosar, Cordarone, Dilantin (phenytoin), ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, itraconazole, ketoconazole, Lescol, Levitra, lidocaine, Lipitor, lovastatin, midazolam, Mylanta, pimozone, pravastatin, proton-pump inhibitors (Aciphex, Nexium, Prevacid, Prilosec-OTC), quinidine, rifabutin, rifampin, simvastatin, St. John’s wort, Sustiva, triazolam, trazodone, Vfend, Viagra, Videx and Videx-EC, Viread, Vytorin, and warfarin. |
| **Viracept** (nelfinavir) | Advicor, Altoprev, birth control pills, Cialis, Cordarone, Crixivan, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), fluticasone (Advair, Flonase, Flovent), garlic supplements, Invirase, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam, Mycobutin, phenobarbital, phenytoin (Dilantin and others), pravastatin, Prilosec-OTC, rifampin, simvastatin, St. John’s wort, Tegretol (carbamazepine), triazolam, trazodone, Vfend, Viagra, and Vytorin. |

### Entry Inhibitors

| **Fuzeon** (enfuvirtide, or T-20) | None found to be clinically significant. |
| **Selzentry** (maraviroc) | Biaxin, Intenence, Invirase, itraconazole, Kaletra, ketoconazole, Mycobutin, Norvir, Reyataz, rifampin, St. John’s wort, Sustiva, Tegretol (carbamazepine), Vfend, Viramune, and warfarin. |

### Integrase Inhibitor

| **Isentress** (raltegravir) | Aptivus/Norvir, omeprazole, Reyataz, Reyataz/Norvir, and rifampin. |
Please see the drug’s page for details, or refer to the manufacturer’s package insert for a full, comprehensive list of potential drug side effects. Remember that side effects may or may not occur. Some are more common than others, and individuals react differently to the same drug. A drug regimen cannot be chosen solely on the basis of minimal potential for side effects. Discuss any changes, however minor, with your health care providers, including your pharmacist, since small reactions may become serious. There may also be management techniques for the side effect. Visit http://www.acria.org/index.php?q=publications/educational-booklets/side-effects.

### Nucleoside Reverse Transcriptase Inhibitors (also called nucleoside analogs, NRTIs, or nukes)

<table>
<thead>
<tr>
<th>Potential drug class side effects</th>
<th>Enlarged, fatty liver and lactic acidosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combivir</strong>&lt;br&gt;(Retrovir and Epivir)</td>
<td>See Epivir and Retrovir.</td>
</tr>
<tr>
<td><strong>Emtriva</strong>&lt;br&gt;(emtricitabine, or FTC)</td>
<td>A very tolerable drug, but side effects may include headache, diarrhea, nausea and rash. Darkening of the skin on the palms and the soles of the feet has also been reported.</td>
</tr>
<tr>
<td><strong>Epivir</strong>&lt;br&gt;(lamivudine, or 3TC)</td>
<td>A very tolerable drug, but side effects may include headache, nausea, vomiting, diarrhea, fever, fatigue, hair loss, insomnia, malaise, nasal symptoms, cough, peripheral neuropathy, low white blood cell count, and anemia.</td>
</tr>
<tr>
<td><strong>Epzicom</strong>&lt;br&gt;(Epivir and Ziagen)</td>
<td>See Epivir and Ziagen.</td>
</tr>
<tr>
<td><strong>Retrovir</strong>&lt;br&gt;(zidovudine, or AZT)</td>
<td>Headaches, fever, chills, muscle soreness and/or damage, fatigue, nausea, lipodystrophy, fingernail discoloration, anemia (low red blood cell count), and neutropenia (low white blood cell count).</td>
</tr>
<tr>
<td><strong>Trizivir</strong>&lt;br&gt;(Epivir, Retrovir, and Ziagen)</td>
<td>See Epivir, Retrovir, and Ziagen.</td>
</tr>
<tr>
<td><strong>Truvada</strong>&lt;br&gt;(Viread and Emtriva)</td>
<td>See Viread and Emtriva. Abdominal distension/pain.</td>
</tr>
<tr>
<td><strong>Videx &amp; Videx EC</strong>&lt;br&gt;(didanosine, or ddI)</td>
<td>Peripheral neuropathy, upset stomach, diarrhea, headache, pancreatitis (inflammation of the pancreas), eye changes and optic neuritis, increased uric acid levels, insomnia, and body fat redistribution.</td>
</tr>
<tr>
<td><strong>Viread</strong>&lt;br&gt;(tenofovir)</td>
<td>Overall fairly well tolerated; however, side effects may include nausea, diarrhea, vomiting, flatulence (gas), bone changes, kidney toxicities, and low blood phosphate.</td>
</tr>
<tr>
<td><strong>Zerit</strong>&lt;br&gt;(stavudine, or d4T)</td>
<td>Peripheral neuropathy, facial wasting, mitochondrial toxicities (a variety of symptoms caused by cell damage), lipodystrophy, pancreatitis (inflammation of the pancreas), headache, chills/fever, malaise, insomnia, anxiety, depression, rash, upset stomach, diarrhea, abdominal pain, and blood lipid increases.</td>
</tr>
<tr>
<td><strong>Ziagen</strong>&lt;br&gt;(abacavir sulfate)</td>
<td>Hypersensitivity reaction, nausea, vomiting, diarrhea, fatigue, headache, fever, rash, and loss of appetite.</td>
</tr>
</tbody>
</table>
## Non-Nucleoside Reverse Transcriptase Inhibitors (also called non-nucleoside analogs, NNRTIs, or non-nukes)

<table>
<thead>
<tr>
<th>Potential drug class side effects</th>
<th>Rash.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inteience</strong> (etravirine, or TMC-125)</td>
<td>Rash, diarrhea, nausea, nasopharyngitis (symptoms like a common cold), headache, hypersensitivity, and increased liver enzyme levels.</td>
</tr>
<tr>
<td><strong>Rescriptor</strong> (delavirdine)</td>
<td>Headache, nausea, vomiting, diarrhea, fatigue, increased liver enzyme levels, itchy skin or rash, and body fat accumulation or redistribution.</td>
</tr>
<tr>
<td><strong>Sustiva</strong> (efavirenz)</td>
<td>Central nervous system (CNS) and psychiatric symptoms. Rash, nausea, vomiting, diarrhea, fever, insomnia, and increases in triglycerides, good cholesterol (HDL), and liver enzymes. False positive tests for marijuana. Birth defects.</td>
</tr>
<tr>
<td><strong>Viramune</strong> (nevirapine)</td>
<td>Headache, nausea, vomiting, fever, rash, Stevens-Johnson syndrome, increased liver enzyme levels, liver damage, and drug-induced hepatitis.</td>
</tr>
</tbody>
</table>

