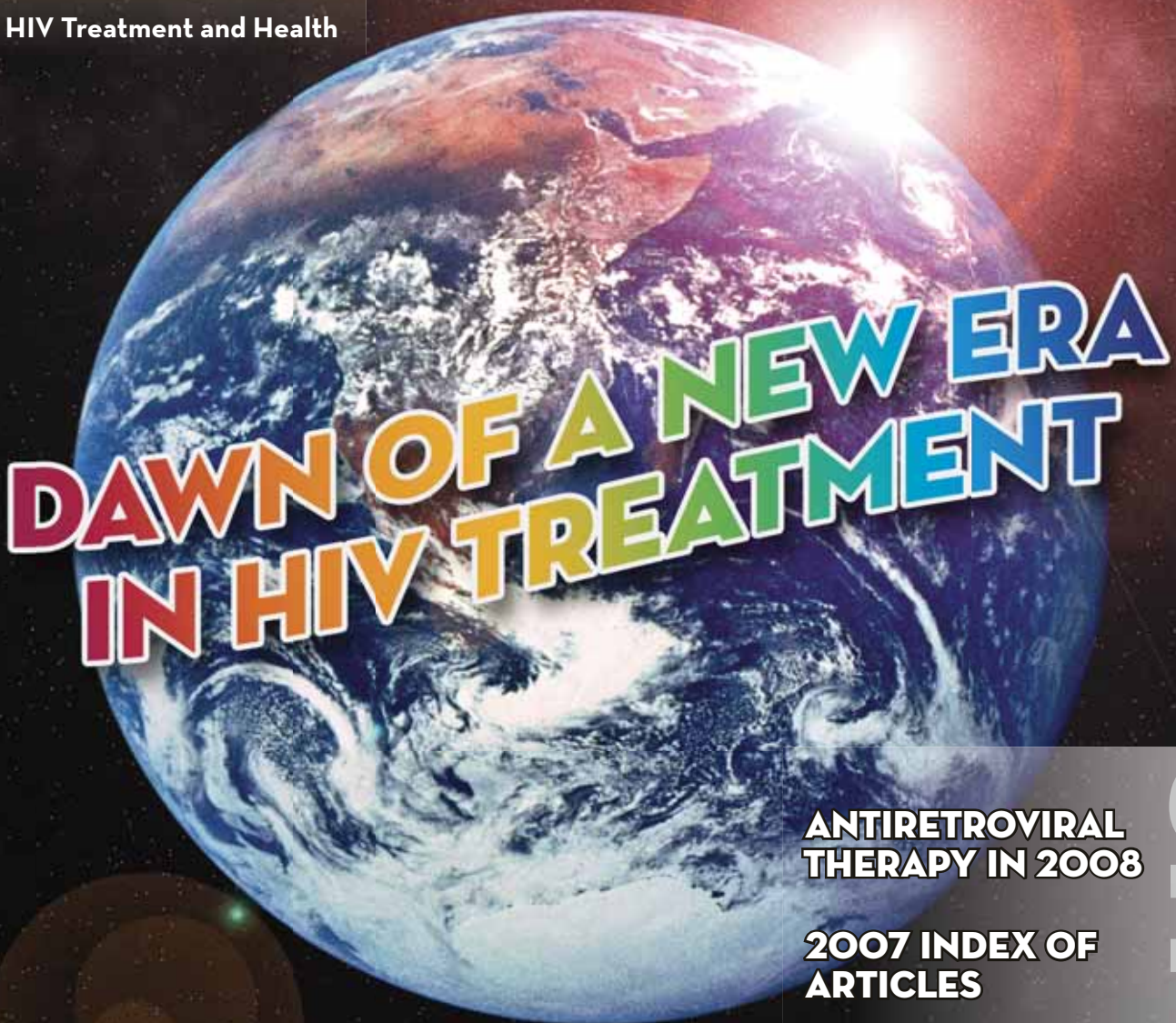
POSITIVELY AWARE
HIV Treatment and Health

THE 12TH ANNUAL HIV DRUG GUIDE



DAWN OF A NEW ERA IN HIV TREATMENT

PLUS

ANTIRETROVIRAL THERAPY IN 2008

2007 INDEX OF ARTICLES

SPECIAL PULL-OUT DRUG CHART

JANUARY / FEBRUARY 2008
THE JOURNAL OF TEST POSITIVE AWARE NETWORK

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In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults

You control your life. Take an active role in your HIV treatment.

Once a day TRUVADA® can help get you to undetectable and keep you there. As part of an HIV regimen, the meds in TRUVADA:

- Can be taken with or without food
- Reduce viral load and increase CD4 cell count

Ask your doctor how TRUVADA can be part of a complete once a day regimen.

Truvada®

200 mg emtricitabine · tenofovir disoproxil fumarate 300 mg

Move On

TRUVADA is the #1 Prescribed HIV Med*

TRUVADA® does not cure HIV infection or lower your chance of passing HIV-1 to others and must be used as part of combination therapy. **TRUVADA should not be used with ATRIPLA™, VIREAD®, EMTRIVA®, Combivir®, Epivir®, Epivir-HBV®, Epzicom™, or Trizivir®.**

USE OF TRUVADA:

TRUVADA is indicated in combination with other antiretroviral agents (such as non-nucleoside reverse transcriptase inhibitors or protease inhibitors) for the treatment of HIV-1 infection in adults.

IMPORTANT SAFETY INFORMATION:

- **Lactic acidosis** (a buildup of acid in the blood) can be a medical emergency and may need to be treated in the hospital. **Call your healthcare provider right away** if you have nausea, vomiting, unusual muscle pain, and/or weakness
- **Serious liver problems** (hepatotoxicity), with liver enlargement (hepatomegaly) and fat in the liver (steatosis), may occur. Call your healthcare provider right away if you have light colored stools, dark colored urine, and/or if your skin or the whites of your eyes turn yellow
- **Flare-ups of hepatitis B virus (HBV) infection:** If you have HIV and HBV, your liver disease may suddenly get worse if you stop taking TRUVADA. Do not stop taking TRUVADA unless directed by your healthcare provider
- Kidney problems: If you have had kidney problems or take other medicines that can cause kidney problems, your healthcare provider should do regular blood tests to check your kidneys
- Bone changes: It is not known whether long-term use of TRUVADA causes damage to your bones. If you have had bone problems in the past, talk to your healthcare provider before taking TRUVADA

Changes in body fat have been seen in some people taking anti-HIV medicines. The most common side effects of TRUVADA when taken with other anti-HIV medicines are dizziness, diarrhea, nausea, vomiting, headache, abdominal pain, depression, rash, and gas. Skin discoloration (spots and freckles) may also occur.

Discuss all medicines you take with your healthcare provider and be aware:

- Your healthcare provider may need to follow you more closely or adjust your therapy if you are taking Videx®, Videx® EC, Reyataz®, or Kaletra® with TRUVADA

For more information, please visit **www.TRUVADA.com** or call **1-800-GILEAD-5 (1-800-445-3235)** and select option 2. **Please see Patient Information on the next page.**

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.

TRUVADA, VIREAD, and EMTRIVA are registered trademarks of Gilead Sciences, Inc. ATRIPLA is a trademark of Bristol-Myers Squibb and Gilead Sciences, Inc. All other trademarks are the property of their respective owners.

*Based on data from PHAST retail monthly data, April 2006–February 2007, Wolters Kluwer Health.

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Patient Information

TRUVADA® (tru-VAH-dah) Tablets

Generic name: emtricitabine and tenofovir disoproxil fumarate
(em tri SIT uh bean and te NOE' fo veer dye soe PROX il FYOU mar ate)

Read the Patient Information that comes with TRUVADA before you start taking it and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. You should stay under a healthcare provider's care when taking TRUVADA. **Do not change or stop your medicine without first talking with your healthcare provider**. Talk to your healthcare provider or pharmacist if you have any questions about TRUVADA.