### Dual-class Fixed Dose Combination

Atripla (Sustiva/Truvada)


### Protease inhibitors (PIs)

<table>
<thead>
<tr>
<th>Potential drug class side effects</th>
<th>Increased levels of cholesterol and triglycerides (except unboosted Reyataz), lipodystrophy, onset of new cases or worsening of diabetes, Immune Reconstitution Inflammatory Syndrome (IRIS), and increased bleeding in hemophiliacs.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aptivus</strong> (tipranavir) (must be taken with Norvir)</td>
<td>Mild diarrhea, nausea, vomiting, and abdominal pain. Headaches, fever, fatigue, dry mouth, rash (including sensitivity to sun), dizziness, liver toxicity, and bleeding in the brain. Aptivus has a sulfa component, and should be used with caution in patients with allergies to sulfa drugs. Also see Norvir.</td>
</tr>
<tr>
<td><strong>Crixivan</strong> (indinavir sulfate)</td>
<td>Headache, fatigue or weakness, malaise, nausea, diarrhea, stomach pains, loss of appetite, yellowing of skin/eyes, changed skin color, dry mouth/sore throat, taste changes, painful urination, indigestion, joint pain, hives, liver toxicity, kidney stones, increased bilirubin, itchy/dry skin, ingrown toenails, and hair loss.</td>
</tr>
<tr>
<td><strong>Invirase</strong> (saquinavir) (must be taken with Norvir)</td>
<td>Diarrhea, abdominal discomfort, vomiting, and nausea. Also see Norvir.</td>
</tr>
<tr>
<td><strong>Kaletra</strong> (lopinavir/ritonavir)</td>
<td>Rash, diarrhea, nausea, vomiting, stomach pain, headache, muscle weakness, increased cholesterol and triglycerides, and increased liver enzyme levels. Also see Norvir.</td>
</tr>
</tbody>
</table>
### Lexiva
(fos-amprenavir calcium)

- Nausea, rash, diarrhea, headache, vomiting, fatigue, and abdominal pain. Lexiva has a sulfa component, and should be used with caution in patients with allergies to sulfa drugs.

### Norvir
(ritonavir)

- Weakness, stomach pain, upset stomach, tingling/numbness around the mouth, hands or feet, loss of appetite, taste disturbance, weight loss, headache, dizziness, pancreatitis, alcohol intolerance, liver problems, increased muscle enzyme levels, and uric acid.

### Prezista
(darunavir)

- Rash, diarrhea, nausea, headache, abdominal pain, and increased liver enzyme levels. Prezista contains a sulfa component and should be used cautiously in patients with sulfa allergies. Also see Norvir.

### Reyataz
(atazanavir sulfate)

- Dizziness, lightheadedness, rash, kidney stones, and elevated liver function test results, including elevated levels of unconjugated bilirubin.

### Viracept
(nelfinavir)

- Diarrhea, stomach discomfort, nausea, gas, weakness, and rash.

### Entry Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuzeon</td>
<td>Injection site reactions (ISRs), Immune Reconstitution Inflammatory Syndrome (IRIS), pneumonia, diarrhea, nausea, and fatigue. Hypersensitivity reactions are possible.</td>
</tr>
<tr>
<td>Selzentry</td>
<td>Cough, fever, cold, rash, muscle and joint pain, stomach pain, dizziness, liver toxicity, allergic reaction, low blood pressure, possible increased risk of infections and cancer.</td>
</tr>
</tbody>
</table>

### INTEGRASE INHIBITOR

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isentress</td>
<td>A very tolerable drug, but side effects may include diarrhea, nausea, vomiting, headache, fever, abdominal pain, fatigue, weakness, dizziness, lipodystrophy, increased levels of liver enzymes and creatine kinase, allergic reaction, and Immune Reconstitution Inflammatory Syndrome (IRIS).</td>
</tr>
</tbody>
</table>

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**NEW TO THE GAME?**

Current DHHS treatment guidelines for first time therapy*

**Patients naïve to antiretroviral therapy** should be started on one of the following three types of combination regimens:

- **NNRTI + 2 NRTIs; or**
- **PI (preferably boosted with ritonavir) + 2 NRTIs; or**
- **INSTI + 2 NRTIs**

<table>
<thead>
<tr>
<th>Preferred Regimens</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTI-based</strong></td>
<td>Sustiva (efavirenz) 1 + Truvada (emtricitabine/tenofovir)</td>
</tr>
<tr>
<td><strong>PI-based</strong></td>
<td>Boosted Reyataz (atazanavir/ritonavir) + Truvada (emtricitabine/tenofovir)</td>
</tr>
<tr>
<td></td>
<td>Boosted Prezista (darunavir/ritonavir) + Truvada (emtricitabine/tenofovir)</td>
</tr>
<tr>
<td><strong>INSTI-based</strong></td>
<td>Isentress (raltegravir) + Truvada (emtricitabine/tenofovir)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preferred for Pregnant Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PI-based</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alternative Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTI-based</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>PI-based</strong></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

Visit www.aidsinfo.nih.gov for the complete set of guidelines and for more detailed information, including “acceptable regimens,” “regimens that may be acceptable, but more definitive data are needed,” and “regimens to be used with caution.”

1 Except during first trimester of pregnancy or in women with high pregnancy potential
2 Viramune (nevirapine) should not be initiated in women with CD4+ T-cell count greater than 250 cells/mm3 or in men with CD4+ T-cell count greater than 400 cells/mm3
3 Emtriva (emtricitabine) and Epivir (lamivudine) are interchangeable

Abbreviations: INSTI = integrase strand transfer inhibitor, NNRTI = non-nucleoside reverse transcriptase inhibitor, NRTI = nucleos(t)ide reverse transcriptase inhibitor, PI = protease inhibitor
ABC = abacavir, ATV = atazanavir, 3TC = lamivudine, ddI = didanosine, DRV = darunavir, EFV = efavirenz, FPV = fosamprenavir, FTC = emtricitabine, LPV = lopinavir, NVP = nevirapine, RAL = raltegravir, r = low dose ritonavir, SQV = saquinavir, TDF = tenofovir, ZDV = zidovudine

Jeff Berry: What do you see as some of the most challenging issues you encounter as a clinician in treating patients with HIV?

Cal Cohen: There are a number of infectious diseases that you take a pill for a couple of days and they’re gone. If you have pneumonia, if you have strep throat, if you have syphilis… you treat it and it’s gone. Unfortunately, HIV is the opposite model. As far as we know, it will probably never leave the body. And therefore, we’re talking about stalemate, we’re not talking about checkmate. We’re talking about a regimen that maintains control of this virus because when it grows, it causes damage. So we have to stop its growth, for as long as people are alive.

To me, that’s what continues to be the most fulfilling part of this field: for almost everybody—we can get the virus under control these days. Almost everybody. Obviously, that’s terrific. The days of pneumocystis and cryptococcal meningitis and resistant viruses and all that stuff – those were miserable days and those were miserable diseases. Dealing with death and disease you can’t stop is a miserable, sad story.

These days, treatment is way better than that. That’s great. When HIV is controlled, it’s quite remarkable how well people do. We know at the current time that when somebody starts on a regimen, that most people who take most of their meds will do fine [emphatic pause], and most people won’t have virologic breakthrough.

That’s the importance of adherence. That’s what creates the dividing line – between the likelihood of treatment failure, that the regimen is going to fail and then if all doesn’t get better the next time, you’re going to be stuck with untreatable HIV vs., hey, no, your HIV is under control and we can focus on the fact that you don’t like your job and you don’t like your boyfriend. Or you do and what do you plan to do to celebrate? And those kinds of things are very important, but obviously they are a luxury to focus on if your viral load is 200,000 and your CD4 is 20, and you’re coughing.

We’re not glib enough to think HIV is irrelevant even if the viral load is undetectable. Nevertheless, most of us are very confident that if the viral load is undetectable, most people are fine most of the time.

But on the other hand, it’s taking medicine every day, every day, every day, at least so far. We’ve done some research, called the FOTO study, to show that daily meds are not necessarily the only way to go about this, at least for those whose virus is suppressed on three of the longer-acting antiviral medications. But for now, even with the possibility of short breaks, we are talking meds most every day. For some people that’s fine, but there are some people for whom that’s just hard to do, for whatever reason. And for the people for whom it’s easy, it is in some ways incomprehensible that it’s ever hard. But a clinician’s job, obviously, is to take care of both kinds of people.

There are times in which people can go from one category to another. For example, there’s someone whose life is going well and they’re taking their meds, and life is good, and they have access to health care. But things can change. Depression is certainly among the most common reasons why some people may just say, “The heck with it. It isn’t worth it anymore. I don’t care about my HIV meds because I don’t care about a long and healthy life anymore.” Other people slip into drug abuse, whether it’s crystal meth or other drugs, and they’re no longer so dedicated to the ongoing daily medicines to control their HIV because other things sometimes take precedence. For others, it’s economics, which is obviously a worry for our health care system nowadays. Can I afford these meds? A clinician needs to ensure that those issues are handled, because that makes the difference for those people who will maintain control of HIV so that it may not even be in the top 10 medical concerns in their lives. Or it may be at the bottom of the top 10, but not at the top of the top 10.

JB: We’re seeing an aging population of people living with HIV. Any idea about the complications of inflammation, whether as a result of HIV or the medications used to treat it?
CC: I think it’s worth noting the obvious, that this is part of the point of getting HIV under control. It’s worth reminding ourselves that as we all age, things can and often do start to go wrong. Putting that into context, yes, we are, as a field, now concentrating on changes that happen to people as they mature, and since heart disease is very common, there’s been a lot of interest and focus on that. In addition, we’re certainly worried that when HIV is uncontrolled, it increases the risk of heart damage and heart attack.

Similarly, when we treat HIV with some medications, the risk is also higher than with other medications. There are two versions of that story. There are medicines that change the known risk factors, meaning that they change your cholesterol values in ways that we think is unfavorable. That’s real and we try to avoid those meds as much as we can. These days, most of us start people on the most cholesterol and lipid-friendly regimen we have, and that’s great.

At the same time, though, we are aware of some studies that show that some of these medications contribute to an increased risk of heart attack despite, or in addition to, whatever they do to cholesterol and other changes. That’s been the focus of the past couple of years of work, mainly around the drug abacavir [Ziagen], and also to some extent around the use of [lopinavir/ritonavir] Kaletra, the protease inhibitor. And a few of the other protease inhibitors, for example, fos-amprenavir [Lexiva], all are in this category of medications that at least have an association with a higher than predicted risk of heart attack in people who are on them vs. people who are on other treatments.

These data are certainly controversial. There are studies that see this, there are studies that don’t. There are people who feel that this is some important signal to respect and there are other people who feel that the whole thing is probably just a mis-reading of the data we have. So there’s controversy. And each clinician has to decide how much they want to use that information to make judgments.

Nevertheless, even with the controversy it’s important to recognize that we do have some medications that consistently are not shown to be associated with a higher risk of these problems. I think many of the revisions in the most recent guidelines from the DHHS in 2009, which just came out on December 1st, summarize which medicines at the current time seem to have the lowest risk of changing both the known factors—like changes in cholesterol—and changes in the unknown risk factors. And do well to control HIV with fewer risks.

JB: In your opinion, if you had a patient who was on, say, Kaletra and they were experiencing these changes over a long period of time, would you switch them? Or is that irreversible once that damage is done?

CC: Let me make sure I understand. Let’s define irreversible—like for somebody who had a heart attack?

JB: No, just elevated triglycerides over a period of time.

CC: There’s no doubt that if somebody is on, say, Kaletra and has elevated triglycerides, that we have a lot of studies, all of which have shown we have medications to use instead of Kaletra that would reliably lower the triglyceride fraction.

There’s actually some ambiguity about this topic—in terms of which of the lipid fractions are important. There’s controversy in, for example, how important triglycerides are in predicting the risk of heart disease. Nevertheless, let’s just say we have someone with what we call globally abnormal lipids. We do have a number of studies that show we have medicines that can usually improve the lipid profile. We also know there are rules for how to switch without creating virologic breakthrough.