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

- **Some people who have taken medicine like TRUVADA (nucleoside analogs) have developed a serious condition called lactic acidosis** (build up 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 the following signs or symptoms of lactic acidosis.**
  - You feel very weak or tired.
  - You have unusual (not normal) muscle pain.
  - You have trouble breathing.
  - You have stomach pain with nausea and vomiting.
  - You feel cold, especially in your arms and legs.
  - You feel dizzy or lightheaded.
  - You have a fast or irregular heartbeat.
- **Some people who have taken medicines like TRUVADA have developed serious liver problems called hepatotoxicity,** with liver enlargement (hepatomegaly) and fat in the liver (steatosis). **Call your healthcare provider right away if you get the following signs or symptoms of liver problems.**
  - Your skin or the white part of your eyes turns yellow (jaundice).
  - Your urine turns dark.
  - Your bowel movements (stools) turn light in color.
  - You don't feel like eating food for several days or longer.
  - You feel sick to your stomach (nausea).
  - You have lower stomach area (abdominal) pain.
- **You may be more likely to get lactic acidosis or liver problems** if you are female, very overweight (obese), or have been taking nucleoside analog medicines, like TRUVADA, for a long time.
- **If you are also infected with the Hepatitis B Virus (HBV),** you need close medical follow-up for several months after stopping treatment with TRUVADA. Follow-up includes medical exams and blood tests to check for HBV that could be getting worse. **Patients with Hepatitis B Virus infection, who take TRUVADA and then stop it, may get "flare-ups" of their hepatitis. A "flare-up" is when the disease suddenly returns in a worse way than before.**

What is TRUVADA?

TRUVADA is a type of medicine called an HIV (human immunodeficiency virus) nucleoside analog reverse transcriptase inhibitor (NRTI). TRUVADA contains 2 medicines, EMTRIVA® (emtricitabine) and VIREAD® (tenofovir disoproxil fumarate, or tenofovir DF) combined in one pill. TRUVADA is always used with other anti-HIV medicines to treat people with HIV infection. TRUVADA is for adults age 18 and older. TRUVADA has not been studied in children under age 18 or adults over age 65.

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, acquired immune deficiency syndrome (AIDS) develops.

TRUVADA helps block HIV reverse transcriptase, a chemical in your body (enzyme) that is needed for HIV to multiply. TRUVADA lowers the amount of HIV in the blood (viral load). TRUVADA may also help to increase the number of T cells (CD4 cells). Lowering the amount of HIV in the blood lowers the chance of death or infections that happen when your immune system is weak (opportunistic infections).

TRUVADA does not cure HIV infection or AIDS. The long-term effects of TRUVADA are not known at this time. People taking TRUVADA 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) infection. **It is very important that you see your healthcare provider regularly while taking TRUVADA.**

TRUVADA 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 TRUVADA?

- Do not take TRUVADA if you are allergic to TRUVADA or any of its ingredients. The active ingredients of TRUVADA are emtricitabine and tenofovir DF. See the end of this leaflet for a complete list of ingredients.
- Do not take TRUVADA if you are already taking ATRIPLA™, Combivir (lamivudine/zidovudine), EMTRIVA, Epivir or Epivir-HBV (lamivudine), Epzicom (abacavir sulfate/lamivudine), Trizivir (abacavir sulfate/lamivudine/zidovudine), or VIREAD because these medicines contain the same or similar active ingredients.

What should I tell my healthcare provider before taking TRUVADA?

Tell your healthcare provider if you:

- **are pregnant or planning to become pregnant.** We do not know if TRUVADA can harm your unborn child. You and your healthcare provider will need to decide if TRUVADA is right for you. If you use TRUVADA while you are pregnant, talk to your healthcare provider about how you can be on the TRUVADA Antiviral Pregnancy Registry.
- **are breast-feeding.** You should not breast feed if you are HIV-positive because of the chance of passing the HIV virus to your baby. Also, it is not known if TRUVADA 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.
- **have kidney problems or are undergoing kidney dialysis treatment.**
- **have bone problems.**
- **have liver problems including Hepatitis B Virus infection.**

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements Especially tell your healthcare provider if you take:

- Videx, Videx EC (didanosine). Tenofovir DF (a component of TRUVADA) may increase the amount of Videx in your blood. **You may need to be followed more carefully if you are taking TRUVADA and Videx together.** Also, the dose of didanosine may need to be reduced.
- Reyataz (atazanavir sulfate) or Kaletra (lopinavir/ritonavir). These medicines may increase the amount of tenofovir DF (a component of TRUVADA) in your blood, which could result in more side effects. You may need to be followed more carefully if you are taking TRUVADA and Reyataz or Kaletra together. TRUVADA may decrease the amount of Reyataz in your blood. If you are taking TRUVADA and Reyataz together, you should also be taking Norvir (ritonavir).

Keep a complete list of all the medicines that you take. Make a new list when medicines are added or stopped. Give copies of this list to all of your healthcare providers and pharmacist **every** time you visit your healthcare provider or fill a prescription.

How should I take TRUVADA?

- Take TRUVADA exactly as your healthcare provider prescribed it. Follow the directions from your healthcare provider, exactly as written on the label.
- The usual dose of TRUVADA is 1 tablet once a day. TRUVADA is always used with other anti-HIV medicines. If you have kidney problems, you may need to take TRUVADA less often.
- TRUVADA may be taken with or without a meal. Food does not affect how TRUVADA works. Take TRUVADA at the same time each day.
- If you forget to take TRUVADA, take it as soon as you remember that day. **Do not** take more than 1 dose of TRUVADA in a day. **Do not** take 2 doses at the same time. Call your healthcare provider or pharmacist if you are not sure what to do. **It is important that you do not miss any doses of TRUVADA or your anti-HIV medicines.**
- When your TRUVADA 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 TRUVADA and become harder to treat.
- Do not change your dose or stop taking TRUVADA without first talking with your healthcare provider. Stay under a healthcare provider's care when taking TRUVADA.
- If you take too much TRUVADA, call your local poison control center or emergency room right away.

What should I avoid while taking TRUVADA?

- **Do not breast-feed.** See "What should I tell my healthcare provider before taking TRUVADA?"
- **Avoid doing things that can spread HIV infection** since TRUVADA does not stop you from passing the HIV infection to others.
  - **Do not share needles or other injection equipment.**
  - **Do not share personal items that can have blood or body fluids on them, like toothbrushes or razor blades.**
  - **Do not have 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.
- ATRIPLA, Combivir (lamivudine/zidovudine), EMTRIVA, Epivir or Epivir-HBV (lamivudine), Epzicom (abacavir sulfate/lamivudine), Trizivir (abacavir sulfate/lamivudine/zidovudine), or VIREAD. **TRUVADA should not be used with these medicines.**

What are the possible side effects of TRUVADA?

TRUVADA may cause the following serious side effects (see "What is the most important information I should know about TRUVADA?"):

- **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 doctor right away if you get signs of lactic acidosis.** (See "What is the most important information I should know about TRUVADA?")
- **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 TRUVADA?")
- **"Flare-ups" of Hepatitis B Virus infection,** in which the disease suddenly returns in a worse way than before, can occur if you stop taking TRUVADA. Your healthcare provider will monitor your condition for several months after stopping TRUVADA if you have both HIV and HBV infection. TRUVADA is not approved for the treatment of Hepatitis B Virus infection.
- **Kidney problems.** 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.
- **Changes in bone mineral density (thinning bones).** It is not known whether long-term use of TRUVADA will cause damage to your bones. If you have had bone problems in the past, your healthcare provider may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density.

Other side effects with TRUVADA when used with other anti-HIV medicines include:

- Changes in body fat have been seen in some patients taking TRUVADA and other anti-HIV medicines. These changes may include increased amount of fat in the upper back and neck ("buffalo hump"), breast, and around the main part of your body (trunk). Loss of fat from the legs, arms and face may also happen. The cause and long term health effect of these conditions are not known at this time.

The most common side effects of EMTRIVA or VIREAD when used with other anti-HIV medicines are: dizziness, diarrhea, nausea, vomiting, headache, rash, and gas. Skin discoloration (small spots or freckles) may also happen with TRUVADA.

These are not all the side effects of TRUVADA. This list of side effects with TRUVADA is **not complete** at this time because TRUVADA is still being studied. If you have questions about side effects, ask your healthcare provider. Report any new or continuing symptoms to your healthcare provider right away. Your healthcare provider may be able to help you manage these side effects.

How do I store TRUVADA?

- **Keep TRUVADA and all other medicines out of reach of children.**
- Store TRUVADA at room temperature 77 °F (25 °C).
- Keep TRUVADA 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.

General information about TRUVADA:

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use TRUVADA for a condition for which it was not prescribed. Do not give TRUVADA to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about TRUVADA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about TRUVADA that is written for health professionals. For more information, you may also call 1-800-GILEAD-5 or access the TRUVADA website at www.TRUVADA.com.

Do not use TRUVADA if seal over bottle opening is broken or missing.

What are the ingredients of TRUVADA?

Active Ingredients: emtricitabine and tenofovir disoproxil fumarate

Inactive Ingredients: Croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and pregelatinized starch (gluten free). The tablets are coated with Opadry II Blue Y-30-10701 containing FD&C Blue #2 aluminum lake, hydroxypropyl methylcellulose 2910, lactose monohydrate, titanium dioxide, and triacetin.