So, in recent years, we’ve had a lot of information about how to switch and how to switch correctly. We also have recent studies to show us that sometimes we get it wrong and that there are rules to the game and that switching should be done by somebody who knows the rules of the game. It shouldn’t be done by somebody who doesn’t understand HIV medications.

JB: Do you think there’s still a need for expanded access to newer agents for those currently failing therapy or will there be over the next year or two? If so, should the drug companies always provide an EAP [expanded access program] or only in certain circumstances? And if so, what should those be?

CC: At the current time, probably the only expanded access likely to be relevant are for drugs that offer advantages to people whose virus can’t be controlled without that drug. The only drug that I’m aware of for which that may be potentially true is the maturation inhibitor called bevirimat. It’s being developed as it often, though not always, is active against resistant viruses—resistance specifically to other drugs in other classes. So that’s the drug that, in the next year or so, may be critical to have in an EAP. Others may also be identified, such as newer integrase inhibitors. We shall see.

JB: Can you talk a little bit about treatment as prevention?

CC: First, let’s review the basics. We know enough intellectually so that we don’t need to use treatment as prevention, right? We know how the virus is transmitted and therefore, people who are negative can stay negative, even if they have sex with positive people. I’m saying the obvious, but it is true. I think it’s reasonable to reassure the negative partner of an HIV-positive person that we know the rules of the game of sex and we know, for example, kissing is not going to transmit this virus and that there are things that they can do sexually that just don’t transmit HIV.

So, if we then accept that despite knowing that, we still have an epidemic of 55,000 new infections in the U.S. every year, many suggest we need to try something else. In other words, our strategy historically that says only that people should be protecting...
themselves—it just hasn’t fully worked, so what else can we do?

If somebody says, “I’m positive in a relationship where my partner is negative, and I would like to go on treatment so I can protect him or her,” that approach seems very much supported by the data we have so far. There’s very little doubt that when somebody is positive and on treatment they’re much less infectious to partners than if they’re off treatment. I think that’s pretty clear, even if not guaranteed.

I think the piece of this that is going to get a lot more interesting next year is what do we do for treatment as prevention for the negative person, what’s called pre-exposure prophylaxis. I think that’s now become very interesting because that changes the whole story line. Now, somebody who’s positive can be on treatment to protect their partner, but somebody who’s negative can potentially go on treatment to protect themselves.

Where some people get nervous with this conversation is if people then say, “Now that I’m on treatment and my viral load is undetectable, my partner and I can do anything we want because the risk is essentially zero.” I think that’s where the controversy brews because it is entirely possible that their risk still isn’t zero, because there are men who have HIV in their seminal fluid even though in their blood it is undetectable. We know that’s real and there are studies showing that three to four percent of men fall into that category – and we don’t know who they are unless we do viral load in seminal fluid and most labs don’t have that capability. So the messaging still has to be “Yes, it’s much less risky to you—on the other hand, this doesn’t mean that you can feel as confident as we wish you could feel.” So this is better and may make the odds go from one percent risk to one in a thousand risk, but it doesn’t make it zero.

**JB:** We’re seeing more and more individuals being diagnosed and coming into care with substance abuse and mental health issues. What are you seeing in your patients and how are you addressing those issues?

**CC:** Well, in my personal practice I’m not seeing more and more. I’m seeing a steady amount. I think the drug many of us are challenged by the most is crystal methamphetamine. Certainly, its use in urban gay men is well-documented and of concern to many of us, partly because of what it does to people. It seems to have a power to make people prioritize sexual experiences at the expense of other things in life, like holding a job, like having an income, and even taking HIV meds. And that’s always regrettable, and when people are in that struggle, sometimes it’s hard to convince them that they’re in it.

Sometimes it takes lots of discussions and lots of time. Sometimes it takes multiple discussions with multiple people. A very wise psychiatrist named Glen Treisman in Baltimore, whose life’s work is dealing with psychiatric issues and substance abuse, said the key to dealing with substance abuse is you confront it. You’re honest and you confront it. You say, “This is what’s going on with your life. You don’t think so, but it is. And if you are able to change this direction, your life won’t be going in this downhill direction. That doesn’t mean that your life will be perfect. There are always challenges.” Some people say, “I don’t really care.” “You don’t understand.” “This is way better than you’ll ever find out” and that’s it. But, as Glen said, part of medicine is this persistent optimism that you are an agent of people’s health for whatever it is that they’re ready to change. You say this is where this is going and if you want help to go somewhere else, that’s why I’m here.

**JB:** What do you find most exasperating about your work?

**CC:** Exasperating? Probably for me the biggest exasperation is the intrusion of for-profit insurance companies on decision-making that we want to do, because they are prioritizing expense rather than health. Being told that when I prescribe a new regimen for somebody, oh, let’s say [Isentress, Intelence, and Prezista], and being told the pharmacy can’t dispense one of those three because the insurance company doesn’t approve that. To me that’s just profoundly irritating that some likely extraordinarily ignorant human being – ignorant meaning they don’t know what I’m about to talk to them about – is going to answer the phone and through a series of buttons, allow me to take care of somebody who I have spent 20 years figuring out how to prescribe for, and I think that they have no business in intruding on it. I appreciate the economics, but it makes me craaaazy that the system doesn’t seem to figure out that some of us should be allowed to do what we do without the intrusion of that stuff.

**JB:** Wow. I never thought about that aspect of it.

**CC:** It’s even worse, in some ways, because when the pharmacy or pharmacist is under-informed and they give that person two of the three meds but not all three, because the third one is not approved, and the person then takes the two of the three but not all three, then that is potentially disastrous. I’ve had that thankfully rarely, but those are the kinds of scenarios that I truly want to just put on the front page of the New York Times and say this insurance company just jeopardized this person’s life and if this person’s life is shorter as a result of what just happened here I hope that they pay millions of dollars in fines for the kind of stuff that they do to us. And it makes me enraged, as you maybe can tell. It’s a rare event, but boy, I don’t think it’s going away. 😤
Several new drugs in development offer hope for the future

by Swarup Mehta, PharmD

It has now been over two years since a new anti-HIV medication has come on the market. Some are tired of waiting for new drugs and new classes to be approved. However, with over 60 new drugs in development, it’s time to get excited again. Here are some highlights of drugs from both existing classes and new ones that are in the pipeline.

**New nukes**

The oldest class of drugs, the nucleoside reverse transcriptase inhibitors (NRTIs) or nukes, may have some new drugs on the horizon. The advantage of new medications is the hope that they will be active against HIV if an older nuke no longer works due to drug resistance.

Apricitabine, being developed by Avexa, is structurally similar to Epivir and Emtriva. Side effects include nausea, diarrhea, nasal and chest congestion, and increases in triglycerides. It was in a Phase 3 study, but was stopped early for analysis—more information coming soon.

Amdoxovir (DAPD) is another NRTI currently under development by RFS Pharma, and is currently in Phase 2. Studied doses are 300 or 500 mg taken by mouth twice daily. Reports of eye problems or visual disturbances have been noted, and resolved upon discontinuation of the medication.

Elvucitabine is currently in Phase 2 and is being developed by Achillion Pharmaceuticals. Studied doses are 5 or 10 mg by mouth once daily. This drug shows activity against hepatitis B as well as HIV.

However, apricitabine, mdoxovir, and elvucitabine may have activity against HIV strains that are resistant to other NRTIs, including Epivir and Retovir.

Racivir is an NRTI being developed by Pharmasset, Inc. and also has activity against hepatitis B as well as HIV. Currently in Phase 2 studies, a standard dose has yet to be determined. However, it will most likely be once daily. Racivir is structurally similar to Epivir and Emtriva, but it is undetermined whether or not it has activity against HIV strains already resistant to Epivir and Emtriva.
One of the most exciting drugs in development is a new “booster” drug, GS-9350, being developed by Gilead. It may be the first alternative to taking low-dose Norvir to increase concentrations of other drugs, including elvitegravir, and may be more lipid-friendly when compared to Norvir.

**More non-nukes**

Rilpivirine (TMC-278) is a second generation non-nucleoside reverse transcriptase inhibitor (non-nuke or NNRTI) in development by Tibotec. It is in Phase 3 studies. Similar to Intellence, it seems to be active against HIV strains that are resistant to other NNRTIs. Current dose is yet to be determined, but will most likely be once daily. Tibotec is going to work with Gilead using their blockbuster drug Truvada to make a once-daily fixed dose tablet to compete with Atripla.

GS-9350 is currently in two Phase 2 studies, one comparing a once-daily, fixed dose “Quad” regimen (four-in-one drug combo with GS-9350, elvitegravir, and Truvada) with once-daily, fixed dose Atripla. The “Quad” was non-inferior to Atripla, based on 24-week data.

Another study compares either GS-9350-boosted or Norvir-boosted Reyataz, both combined with Truvada. Similar efficacy was seen at 24 weeks.

ViiV Healthcare, formerly GlaxoSmithKline (GSK), in collaboration with Shionogi, also has several integrase inhibitors in development. S/GSK1349572 (or 572 for short) is a once daily unboosted drug. Last year, GSK reported a significant 1.5 log drop in viral load to a very substantial 2.5 drop in people taking 2 to 50 mg of 572 during a 10-day dose-ranging study. Limited cross-resistance to Isentress and elvitegravir is expected. The drug is now in Ph. 2 study.

**Maturation inhibitors, CCR5 antagonists, and monoclonal antibodies**

Bevirimat (PA457, now MPC-4326) is one of two drugs in a new class called maturation inhibitors being developed by Myriad Pharmaceuticals, Inc. It is taken twice daily. They are now enrolling individuals in their Phase 2 study. The direct link is http://clinicaltrials.gov/ct2/show/NCT01026727?term=mpc-4326&rank=1.

Vivecon (MPC 9055) is the other maturation inhibitor in development. It is currently in Phase 2 and is available in a pill or capsule form.

Selzentry is the only CCR5 antagonist currently on the market. With the recent setback of vicriviroc (being developed by Schering-Plough/Merck), it may stay that way for a long time. There were two Phase 3 studies of vicriviroc in treatment-experienced patients. Both failed to meet their primary endpoints. The company is not giving up on this drug. They are continuing a Phase 2 study for use in treatment-naïve individuals (those who have never been on HIV treatment before). It is being used once daily, with respiratory infection being one of the most common side effects. The drug levels are increased significantly by Norvir and reduced significantly by Sustiva. Vicriviroc is active against HIV strains that are resistant to other entry inhibitors, like Fuzeon.

Two new entry inhibitors are currently being developed, PRO-140, by Progenics, and ibalizumab (TNX-355), by Tanox, which was bought out by Genentech. Both are monoclonal antibodies that bind to CCR5 receptors on CD4 cells, preventing HIV from entering the cell. Because of the different mechanism of action when compared to the CCR5 inhibitor Selzentry, there seems to be low cross-resistance. Both are administered intravenously every two weeks. Both are now in Phase 2 as well.

**Summary**

It’s exciting to see what the future of HIV therapy will bring. But remember, highly active drugs are already available. Make sure to be compliant on your current regimen to avoid resistance and live a long, healthy life. 🌻
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Please see Important Safety Information and Medication Guide for VIRAMUNE on the following pages.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
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Important Safety Information

VIRAMUNE is indicated for use in combination with other antiretroviral agents for the treatment of HIV infection.

VIRAMUNE does not cure HIV or AIDS, and has not been shown to reduce the risk of passing HIV to others through sexual contact or blood contamination. VIRAMUNE can cause severe liver disease and skin reactions that can cause death. These reactions occur most often during the first 18 weeks of treatment, but can occur later. Ask your healthcare provider about how to recognize symptoms of skin and liver problems. Stop taking VIRAMUNE if you have any of these reactions. Do not restart VIRAMUNE if you experience any of these reactions. Call your healthcare provider immediately if you have any of these reactions.

Any patient can experience liver problems with VIRAMUNE, but women and patients who have higher CD4 counts when they begin VIRAMUNE treatment have a greater risk. If you are a woman with CD4+ >250 cells/mm³, or a man with CD4+ >400 cells/mm³, you should not begin taking VIRAMUNE unless you and your doctor have decided that the benefit of doing so outweighs the risk. Women, including pregnant women, with CD4+ cell counts >250 cells/mm³ are at the greatest risk.

Do not take VIRAMUNE if you have severe liver problems.