℞ Only

May 2007

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GILEAD

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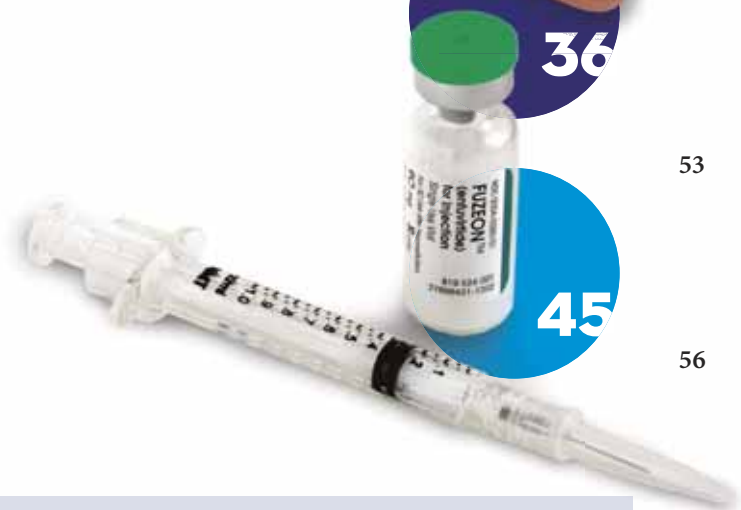

Photo © Russell McGonagle

Articles continued

Distribution of *Positively Aware* is supported in part through unrestricted grants from GlaxoSmithKline and Abbott Laboratories.

A model, photograph, 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

TPAN PROGRAMS AND MEETINGS

- Support Groups
- Rapid HIV Testing
- Yoga, Reiki and Massage
- Needle Exchange Program
- Buddy Program
- Access Medical Clinic at TPAN
- PULSE, an HIV-positive Weekly Social
- Positively Aware Party at Hydrate
- POWER—Positive Outcomes for Wellness, Education and Recovery
- TEAM (Treatment Education Advocacy Management)
- SMART Sex—Prevention and Outreach Program
- TRADE (Teachin', Reachin', Advocatin', Demonstratin', Empowerin') — Prevention and Outreach Program
- Monthly Educational Forums and Trainings

For detailed descriptions of programs, including dates, times and locations, visit www.tpan.com and click on Client Services, or call (773) 989-9400.

TPAN EVENTS

- Jackets Required
  Sunday, March 9th, 2008
  visit www.tpan.com
- Ride for AIDS
  June 7–8, 2008
  visit www.rideforAIDS.org
- Aware Affair Gala
  Saturday, September, 13th, 2008
  visit www.tpan.com
- Other Special Events

For detailed descriptions of these and other TPAN events visit www.tpan.com and click on Events, or call (773) 989-9400.

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The Numbers Game

Sometimes what you do know can hurt you.

When I first started antiretroviral therapy nearly 20 years ago, I would watch my T-cells like a hawk. Initially they hovered at around 500, and since I was experiencing repeated episodes of oral thrush, therapy at that time was recommended. After I started on drugs, my CD4 count shot up to about 800, and I felt victorious, as though I had won the "HIV" lottery.

The numbers quickly fell back down to 500, though, and I thought maybe I had read the numbers on my lottery ticket incorrectly, and that I had actually been given a losing ticket instead. And as those numbers continued to steadily creep down, down, down over the next few years, I began to feel really, really cheated—in fact, I felt robbed.

Those absolute numbers seemed so very important to me at the time, because I had learned that they were a measurement of how my immune system was functioning, and I have a virus which compromises the immune system. But the funny thing was, it was just a number. I felt pretty much the same, physically. A few skin rashes with the occasional bout of thrush, but otherwise, that was about it.

I have learned—at least for myself—that it is a very tricky game, this numbers game.

I decided very early on to put the numbers in their place, so to speak. I realized that they indeed had their place, and that they served their function, so I gave them their due. But I also learned not to invest too much power in them, or risk falling into despair over the fact that my body was failing me, so that it then became this vicious cycle that fed off of itself, kind of a catch-22 with the virus, if you will.

Yes, it was important to take the tests, and yes, it was important to get the results, but, no, I couldn't give in to what they were actually telling me, that I was getting sicker and weaker every day. If I had taken those numbers at face value, I probably would have convinced myself to stop taking the drugs, thinking they weren't doing me any good anyway.

I think that ultimately I found a good balance in my life, and I learned to listen to my own body, and to trust what it was telling me. I weighed how I felt physically against the numbers in my test results when it came time to making important decisions regarding my own healthcare. To be fair, I've also had the luxury of adding more effective drugs to my regimen, which luckily came along for me at just the right time. I've also always had exceptional physicians, whom I could trust, and access to accurate and reliable sources of information about HIV and its treatment. But equally important, for me at least, was that I was beginning to see the value in taking care of myself mentally, emotionally, and spiritually as well.

Today, with even more new drugs, keeping my balance continues to be important. I haven't had to change my therapy in years, but for those who do, our annual HIV Drug Guide provides handy information.

2007 was a banner year in the treatment of HIV. With the approval of two new drugs and another expected to be approved in early 2008, and dozens more in the pipeline, suddenly there is hope on the horizon. Hope for regimens that are simpler to follow. Hope for drugs that are much more tolerable. And hope for fewer pills that are easier to swallow.

This year's *Positively Aware* HIV Drug Guide contains all sorts of helpful, reliable and really useful information about the treatment of HIV. You'll read about drug side effects, some of which you may experience, most of which hopefully you never will. You'll also find helpful tips on what you can do to minimize or avoid some side effects altogether. And you will learn about potential drug interactions, and in so doing learn to avoid drugs that, if taken together, could harm you, or cause them to not work in the way that they should.

But still important as ever—adherence. A one-pill, once a day regimen might be easier to take, but it is also going to be less forgiving if you regularly miss doses. And these newer drugs need to be chosen wisely, lest we unwittingly create drug resistant strains of the virus by choosing powerful regimens that we can't adhere to, thereby quickly knocking out the promise of the new drugs before they are ever realized.

New with this year's drug guide is an introductory page by Joel Gallant, MD, which is a good, basic primer on the different drug classes and how they work. Thanks, Joel! Special thanks, as always, to our drug guide pharmacist, who this year is Mariela Diaz-Linares, Pharm.D.

And finally, it's been seven years since we've given the magazine a facelift, and so with this issue you'll find some changes—among them a new logo, and a new look. We trust you'll like these changes, and hope they will make reading *Positively Aware* an even more enjoyable and rewarding experience for you, our readers. Look for more improvements and changes throughout the coming year. As always, we welcome your comments and suggestions.

Knowledge is strength, and knowledge is power. But all of this information is really just a guide, a tool, a roadmap to living a healthier, smarter life with HIV. What you do with that life, and how you ultimately choose to lead it, is going to be up to you.

Take care of yourself, and each other.

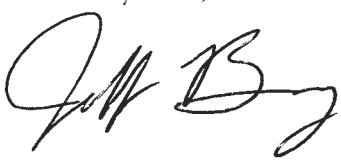

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Photo © Russell McGonagle

READERS FORUM

Woman to woman

I just read your letter; it is so uplifting ["An Open Letter: Woman to Woman," September/October]. Your approach to the virus and the stigma does make people like us who are still not so open about our status want to ask ourselves: "How long will you continue living a lie?" Strangely, I have disclosed to my partner who is negative and who [now] loves me more, just like you put it in your letter. My family members and my girlfriend know, and none of those people are treating me differently. But I cannot get myself to telling many other people in my life and that is so demeaning to me. I sometimes sit and wonder how other people would treat me [if they knew] my status. Would they still trust me if they eventually find out that I have been living silently with my condition? I think I am going to read the letter again and again until I get the right mental attitude toward the condition. I am really happy to have come across your article.

Name withheld, South Africa, via the Internet

HIV 101

I am a case manager and a social worker at the AIDS Resource Center of Wisconsin in the Green Bay office. I had the opportunity to read the issue with the tag line "Everything You Always Wanted to Know About HIV," [September/October] and I wanted to let you know I thought the issue was very well done. The articles were clear, concise, and comprehensive. We get many magazines and journals in our office every month, so I made sure to let my colleagues know how good a resource I think this particular issue could be. I wanted to express my thanks to your staff for their hard work. I think this will definitely be of assistance to the clients with whom I work.