The dose of VIRAMUNE for adults is one 200-mg tablet daily for the first 14 days, followed by one 200-mg tablet twice daily. VIRAMUNE is always taken with other anti-HIV medications. The 14-day lead-in period is important because it can help reduce your chances of getting a potentially serious skin rash. If you have a skin rash during the first 14 days, immediately contact your doctor and do not increase your VIRAMUNE dose to twice a day. The total duration of the once daily lead-in dosing period should not exceed 28 days, at which point an alternative regimen may need to be started.

Other side effects that patients have experienced include nausea, fatigue, fever, headache, vomiting, diarrhea, abdominal pain, and myalgia. Changes in body fat may occur in patients receiving antiretroviral therapy. Immune reconstitution syndrome has been reported in patients treated with combination ARV therapy.

Please see Medication Guide for VIRAMUNE on the following pages.
MEDICATION GUIDE

VIRAMUNE® (VIH-rah-mune) Tablets

VIRAMUNE® Oral Suspension

Generic name: nevirapine tablets and oral suspension

Read this Medication Guide before you start taking VIRAMUNE and each time you get a refill because there may be new information. This information does not take the place of talking with your doctor. You and your doctor should discuss VIRAMUNE when you start taking your medicine and at regular checkups. You should stay under a doctor’s care while using VIRAMUNE. You should consult with your doctor before making any changes to your medications, except in any of the special circumstances described below regarding rash or liver problems.

What is the most important information I should know about VIRAMUNE?

Patients taking VIRAMUNE may develop severe liver disease or skin reactions that can cause death. The risk of these reactions is greatest during the first 18 weeks of treatment, but these reactions also can occur later.

Liver Reactions

Any patient can experience liver problems while taking VIRAMUNE. However, women and patients who have higher CD4 counts when they begin VIRAMUNE treatment have a greater chance of developing liver damage. Women with CD4 counts higher than 250 cells/mm³ are at the greatest risk of these events. If you are a woman with CD4 >250 cells/mm³ or a man with CD4 >400 cells/mm³ you should not begin taking VIRAMUNE unless you and your doctor have decided that the benefit of doing so outweighs the risk. Liver problems are often accompanied by a rash. Patients starting VIRAMUNE with abnormal liver tests and patients with hepatitis B or C have a greater chance of developing further increases in liver tests after starting VIRAMUNE and throughout therapy.

In rare cases liver problems have led to liver failure and can lead to a liver transplant or death. Therefore, if you develop any of the following symptoms of liver problems stop taking VIRAMUNE and call your doctor right away:

• general ill feeling or “flu-like” symptoms
• dark urine (tea colored)
• tiredness
• pale stools (bowel movements)
• nausea (feeling sick to your stomach)
• pain, ache, or sensitivity to touch on your right side below your ribs
• lack of appetite
• yellowing of your skin or whites of your eyes

Your doctor should check you and do blood tests often to check your liver function during the first 18 weeks of therapy. Checks for liver problems should continue regularly during treatment with VIRAMUNE.

Skin Reactions

Skin rash is the most common side effect of VIRAMUNE. Most rashes occur in the first 6 weeks of treatment. In a small number of patients, rash can be serious and result in death. Therefore, if you develop a rash with any of the following symptoms stop using VIRAMUNE and call your doctor right away:

• general ill feeling or “flu-like” symptoms
• blisters
• fever
• mouth sores
• muscle or joint aches
• swelling of your face
• conjunctivitis (red or inflamed eyes, like “pink eye”)
• tiredness
• any of the symptoms of liver problems discussed above

If your doctor tells you to stop treatment with VIRAMUNE because you have experienced the serious liver or skin reactions discussed above, never take VIRAMUNE again. These are not all the side effects of VIRAMUNE. See the section “What are the possible side effects of VIRAMUNE?” for more information. Tell your doctor if you have any side effects from VIRAMUNE.

What is VIRAMUNE?

VIRAMUNE is a medicine used to treat Human Immunodeficiency Virus (HIV), the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

VIRAMUNE is a type of anti-HIV medicine called a “non-nucleoside reverse transcriptase inhibitor” (NNRTI). It works by lowering the amount of HIV in the blood (“viral load”). You must take VIRAMUNE with other anti-HIV medicines. When taken with other anti-HIV medicines, VIRAMUNE can reduce viral load and increase the number of CD4 cells (“T cells”). CD4 cells are a type of immune helper cell in the blood. VIRAMUNE may not have these effects in every patient.

VIRAMUNE does not cure HIV or AIDS, and it is not known if it will help you live longer with HIV. People taking VIRAMUNE may still get infections common in people with HIV (opportunistic infections). Therefore, it is very important that you stay under the care of your doctor.

Who should not take VIRAMUNE?

• Do not take VIRAMUNE if you are allergic to VIRAMUNE or any of its ingredients. The active ingredient is nevirapine. Your doctor or pharmacist can tell you about the inactive ingredients.
• Do not restart VIRAMUNE after you recover from serious liver or skin reactions that happened when you took VIRAMUNE.
• Do not take VIRAMUNE if you have severe liver problems.
• Do not take VIRAMUNE if you take certain medicines. (See “Can I take other medicines with VIRAMUNE?” for a list of medicines.)
• Do not take VIRAMUNE if you are not infected with HIV.

What should I tell my doctor before taking VIRAMUNE?

Before starting VIRAMUNE, tell your doctor about all of your medical conditions, including if you:

• have problems with your liver or have had hepatitis
• are undergoing dialysis
• have skin conditions, such as a rash
• are pregnant, planning to become pregnant, or are breast feeding

How should I take VIRAMUNE?

Take the exact amount of VIRAMUNE your doctor prescribes. The usual dose for adults is one tablet daily for the first 14 days followed by one tablet twice daily. Starting with one dose a day lowers the chance of rash, which could be serious. Therefore, it is important to strictly follow the once daily dose for the first 14 days. If you have a skin rash during the first 14 days immediately contact your doctor and do not increase your dose to VIRAMUNE twice a day. The total duration of the once daily lead-in dosing period should not exceed 28 days at which point an alternative regimen may need to be started. See the first section “What is the most important information I should know about VIRAMUNE?”

The dose of VIRAMUNE for children is based on their size. Children’s dosing also starts with once a day for 14 days and then twice a day after that.