Michael Larkey, MSW, via the Internet

Prevention

Thanks, Jeff, for your editorial in Positively Aware [July/August]. This is the first time I've read this magazine and found this issue helpful. You raise the issue of prevention efforts. I don't know how helpful they've been, but I suspect not much. Why? Maybe they're not targeting the sources of the issue of HIV infection, drug addiction, suicidal thoughts, and so on. I find the same lack of focus to be the case with such organizations as the Human Rights Campaign and others. I work as an addictions counselor among gay and bi men (little do these labels reflect reality) of all races. The same shit keeps coming up… self-image. And, our fellow gays don't help strengthen self-esteem among each other. I'm suggesting that a more varied approach is needed to target all the issues surrounding becoming infected with HIV. Self-esteem, child molestation, sexism/heterosexism and how we have been taught to suck it up like mother's milk and live it out in our stereotypes of what it means to be queer/gay/masculine/men. I know this is brief and far from comprehensive, but you get, I hope, the drift of what I'm talking about. Until we start addressing sexism/heterosexism in our own midst, we will continue to seek other ways of being true to ourselves… or else run, hide, numb ourselves from feeling those feelings of "not good enough" with drugs, liposuctions, sarcasm, isolation, depression, etc.

I wish you the best in your work and life. We need loud voices of reason and compassion like yours.

Ken, via the Internet,
www.transitionpower.com

Many thanks

I am writing to thank [Keith Green] for your inspiring story about your journey through life being HIV-positive [What's Goin' On: The Little Voice Within, July/August 2006]. I greatly admire the strength and zeal that you have for your life's work. I have come across your story at a time in my life where I needed it a lot. Reading your story and becoming more educated on the life quality and life expectancy of HIV-positive people has really made me feel better about my prospects in life if, the Most High forbid, I come up to be HIV-positive. Again I must say that I thank you so very much and will most definitely pray for your health and happiness tonight before bed. I would greatly appreciate even a short e-mail of encouragement. If not I will still be so thankful for your openness and strength. May your faith keep you strong.

Crios, via the Internet

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Add us as your friend and check out some of our other community friends.

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Do you know enough about the current classes of drugs and how they work that you feel comfortable in helping to manage your own care?

Vote at www.tpan.com

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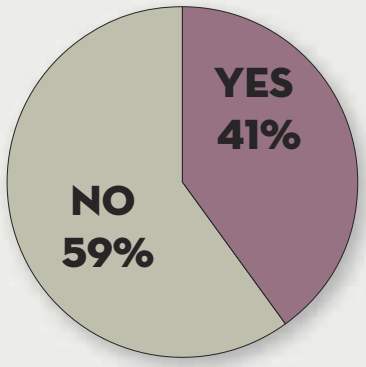
YES:

- Our organization is "planting" 618 red ribbons on a park hillside and walking in our city's holiday parade in honor of those we've lost.
- I plan to attend a memorial service at an organization I know nothing about in order to learn about what they do.
- I like many others have this chronic manageable disease. I have lost many friends due to it, the OI's and ignorance. I feel it's my way of remembering my lost brothers and sisters worldwide!
- We are having a World AIDS Day March, and a memorial for a local HIV/AIDS activist. We will hold a candlelight march through our community and have speakers to talk on the subject of SILENCE=DEATH.
- I'm going to attend and volunteer at the Candlelight Vigil in Chicago's Lakeview neighborhood; www.chicagoworldaidsday.com.

NOVEMBER / DECEMBER POLL RESULTS

Do you plan to do anything special this year in commemoration of World AIDS Day?



NO:

- I'll continue my education and progress towards my degree in studies of pharmacy specializing in infectious disease. I believe this is the best I can contribute toward the fight against HIV/ AIDS and to coming closer to finding a cure. If not in my lifetime, maybe I will have done enough to help the medical community after me to find a cure.
- Not sure, so I said no. I do send letters to Congress from one organization, but that's as far as I've gone this year so far.

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ANTIRETROVIRAL THERAPY UPDATE

EVERYTHING YOU NEED TO KNOW, IN A NUTSHELL

BY JOEL GALLANT, MD, MPH

In the two decade history of antiretroviral therapy (ART), 2007 will be viewed as a banner year, marked by the approval of the first integrase inhibitor and the first CCR5 inhibitor, together with the availability of the first "2nd generation" non-nucleoside reverse transcriptase inhibitor (NNRTI). What we once called "untreatable virus" has essentially become a thing of the past. In the developed world, just about anyone with a knowledgeable provider and the ability to take medication regularly should be able to have an undetectable viral load.

This progress has also come with improvements in the convenience, tolerability, and toxicity of ART. Simple, once-daily regimens are now standard for initial therapy, and are even becoming possible for those on second-line regimens and beyond. The lipoatrophy that was once an almost inevitable result of treatment is now disappearing as we move away from using d4T (Zerit) and AZT (zidovudine, Retrovir, and included in Combivir and Trizivir). Protease inhibitors (PIs) are becoming easier to take and better tolerated, and the new medications appear to have few side effects, at least in the short term.

When to start

There is a growing move toward starting ART earlier, in part because our treatment options today are more effective, better tolerated, and have less long-term toxicity. Studies are also beginning to show that people are healthier and may even live longer when they start ART at higher CD4 counts. Some of these benefits have been surprising, because not only are people on ART less likely to develop AIDS, but they also seem to be at lower risk of problems not usually thought of as being HIV-related, such as heart disease, liver disease, and some cancers. Treatment guidelines will probably soon recommend treatment at CD4 counts below 350, but in my own opinion you can probably justify therapy at even higher CD4 counts, especially if there is evidence of progression (CD4 decline) or a high viral load.

There are a few situations that would push me to recommend treatment regardless of CD4 count. People who are co-infected with hepatitis B virus (HBV) and who need treatment for it should consider starting ART regardless of their numbers, because it's a lot easier to treat both viruses (usually with either Atripla or a combination that includes Truvada) than to try to use HBV drugs without activity against HIV, which are often less effective or more toxic. People with HIV-negative partners might also consider starting therapy, since it may lower the risk of sexual transmission.

There are also two good reasons *not* to start therapy: (1) If you've got a high and stable CD4 count and a low viral load, your immune system might be handling the infection well on its own. (2) If you're not ready to make the commitment to adherence that's required to make ART last, you should wait until you're ready.

What to start with

Before you start, make sure you've been tested for resistance. It's not unusual to be infected with a resistant virus, which you

Photo © Russell McGonagle

need to know about before you choose a regimen. Don't wait until you need ART before getting the test: the sooner you get it after you're infected, the more accurate it will be.

There are a lot of great choices for initial therapy. By far the easiest is Atripla, the one pill, once-a-day combination of Viread, Emtriva, and Sustiva. But it's not just a good choice because it's easy; it also appears to be as effective (or better) than anything it's been compared with. However, Atripla is not for everyone. When I'm talking to a patient about what regimen to start, I'm usually thinking about whether there are any reasons *not* to use Atripla. Those reasons would include:

- Kidney problems. The Viread in Atripla could make them worse.

- Baseline resistance to NNRTIs and/or NRTIs. This could increase the chances of failure.

- Pregnancy potential. A woman who is trying to get pregnant or who is having sex with men without using reliable birth control should avoid Atripla because of the risks of birth defects with Sustiva.

- Nonadherence. Atripla is forgiving of the occasional missed dose because the drugs all hang around for a long time in the blood. But interrupting therapy for days or weeks at a time can lead to NNRTI resistance. People who doubt their ability to stay on ART without breaks should consider a Norvir-boosted PI, because the risk of resistance if you fail is much lower.

- Sustiva intolerance. The Sustiva in Atripla has "neuropsychiatric" side effects in the beginning, including vivid dreams, dizziness, and mental "fogginess." Most people get through these problems within a few days or weeks, but there are some who don't tolerate them and have to switch drugs, either because the initial effects are too intense or because they linger too long. It's hard to predict who won't tolerate Sustiva—you never know until you try.

For those who can't take or tolerate Atripla, there are plenty of other great options. If the problem is with Sustiva, you can use one of several Norvir-boosted PIs, including Reyataz, Kaletra, and Lexiva. In a recent study, once-daily Prezista/Norvir looked like a good choice too. If it's Viread you're trying to avoid, then Epzicom is by far the best alternative to Truvada. Now that we have HLA B*5701 testing, there's little reason to fear the abacavir hypersensitivity reaction (HSR). (Abacavir, or Ziagen, is contained in both Epzicom and Trizivir). I avoid Combivir because of its short-term side effects (nausea, anemia, fatigue) and long-term toxicity (lipoatrophy), and there's no reason to use toxic Zerit anymore.

REMEMBER THAT ANTIRETROVIRAL REGIMENS ARE LIKE RELATIONSHIPS—YOU MAY NOT END UP SETTLING DOWN WITH YOUR FIRST ONE.

Let me try to simplify the decision process. When I'm sitting down with a patient to choose an initial regimen, we first look at the resistance test results to make sure all the options are on the table. If they are, then we talk about the three major decisions:

- Use an NNRTI (usually Sustiva, including Atripla) or a boosted PI? The arguments for each are discussed above. Viramune can also be used as an alternative to Sustiva, but not in women with CD4 counts above 250 or men with counts above 400 because of the risk of liver toxicity.

- If a PI, which one? This usually involves a choice of either Kaletra, Reyataz/Norvir, or Lexiva/Norvir, but Prezista/Norvir is starting to look like a good choice, too.

- Which nuke "backbone"? The two best choices are Truvada (including Atripla) and Epzicom. I rarely have a reason to use anything else.

Remember that antiretroviral regimens are like relationships—you may not end up settling down with your first one. During your first few weeks on a new regimen, you need open communication channels with your provider. You should know in advance what side effects to expect and what to do about them if they happen. With Sustiva or Atripla, it's mostly just a matter of waiting out the nervous system side effects. Rashes can occur, but they usually go away on their own. PIs often cause loose stools, but daily use of fiber supplements (Metamucil, Citrucel, Fibercon, and others) will usually restore things to normal. Viread (including Truvada and Atripla) can cause gas—try over-the-counter remedies that contain simethicone. If you have side effects that are unexpected, that go on too long, that seem unusually severe, or that you just can't tolerate, talk to your provider as soon as possible about your alternatives, which might include switching to something else. It's a lot safer to switch than to stop therapy and start over again later. That can lead to resistance that can limit your treatment options down the road.

THE CRITICAL ISSUE WHEN YOU HAVE HIGHLY RESISTANT VIRUS IS TO PROTECT ACTIVE DRUGS. EVERY REGIMEN, WHETHER IT'S THE FIRST OR THE FIFTH, SHOULD INCLUDE AT LEAST TWO, AND PREFERABLY THREE, FULLY ACTIVE DRUGS.

What to do about treatment failure

Treatment failure is less common now that ART is more effective and easier to take. Adherent patients taking a combination chosen carefully based on resistance test results may not have to worry about treatment failure…ever. But failure does happen, usually because of non-adherence, pre-existing resistance, or side effects. When it does, the good news is that there are plenty of good treatment options. We used to say that "the first shot is the best shot," meaning that nothing works as well as the first regimen. That was because most people had drug resistance after their first regimen failed, and the resistance affected the drugs they used in their next combination. That's no longer true now that we have resistance testing and can choose among several drugs for which cross-resistance is not an issue.

Your viral load should be undetectable (less than 50 or 75 copies/mL, depending on which test you're using) within 4-6 months of starting treatment, and it should stay that way. The idea that it's okay to have detectable virus as long as you "feel good" or have a high CD4 count is a concept dating back to the dark ages of the late 20th century. If your viral load is detectable on a regimen that should be keeping it suppressed, you need to find out why.

First, think about your adherence. Are you missing doses? Are you taking medications that need food on an empty stomach (or vice versa)? Are you taking other medications or supplements that could be interacting with your medications? Next, consider the possibility that your detectable viral load is just a harmless "blip." This is likely to be the case if you're adherent, your viral load is low, and all your previous viral loads have been undetectable. Blips happen for all sorts of reasons, but they're not usually a sign of bad things to come. Unfortunately, the only way to know if you're blipping is to repeat the viral load.

If your viral load is repeatedly detectable, then it's time for concern. This is when we use resistance testing to assess the damage. Unfortunately, you generally need a viral load of at least 500 to 1,000 to measure resistance, so it's unclear what to do when your viral load is rising but still too low for the test. Some experts recommend "intensification" (adding another drug) in order to prevent more resistance, but this is still a fairly untested approach.

If you're able to measure resistance, you and your provider should use the results to choose your next regimen. Currently, the usual practice if you fail an NNRTI-containing combination is to switch to a PI, combining it with different or additional NRTIs depending on what the resistance test shows. People who start with a PI have generally switched to an NNRTI. However, the approval of drugs in new classes, especially Isentress, the new integrase inhibitor, may expand the options for second-line therapy.

Managing serious resistance

There was a time, not too long ago, when we lowered our expectations for people who had a lot of drug resistance. Instead of aiming for an undetectable viral load, we were happy when we could just keep the CD4 count from falling. That has changed now that we have more drugs and good evidence that they work. There are still some people out there with virus that can't be suppressed, but a lot fewer of them than there were a few years ago.

The critical issue when you have highly resistant virus is to *protect active drugs*. Using an active agent without backup by other active agents is a recipe for resistance and treatment failure. Every regimen, whether it's the first or the fifth, should include at least two, and preferably three, fully active drugs, chosen carefully based on a review of the treatment history and the appropriate blood tests.

As an example, let's talk about how to select a "salvage regimen" if you have resistance to NRTIs, NNRTIs, and PIs:

- Isentress will work if you've never taken an integrase inhibitor before (and you probably haven't, since it's the first one on the market). But if it's not combined with other active drugs, integrase inhibitor resistance can occur quickly. The only challenge with using Isentress is to know what to use it *with*.

- Selzentry, the new CCR5 inhibitor, *may* work, but only if you have "R5 virus": virus that gets into the CD4 cell by attaching to the CCR5 co-receptor. If you don't understand that, it's okay—just get a *Trofile* test, which will tell you whether you've got the right kind of virus for Selzentry. If you don't, there's no point in using it—it won't suppress

your virus, and it won't protect the other drugs in the regimen.

- PIs may still be an option, depending on how much resistance you have. The PIs most likely to work are Prezista and Aptivus. You need a resistance test to find out which PI is most active, or if your virus is resistant to all of them. In people with a lot of PI mutations, genotype resistance tests can be hard to interpret. Many of us prefer phenotypes (such as PhenoSense or PhenoSense GT) or a virtual phenotype (VircoTYPE) in these situations. The resistance test should be drawn while you're still taking a PI. If you're not, you need to go back to older resistance tests to figure things out.

- You may still be able to use NNRTIs even if you're resistant to Viramune and Sustiva. Intelence is a new "second generation NNRTI." It's effective in most people with resistance to the other NNRTIs, but you need to look at genotypes to be sure. If you took Viramune or Sustiva in the past, older genotypes are more accurate than recent ones—you need to look at tests that were drawn while you were taking the NNRTI.

- NRTIs are sometimes included in salvage regimens, even when resistance tests show complete resistance to the class. We don't know whether that's necessary or helpful, but if you're using nukes despite NRTI resistance, don't count on them. You still need "at least two and preferably three" active drugs, which usually doesn't include the nukes.

- If you and your provider have followed these steps, you should have a pretty good idea of whether you've got the required number of active drugs to form a regimen. If you don't have enough active agents, this is where Fuzeon comes in. Fewer people need Fuzeon now that we have other options, but there's still a place for it. If you're about to start Isentress, but your virus isn't R5 tropic and you've got cross-resistance to Prezista, Aptivus, and etravirine, then you may need this drug.

IF YOU AND YOUR PROVIDER HAVE FOLLOWED THESE STEPS, YOU SHOULD HAVE A PRETTY GOOD IDEA OF WHETHER YOU'VE GOT THE REQUIRED NUMBER OF ACTIVE DRUGS TO FORM A REGIMEN.

Conclusions

ART is getting easier for those who are taking it but more challenging for the clinicians who are prescribing it. In the example I just described—choosing a regimen for someone with a lot of drug resistance—there were at least three different tests that required expert interpretation: the Trofile assay to assess tropism, the phenotype or virtual phenotype to decide on PI susceptibility, and old genotypes to decide whether etravirine would work. And while decisions about the first regimen may be a lot simpler, they still require an understanding of baseline resistance, drug interactions, and the importance of adherence. This is *not* a disease that should be managed by providers without a lot of experience in the field. That doesn't mean you have to leave your primary care provider and switch doctors, but if your primary provider isn't an HIV expert, you should be referred to an expert who can consult with your primary provider about managing your HIV disease. People with HIV infection often need to advocate for their own access to expert care.