• You may take VIRAMUNE with water, milk, or soda, with or without food.
• If you or your child uses VIRAMUNE suspension (liquid), shake it gently before use. Use an oral dosing syringe or dosing cup to measure the right dose. After drinking the medicine, fill the dosing cup with water and drink it to make sure you get all the medicine. If the dose is less than 5 mL (one teaspoon), use the syringe.
• Do not miss a dose of VIRAMUNE, because this could make the virus harder to treat. If you forget to take VIRAMUNE, take the missed dose right away. If it is almost time for your next dose, do not take the missed dose. Instead, follow your regular dosing schedule by taking the next dose at its regular time.
• If you stop taking VIRAMUNE for more than 7 days, ask your doctor how much to take before you start taking it again. You may need to start with once-a-day dosing.
• If you suspect that you have taken too much VIRAMUNE, contact your local poison control center or emergency room right away.

Can I take other medicines with VIRAMUNE?

• VIRAMUNE may change the effect of other medicines, and other medicines can change the effect of VIRAMUNE. Tell your doctors and pharmacists about all medicines you take, including non-prescription medicines, vitamins and herbal supplements.
• Do not take Nizoral® (ketocanazole) or Rifadin®/Rifamate®/Riftater® (rifampin) with VIRAMUNE.
• Tell your doctor if you take Biaxin®
(clarithromycin), Diflucan® (fluconazole), methadone, or Mycobutin® (rifabutin).

VIRAMUNE may not be right for you, or you may need careful monitoring.

- It is recommended that you not take products containing St. John’s wort, which can reduce the amount of VIRAMUNE in your body.
- If you take birth control pills, you should not rely on them to prevent pregnancy. They may not work if you take VIRAMUNE. Talk with your doctor about other types of birth control that you can use.

What should I avoid while taking VIRAMUNE?

Avoid doing things that can spread HIV infection, as VIRAMUNE does not stop you from passing HIV infection to others. Do not share needles, other injection equipment or personal items that can have blood or body fluids on them, like toothbrushes and razor blades. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

The Centers for Disease Control and Prevention advises mothers with HIV not to breast feed so they will not pass HIV to the infant through their milk. Ask your doctor about the best way to feed your infant.

What are the possible side effects of VIRAMUNE?

VIRAMUNE can cause serious liver damage and skin reactions that can cause death. Any patient can experience such side effects, but some patients are more at risk than others. See “What is the most important information I should know about VIRAMUNE?” at the beginning of this Medication Guide.

Other common side effects of VIRAMUNE include nausea, fatigue, fever, headache, vomiting, diarrhea, abdominal pain, and myalgia. This list of side effects is not complete. Ask your doctor or pharmacist for more information.

Changes in body fat have also been seen in some patients taking antiretroviral therapy. The changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these conditions are not known at this time.

How do I store VIRAMUNE?

Store VIRAMUNE at room temperature, between 59° to 86°F (15° to 30°C).

Throw away VIRAMUNE that is no longer needed or out-of-date.

Keep VIRAMUNE and all medicines out of the reach of children.

General information about VIRAMUNE

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use VIRAMUNE for a condition for which it was not prescribed. Do not give VIRAMUNE to other people, even if they have the same condition you have. It may harm them.

This Medication Guide summarizes the most important information about VIRAMUNE. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about VIRAMUNE that is written for health professionals, or you can call 1-800-542-6257 for additional information.
**PICK A CARD, PICK A PLAN**

How and where to get financial support to help pay for your meds

*by Jeff Berry*

With the ongoing economic crisis, plus the large number of people who are unemployed, and the mounting costs associated with health care, patient assistance and drug co-pay programs may be a way to offer much-needed assistance to those who are uninsured and underinsured, or are being adversely affected by the rising costs of drug co-pays, health insurance premiums, and other expenses associated with health care.

Most, if not all, pharmaceutical companies already provide some level of patient assistance to individuals who are unable to afford their HIV medications. These are typically for uninsured patients only and those who qualify financially. Qualifications vary by program, so individuals and care providers should contact the manufacturer directly to see if an individual is eligible for a specific patient assistance program, or PAP (see sidebar).

Many companies have also recently instituted co-pay assistance programs for their HIV drugs. Co-pay programs may cover all or part of the drug co-pay for many privately-insured individuals, up to a specified amount, and for a pre-determined period of time (for example, up to one year). Certain restrictions and eligibility requirements apply (for example, recipients of ADAP, Medicare, and Medicaid are ineligible), and eligibility requirements may vary from program to program. Individuals usually get their co-pay cards directly from their provider, or in some cases from the manufacturer’s website or by calling a toll-free number. Once enrolled, they then bring the co-pay card to the pharmacy when filling the prescription, and the pharmacy is reimbursed for the amount covered. People who reside in the state of Massachusetts by law are not eligible for drug co-pay programs.

These co-pay programs are the direct result of several years of intense work and negotiations between the Fair Pricing Coalition (FPC) and representatives of the pharmaceutical industry. The FPC, founded by the late Martin Delaney, works with the drug compa-
nies on HIV drug pricing issues in an effort to help control costs and improve access to life-saving medications.

Major health insurance carriers contract with Prescription Benefit Managers (PBMs) to reduce health care costs through the use of mail-order pharmacies. Unfortunately many of the most widely used mail-order pharmacies in the U.S. do not accept co-pay cards, either because their systems are not set up to handle them or they don’t have the software to process this type of reimbursement. This is a problem since more and more patients are required by their company’s health care plan to acquire their medications through a mail-order pharmacy, and it’s an issue that the Fair Pricing Coalition continues to work to address with each individual company.

There may be medications in addition to HIV drugs that individuals have to take, including those needed to control other conditions such as high cholesterol or diabetes. To find patient assistance or drug co-pay programs for these and other types of drugs, visit www.pparx.org or www.needymeds.com.

Together Rx is a prescription savings program for uninsured individuals sponsored by many of the nation’s leading pharmaceutical companies. For more information call toll-free 1-800-966-0407, or enroll online at www.TogetherRxAccess.com.

Additional co-pay and/or patient assistance programs are available for hepatitis B and hepatitis C drugs, as well as some medications or treatments used for other HIV-related conditions such as lipodystrophy. Contact the manufacturer directly or visit www.positivelyaware.com and enter “co-pay programs” in the search box for more information.

Below is a brief description of currently available HIV co-pay programs. For more information, or if you have a problem accessing or using a specific program, call the Project Inform Hotline at 1-800-822-7422, or call the number listed for that program. Visit www.positivelyaware.com for more information, as this article is regularly updated as details of specific programs change.