Joel Gallant, MD, MPH, is Professor of Medicine and Epidemiology in the Division of Infectious Diseases at the Johns Hopkins University School of Medicine, and Associate Director of the Johns Hopkins AIDS Service. He conducts clinical trials on new antiretroviral agents, and writes and speaks throughout the world on the subject of HIV infection and its treatment. He is well known for his online, interactive "Patient Forum" at the Johns Hopkins HIV Guide (http://www.hopkins-hivguide.org), where he answers questions from readers. His new book, 100 Questions and Answers about HIV and AIDS will be published soon and is now available for pre-order at Amazon.com. Dr. Gallant would like to disclose that he has received research support and has served as a paid consultant for a number of pharmaceutical companies.

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January 2008

HIV DRUG GUIDE INTRODUCTION

A brief description of the drug classes and how they work

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. 2007 brought us two new drug classes: the CCR5 antagonists (a type of entry inhibitor) and the integrase inhibitors, so there are now six classes to choose from. 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 with more classes, we'll begin to see the emergence of new approaches and more options for therapy.

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-80's. Most ART combinations today consist of a combination 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.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) or "Non-Nukes"

The NNRTIs, or "non-nukes," are powerful, convenient drugs with little long-term toxicity. 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 PIs, 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.

Protease Inhibitors (PIs)

The PIs are the drugs that changed everything. It was the combination of NRTIs plus PIs 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 given 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 may cause body shape changes, specifically fat accumulation. 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.)

Entry Inhibitors

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 coreceptor (either CCR5 or CXCR4). This year, the first CCR5 antagonist, Selzentry, was approved by the FDA. The final step involves fusion of the envelope of the virus with the membrane of the CD4 cell, a step blocked by Fuzeon, a fusion inhibitor. For more information, see the Selzentry and Fuzeon drug pages.

Integrase Inhibitor

Integrase inhibitors, the newest class of drugs, block the insertion of HIV DNA into human DNA. For more information, see the Isentress drug page.

12TH ANNUAL HIV DRUG GUIDE

A QUICK GUIDE TO USING THIS GUIDE

by Jeff Berry

- Drugs are color-coded by class; drugs are listed alphabetically within each class by brand name.
- Fixed-dose combinations (FDC) are formulations that combine two or more drugs, and are marked "Combo Drug."
- 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 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 those that are FDA-approved, or available in expanded access. Note: Last year Agenerase (amprenavir) was discontinued and removed from the market (an improved formulation, Lexiva, is available which is better absorbed and requires fewer pills).
- The side effects and drug interactions charts make it easier to quickly find some of the more common side effects associated with each drug. Always refer to the individual drug pages, the manufacturer's package insert, and your physician or pharmacist for more information on drug side effects and drug-drug interactions.
- Our special pull-out chart allows you to easily pinpoint dosing information and food and liquid qualifications for each drug. (Intelence is missing because it was not yet approved when the chart was printed.) Refer to the drug pages 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 complete document is available online and contains comprehensive and detailed guidelines on treatment strategies, lab tests, when to start, what to use, special populations, and co-infection.
- Expanded versions of many of the activist's comments, including views on drug development, are available online at www.tpan.com.

Updated by Mariela Diaz-Linares, Pharm.D. and Enid Vázquez.
Doctor's statements by Joel Gallant, MD, MPH.
Activist's statements by Martin Delaney.

Combo Drug

BRAND NAME: **Combivir**

COMMON NAME: **zidovudine (AZT) and lamivudine (3TC)**

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 zidovudine/AZT/Retrovir), twice-a-day (12 hours apart), with no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $838.94 / month

MANUFACTURER CONTACT: GlaxoSmithKline, www.combivir.com, 1 (888) 825–5249

AIDSINFO:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: May be taken with food to decrease potential nausea associated with AZT. See drug pages for lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir) for more details.

POTENTIAL DRUG INTERACTIONS: See the drugs contained in Combivir: lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir). Do not take zidovudine (Retrovir), Epivir, Epzicom, Trizivir, Emtriva, Truvada, or Atripla while taking Combivir, since all or part of these medications are already in Combivir or have equivalent medications.

TIPS: See also the drugs contained in Combivir: lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir). Combivir has been shown in multiple clinical trials to be a potent regimen with either a protease inhibitor or an NNRTI. It is the combination of lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir) into one pill; see the pages of those individual drugs for more information. The AZT in Combivir can cause fatigue and anemia—it isn't pretty in those at risk for developing anemias (see zidovudine). One head-to-head study against Truvada found greater toxicity with Combivir, due to anemia. New Procrit or Epogen warning: if hemoglobin target is above manufacturer's recommendation (12 g/dL), risk for serious and life-threatening cardiovascular complications significantly increases. For AZT patients, measure hemoglobin once a week after starting the anemia drugs until hemoglobin has stabilized. Notify healthcare provider if experiencing pain and/or swelling in the legs, worsening in shortness of breath, increase in blood pressure, dizziness or loss of consciousness, extreme tiredness, or blood clots in hemodialysis vascular access ports. Combivir brings with it one of the "T" drugs, or thymidine analogs (AZT and Zerit)—some clinicians are avoiding those when possible because of implication in lipoatrophy. The wasting of "AZT butt" could be irreversible or take a long time to rebuild. If you are on it though, don't worry—Combivir is still an effective combination. Please see package insert for more complete potential side effects and interactions.

Doctor

I don't use Combivir anymore, mostly for the reasons I've discussed elsewhere (see "Retrovir"). When I do use AZT, it's almost always to take advantage of certain NRTI resistance mutations in someone who is also taking tenofovir. However, rather than use Combivir plus Viread, it's cheaper to give Truvada plus generic AZT. It also means that two of the three nukes (tenofovir and FTC) are being given once a day instead of just one (the Viread in Combivir plus Viread)—a potential advantage in case of a missed dose.—Joel Gallant, M.D.

Activist

Combivir was the first effort to simplify therapy by combining two drugs in a single pill, thus reducing the number of pills needed each day. This approach eventually became known as a "fixed dose combination," or FDC, and several other FDCs followed in later years. Combivir instantly became popular, mostly because it allowed a person to take two of the drugs in a typical three drug combination in the form of just one pill twice daily. Combivir combines AZT (Retrovir) and 3TC (Epivir) and this is both its greatest strength and its greatest weakness. The strength is that it is a well proven combination that doctors and patients are very familiar with. The weakness is that AZT, the oldest and first HIV drug, has a well-known and fairly predictable side effect profile, as does 3TC, and if you want the convenience of two drugs in one pill, this is one of the very few choices available, side effects and all. With so many newer drugs available today, many people are understandably reluctant to use the old standards. Surely, after 20 years, people expect something better than the oldest drug on the shelf. Consequently, though Combivir initially was widely used, over time its share of the market has been dropping. One advantage that the manufacturer, GlaxoSmithKline, achieved by combining two of its drugs has been to overcome some of the deserved or undeserved bad reputation of AZT. Many people who are prescribed Combivir don't even realize that they are taking AZT. They simply assume they are using a different drug called Combivir. Many people readily take Combivir who swear they would never take AZT. This has helped extend the use of AZT for many additional years.—Martin Delaney

CLASS: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)

STANDARD DOSE: One 200 mg capsule once-a-day, with no food restrictions (may be taken with or without food). The dosing needs to be adjusted for people who have decreased kidney function. It is also available as an oral solution, but the dose is 240 mg (or 24 mL). Take missed dose as soon as possible, but do not double up on your next dose. It may be given to children ages 0 to 3 months old at a dose of 3 mg/kg and children 3 months to 17 years old at a dose of 6 mg/kg up to a maximum of 240 mg of the oral solution.

AWP: $368.93 / month; $87.12 for 10 mg/mL, 170 mL

MANUFACTURER CONTACT: Gilead Sciences, www.gilead.com, 1 (800) GILEAD5 (445–3235)

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Very tolerable. Most common side effects (rarely seen) include headache, diarrhea, nausea and rash. Skin discoloration observed as darkening of the skin on the palms and the soles of the feet can occur and usually does not cause any symptoms. More hyperpigmentation seen in pediatric studies than adult studies. Rare but potentially fatal toxicity with all NRTIs is hepatomegaly with steatosis (enlarged, fatty liver) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in patients taking NRTIs but is more common and more severe in women, people who are obese, and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distension, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver.

POTENTIAL DRUG INTERACTIONS: No significant drug interactions. Do not take Truvada, Atripla, Epivir, Epzicom, Combivir, or Trizivir while taking Emtriva, since they contain Emtriva or medication equivalent to Emtriva.

TIPS: Emtriva (FTC) is called a "me-too" drug because of its similarity to Epivir (3TC); both drugs are associated with the M184V mutation (which suggests drug resistance). However, unlike Epivir, Emtriva remains in blood cells in excess of the 24-hour dosing interval (it remains inside of the cell longer).