**HIV Drug Co-pay Programs**

**Abbott: Positive Partnership PLUS Card**—This program includes 12 months of co-pay savings and covers Kaletra plus up to two other ARVs, no income or co-pay eligibility criteria. Patients can save up to $50 per month toward their Kaletra co-pay, plus up to $100 of the cost of other HIV medications (up to $50 for each additional ARV with a limit of $100 total)—must be part of a Kaletra regimen. Patients must get their card from their provider. Call toll-free 1-800-556-8317 or visit www.kaletra.com for more information. (As this issue went to press, plans for a Norvir co-pay program were announced.)

**Boehringer Ingelheim: Viramune Co-Pay Savings Card**—Covers Viramune; card is valid for amount of patient’s out-of-pocket cost up to $50 per month, for a total of 12 months. Patients must get card from their health care provider. The card is in the form of a MasterCard debit card, which can be activated at www.viramune.com or by calling the toll-free number on the card. Debit card should be accepted at any pharmacy which accepts MasterCard, and most mail-order pharmacies as well.

**Bristol-Myers Squibb: Reyataz and Sustiva Co-Pay Benefit Program**—Covers Reyataz and Sustiva; any amount up to $200 per month for each drug. If health care provider does not have card, patients can call toll free 1-888-281-8981; visit www.bms.com.
HIV Patient Assistance Programs

Patient Assistance Programs, or PAPs, offer free HIV drugs for those who can’t afford them or do not have private insurance or drug coverage under another program such as Medicare or a state AIDS Drug Assistance Program (ADAP). Eligibility is based on income and varies from company to company. Exceptions can sometimes be made in certain cases or due to economic hardship, so be sure to ask, even if you may not qualify. See the list below or refer to the individual drug page for more company contact information. For an overview of many prescription assistance programs and their requirements (including other than HIV), visit Partnership for Prescription assistance at www.pparx.org, or call 1-888-4PPA-NOW (1-888-477-2669).

Abbott: Covers Kaletra and Norvir. Call 1-800-222-6885.

Boehringer Ingelheim: Covers Aptivus and Viramune. Call 1-800-556-8317; visit www.rxhope.com.

Bristol-Myers Squibb: Covers Reyataz, Sustiva, Videx, and Zerit. Call 1-888-477-2669 or go to the individual product websites.

Genentech/Roche: Covers Fuzeon and Invirase. Call 1-877-757-6243 or visit www.roche.com.

Gilead Sciences: Covers Atripla, Emtriva, Truvada, and Viread. Call 1-800-226-2056 or visit the individual product websites.

GlaxoSmithKline: See ViiV Healthcare

Merck & Co.: Covers Crixivan and Isentress. Call 1-800-850-3430 or visit www.isentress.com.

Pfizer: See ViiV Healthcare.

Tibotec: Tibotec Therapeutics Patient Savings Program—Covers Prezista and Invegevra. Saves up to 80% of the amount of your actual out-of-pocket cost up to $100 per drug, per month. Visit www.prezista.com/prezista/patient_assistance.html or call toll-free 1-866-961-7169.

ViiV Healthcare: MySupportCard—All former GSK and Pfizer HIV drugs are covered (Combivir, Epivir, Epzicom, Lexiva, Rescriptor, Retrovir, Selzentry, Trizivir, Viracept, and Ziagen). This is still the easiest program to qualify for and to access, with no income criteria. Card is valid for the amount of patient’s actual out-of-pocket cost up to a maximum of $100 for each prescription. Patients can use their current or new card for both Pfizer and GSK drugs, now under one umbrella at ViiV Healthcare. You can get the card from your provider or print out the card online at www.mysupportcard.com, or visit www.gskforyou.com. Call 1-888-825-5249.

Bristol-Myers Squibb and Gilead Sciences: Atripla Co-Pay Assistance Program—Covers Atripla; for high co-pays only. Patient responsible for first $50 plus any amount over $250. If health care provider does not have card, patients can call toll-free 1-866-784-3431 and one will be mailed to them; visit www.atrila.com.

Genentech/Roche: Company does not offer co-pay assistance for HIV medications. However, they do provide patient assistance for both Invirase and Fuzeon. Call 1-877-757-6243 or visit www.roche.com for more information.

Gilead Sciences: Truvada Co-Pay Assistance Program—Covers Truvada, Emtriva, and Viread. For high co-pays only; kicks in above $50 and up to $200/month. If health care provider does not have the card, patients can call toll-free 1-888-358-0398 and one will be mailed to them.

GlaxoSmithKline: See ViiV Healthcare

Merck & Co.: Isentress Patient Savings Coupon Program—Covers Isentress; patient is responsible for the first $30 of out-of-pocket cost. The coupon provides savings towards out-of-pocket cost over $30 up to a maximum of $400 per prescription (regardless of the number of tablets supplied on the prescription) Visit www.isentress.com or call toll-free 1-866-350-9232. (Residents of Colorado and Massachusetts not eligible by law.)

Pfizer: See ViiV Healthcare

Tibotec: Tibotec Therapeutics Patient Savings Program—Covers Prezista and Intelelence. Saves up to 80% of the amount of your actual out-of-pocket cost up to $100 per drug, per month. Visit www.prezista.com/prezista/patient_assistance.html or call toll-free 1-866-961-7169.

ViiV Healthcare: MySupportCard—All former GSK and Pfizer HIV drugs are covered (Combivir, Epivir, Epzicom, Lexiva, Rescriptor, Retrovir, Selzentry, Trizivir, Viracept, and Ziagen). This is still the easiest program to qualify for and to access, with no income criteria. Card is valid for the amount of patient’s actual out-of-pocket cost up to a maximum of $100 for each prescription. Patients can use their current or new card for both Pfizer and GSK drugs, now under one umbrella at ViiV Healthcare. You can get the card from your provider or print out the card online at www.mysupportcard.com, or visit www.gskforyou.com. Call 1-888-825-5249.

* By law, residents of the state of Massachusetts are not eligible for drug co-pay programs. There is legislation pending in the House which, hopefully, will address this issue.

Special thanks to David Evans and the Fair Pricing Coalition for some of the information contained in this article. Note: The author is a member of the Fair Pricing Coalition.
committed to you.

Providing the Resources You Need to Stay Healthy

HIV.walgreens.com/pa

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