Flare up of HBV in people co-infected with HIV/HBV has occurred when Emtriva was discontinued. Patients co-infected with HIV/HBV who stop taking Emtriva should be closely followed by their physician. Emtriva is available as a combination pill with Viread (tenofovir DF), which is called Truvada. In 2006, Emtriva was combined with Sustiva (efavirenz) and Viread in one pill, which is known as Atripla. Please see package insert for more complete potential side effects and interactions.

Doctor

Although it hasn't been around as long, most of my comments about 3TC apply to Emtriva (FTC) as well. I can't think of a reason to use Viread *without* using FTC, which is why my patients on tenofovir are almost always taking it in the form of Truvada or Atripla, which both contain tenofovir and FTC. FTC may also have an advantage over 3TC, at least when it's combined with tenofovir, as it may be less prone to resistance. The reason may be due to the fact that FTC and tenofovir have long and similar half-lives (they stick around for a long time in the blood and the cells). As a result, they're forgiving of the occasional skipped dose (not that I'm recommending skipping doses!).—Joel Gallant, M.D.

Activist

Emtriva, also known as FTC, is very similar to 3TC (Epivir), though it appears to have small competitive advantages over 3TC. The history of the drug is interesting in that, like 3TC, it was once owned by the company known today as GlaxoSmithKline. Many years ago, the company made the decision to develop 3TC as they believed it was the better and safer of the two drugs. Neither had originally been created at the company but were purchased for development. For many years after the launch of 3TC, no one thought or heard of FTC until it was quietly purchased from Glaxo by a small but rapidly growing West Coast company known as Gilead Sciences. Gilead was committed to becoming a major player in the HIV drug field, both by creating new drugs and by purchasing compounds from other companies. Despite the belief of many that FTC/Emtriva offered little or no advantage over 3TC, Gilead invested in its development and conducted the necessary clinical studies to win FDA approval. Over time, FTC/Emtriva was shown to have slightly better efficacy and freedom from developing resistance than 3TC/Epivir. To match and better the simplification advantages of rival Combivir, Gilead quickly developed a pill called Truvada that combined FTC/Emtriva with a second antiviral, tenofovir/Viread.—Martin Delaney

BRAND NAME: **Emtriva**

COMMON NAME: **emtricitabine or FTC**

BRAND NAME: **Epivir**

COMMON NAME: **lamivudine or 3TC**

CLASS: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)

STANDARD DOSE: One 300 mg tablet once-a-day (or one 150 mg tablet twice daily), with no food restrictions (may be taken with or without food). Dose is lowered for people with kidney impairment and in children, to 4 mg/kg/day (a kilogram equals 2.2 pounds). A strawberry/banana flavored liquid is also available. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $386.93 / month for 300 mg

MANUFACTURER CONTACT: GlaxoSmithKline, www.treathiv.com, 1 (888) 825–5249

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: This remains one of the most easily tolerated HIV medications. Potential side effects/toxicities (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 fatal toxicity with all NRTIs is hepatomegaly with steatosis (enlarged, fatty liver) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in patients taking NRTIs but is more common and more severe in women, people who are obese, and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distension, nausea/vomiting, and 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. Children should be watched for signs of pancreatitis.

POTENTIAL DRUG INTERACTIONS: No significant drug interactions. Do not take Epzicom, Combivir, Trizivir, Truvada, or Atripla 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. So 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 followed by their physician. Epivir is also available combined with zidovudine (Combivir, one tablet twice-a-day), in a once-a-day formula with Ziagen (Epzicom, one tablet daily) and in a triple combination with both zidovudine and Ziagen (Trizivir, one tablet twice-a-day). Please see package insert for more complete potential side effects and interactions.

Doctor

Epivir, usually called 3TC, has been and continues to be an incredibly important drug. It's hard to imagine that development of 3TC was almost stopped because resistance occurred so quickly when it was used alone! The mutation that causes resistance to 3TC (M184V) improves the activity of Retrovir, Zerit, and Viread. It can delay resistance to those drugs, and can partially restore their activity if resistance has already occurred. Few drugs in the pharmacy are as safe and well tolerated as 3TC. Either 3TC or its cousin, Emtriva (FTC), should be a part of any initial treatment regimen and of any combination that contains abacavir or AZT. (For convenience, use FTC if you're taking tenofovir, to take advantage of the combined forms: Truvada and Atripla).—Joel Gallant, M.D.

Activist

Epivir has long been a favorite of HIV-treating doctors and is one of the most widely used drugs. On the surface, this has also seemed a little strange because HIV develops resistance to Epivir perhaps more quickly than any other HIV drug. So why does it remain popular? There are a number of reasons. It works well and is one of the more potent drugs of this class. It has a reputation for minimal side effects. But most importantly, it was noted early on that when used with AZT or some other combinations, it seemed to remain effective despite the development of resistance to the drug. The study of this unusual phenomenon led to new knowledge about the interaction of certain antivirals and HIV. Sometimes, a resistant mutation could be a good thing rather than a bad thing. Scientists realized that certain mutations, while giving the virus resistance against a particular drug, weakened the virus in other ways. The mutations that occurred most commonly with Epivir appeared to make the virus more susceptible to AZT and to a lesser extent, to d4T. Additionally, it appeared to make HIV "less fit" or less aggressive in its ability to replicate. This property came to be known as "viral fitness," and Epivir resistance seemed to reduce that fitness. Good thing for Epivir and its maker, GlaxoSmithKline, since these discoveries kept the drug alive and in wide use despite the rapid development of resistance. This not only made Epivir a lasting money maker but helped keep AZT in use for many more years in the form of Combivir.—Martin Delaney

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

STANDARD DOSE: One tablet (600 mg Ziagen/abacavir sulfate and 300 mg Epivir /3TC/ lamivudine), once a day, no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $906.85 / month

MANUFACTURER CONTACT: GlaxoSmithKline, www.epzicom.com, 1 (888) 825–5249

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: The most common side effects of Epzicom are the same as the drugs contained in Epzicom: Epivir and Ziagen. See those pages for more information. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir (Ziagen); see Ziagen. 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, severe nausea, vomiting or abdominal pain, severe tiredness, respiratory symptoms (cough, difficulty breathing and sore throat) and possibly mild rash. These symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should always keep the warning card with you. Hypersensitivity might be confused with flu during flu season, but remember that HSR worsens with every dose. A blood test for HLA-B*5701 can identify people at high risk for this reaction. See tips.

POTENTIAL DRUG INTERACTIONS: See also the drugs contained in Epzicom, Epivir and Ziagen, for more information. Do not take Combivir, Epivir, 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 and Ziagen. Ziagen by itself is FDA approved for either once-a-day or twice-a-day dosing. The once-daily formula in Epzicom was found to have the same amount in the blood over 24 hours (bioequivalency) as Ziagen twice-a-day. Currently, U.S. HIV treatment guidelines recommend Truvada over Epzicom as a preferred agent for the NRTI component of a treatment regimen. Epzicom is not on the preferred list due to the risk of hypersensitivity reactions even though it has demonstrated potency when compared to Combivir. The Ziagen in Epzicom unfortunately has a hypersensitivity reaction (HSR) in about 8% of people taking it. Inexpensive screening, however, can now virtually eliminate HSR! Don't be afraid of genetic testing—it's only looking for one tiny part of your genes. Regardless of the results, it is important to monitor for the potential for this reaction. If HSR is suspected or cannot be ruled out, abacavir products should be discontinued. The test should never be used to diagnose HSR. Healthcare providers should visit www.hlab5701survey.com to learn more and get free tests. The incidence of HSR was the same between Epzicom and Ziagen twice-a-day (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. Check with your doctor if you have any side effects after taking this medicine—don't just stop! Please see package insert for more complete potential side effects and interactions.

Doctor

Epzicom is another great choice. Its main advantage over Truvada is the lack of any kidney toxicity; the disadvantage is the need to get a HLA-B*5701 test first, and then to have to read the "death card" the pharmacist gives you (see "Ziagen"). Studies comparing Truvada and Epzicom are in progress.—Joel Gallant, M.D.

Activist

Epzicom is another fixed dose combination created by GlaxoSmithKline. When Gilead launched Viread/tenofovir, it quickly began to outsell GSK's Ziagen. Both are considered "second generation" drugs and are generally more potent than earlier nucleoside analogue drugs like AZT and ddI. Epzicom combines Ziagen with its earlier drug Epivir/3TC. It is generally considered more potent than GSK's early combination drug Combivir and has the added advantage of once daily dosing. But like any fixed dose combination, Epzicom carries both the strengths and weaknesses of the individual drugs involved. The concern in this case is the Ziagen component, which has high potency but one relatively serious side effect issue. A small percentage of people who use Ziagen, whether alone or in Epzicom (or Trizivir), can suffer a potentially lethal allergic reaction. Physicians are generally knowledgeable in recognizing and handling the problem, but the risk of the problem is enough to discourage many people from trying any form of Ziagen. However, a genetic test is also available which can predict who is likely to have the problem. With the use of this modestly priced test, Epzicom becomes a valid alternative to its main competitor, Truvada from Gilead Sciences. Still, the mere awareness of the allergic reaction problem has limited the sales of Epzicom and Ziagen.—Martin Delaney

Combo Drug

BRAND NAME: **Epzicom**

COMMON NAME: **abacavir sulfate and lamivudine**

BRAND NAME: **Retrovir**

COMMON NAME: **zidovudine (ZDV) or AZT**

CLASS: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)

STANDARD DOSE: One 300 mg tablet twice-a-day (12 hours apart); two 100 mg capsules three times a day also available, no food restrictions (may be taken with or without food). Clear, strawberry-flavored liquid available for pediatric use. Take missed dose as soon as possible, but do not double up on your next dose. Generic Retrovir (zidovudine) is available.

AWP: $432.88 (generic $315) / month

MANUFACTURER CONTACT: GlaxoSmithKline, www.treathiv.com, 1 (888) 825–5249

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Most common side effects include headaches, fever, chills, muscle soreness, fatigue, nausea, and fingernail discloration. Zidovudine (AZT) has been associated with alteration of various cells in the blood through bone marrow suppression resulting in anemia (low red blood cells) and/or neutropenia (low white blood counts), particularly in people with advanced HIV during the first three months. Potential for severe anemia requiring blood transfusion, erythropoietin injections, or hospitalization when used on its own or in combination with hydroxyurea. Prolonged use of high doses of zidovudine has been associated with symptomatic myopathy (muscle damage). Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis (fat) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in patients taking NRTIs but is more common and more severe in women, people who are obese, and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distension, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver. Pancreatitis 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. The risk for pancreatitis with zidovudine is low compared to ddI.

POTENTIAL DRUG INTERACTIONS: Biaxin, Mycobutin, 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 supression 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 healthcare 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: In combination with Epivir, zidovudine is recommended as a preferred NRTI agent in U.S. HIV treatment guidelines in people on HIV therapy for the first time. 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. Also, some clinicians avoid the "T" drugs, or thymidine analogs (zidovudine and Zerit) because of implication in lipoatrophy. Zidovudine has for years been associated with "AZT butt," a disheartening flatness that happens gradually. Taking with food may minimize upset stomach. Please see package insert for more complete potential side effects and interactions.

Doctor

Retrovir, more commonly called AZT, was the first drug approved for the treatment of HIV infection, and it prolonged many lives back in the late '80's and early '90's. It got a new life in the form of Combivir after 3TC became available, experienced another resurrection as part of Trizivir, a once popular "triple-nuke" combination, and has been a cornerstone of therapy in the HAART era. However, AZT's time has finally passed. Compared to the nukes we're using now (namely tenofovir and abacavir), it's weaker, is dosed twice a day, is harder on the stomach, is more prone to resistance, and causes anemia and mitochondrial toxicity, including lipoatrophy. I still have a *few* patients still taking AZT because of resistance to other drugs (it becomes stronger if you have mutations that cause resistance to 3TC, FTC, abacavir, or tenofovir), but that may change as newer, safer agents become available. So long, AZT, and congratulations on a good, long run!—Joel Gallant, M.D.

Activist

Retrovir/AZT was the first drug developed for the treatment of HIV. In subsequent years, activists fought many battles to speed up the drug development process, but the history of AZT demonstrates that the mechanisms and ability to quickly test and approve drugs were present all along. What was lacking, except in the case of AZT, was the will to do it. AZT certainly has served a useful place in the history of treatment for HIV, but it has always come at a price. There is almost a cultural memory of the early and often severe side effects, but people don't always remember that this was primarily the result of overdosing. When dosed properly, AZT can still have side effects but they are seldom severe. Still, many people today believe it is time to reconsider the whole class of drugs that AZT comes from. Most of them have potentially significant side effects that derive from the very nature of what they are doing. It is difficult to conceive of a drug of this type that would be completely free of side effects. With so many new and relatively non-toxic drugs becoming available in recent years, it may be time to ask whether we can build fully effective regimens that don't rely on the old paradigm of "two nukes and a protease inhibitor" or "two nukes and a non-nuke." When this paradigm first became standard in 1996, it wasn't chosen because this was inherently the right or best way to treat HIV. Rather, it was simply the only kind of combination available at the time.—Martin Delaney

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

STANDARD DOSE: One tablet (300 mg Ziagen/abacavir, 150 mg Epivir/3TC/lamivudine, and 300 mg Retrovir/zidovudine/AZT), twice-a-day, no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $1,358.87 / month

MANUFACTURER CONTACT: GlaxoSmithKline, www.treathiv.com, 1 (888) 825–5249

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: The most common side effects of Trizivir are the same as those of the drugs it contains: Epivir, zidovudine (Retrovir), and Ziagen. See those pages for more information. Side effects associated with Trizivir include headache, nausea, upset stomach, and fatigue. May be taken with food to decrease potential nausea associated with zidovudine. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir (Ziagen). See Ziagen. If treatment is stopped because of this serious reaction, never take abacavir or 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, severe nausea, vomiting or abdominal pain, severe tiredness, respiratory symptoms (cough, difficulty breathing and sore throat) and possibly mild rash. These symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should always keep the warning card with you. Hypersensitivity might be confused with flu during flu season, but remember that HSR worsens with every dose. A blood test for HLA-B*5701 can identify people at high risk for this reaction. Check with your doctor if you have any side effects after taking this medicine—don't just stop!

POTENTIAL DRUG INTERACTIONS: See also the drugs contained in Trizivir: Epivir, zidovudine (Retrovir), and Ziagen, for more information. Do not take zidovudine (Retrovir), Epivir, Ziagen, Epzicom, 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, Mycobutin (rifabutin), rifampin, probenecid, methadone, Cytovene (ganciclovir), Valcyte (valganciclovir), Biaxin (clarithromycin), Daraprim (pyramethamine), flucytosine, Fungizone (amphotericin B), doxorubicin, and hydroxyurea.

TIPS: See the drugs contained in Trizivir: Epivir, zidovudine (Retrovir), and Ziagen. 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, when there are concerns of certain toxicities or drug interactions. 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 patients on zidovudine (Retrovir), which is one of the drugs in Trizivir, measure hemoglobin once a week after starting the anemia drugs until hemoglobin has stabilized. Notify healthcare 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. Please see package insert for more complete potential side effects and interactions.

Doctor

Trizivir was the first complete drug regimen available in a single pill (taken twice a day). Compared to the complex, unboosted PI regimens in use at the time, the simplicity of Trizivir was revolutionary, but we now know it's not as effective as the Sustiva- or boosted PI-based regimens that are standard today, and it's not as convenient, either, since most first-line regimens are taken once a day. The use of Trizivir without a fourth drug is no longer recommended, but if you happen to be taking these three drugs along with a PI or NNRTI, then it makes sense to use Trizivir. The 4-drug combination of Trizivir and Viread is sometimes used, but it's still considered experimental.—Joel Gallant, M.D.

Activist

Trizivir was the first fixed dose combination that squeezed three drugs into a single pill. This was a major advance in simplification as it reduced treatment for the first time to a single pill taken once a day. A theoretical weakness of Trizivir though is that all three of the drugs in the combination work against the same step in HIV's replication process. Many researchers believe it is wiser to combine drugs that act against different parts of the virus's reproduction cycle. Trizivir combines AZT, 3TC and Ziagen. Like Epzicom, Trizivir requires that attention be paid to the risk of allergic reactions caused by the Ziagen component. And like Combivir, Trizivir carries the legacy of AZT and the perceptions about its side effects. In clinical studies, Trivizir did quite well and it initially appeared to be about as effective as any other three drug combination. Subsequent studies though showed that it was not quite as effective or long lasting in some patients than the best alternative combinations. The usefulness of the drug is still debated by some. A minority of researchers and doctors point out that even if Trizivir didn't fully succeed in the highest percentage of patients, as compared to the best known combinations, it still worked very well in the great majority of people in clinical studies. The challenge is to figure out who is likely, or not, to benefit. This is no easy task and there are no obvious predictive markers. But some still believe that Trizivir is highly useful for certain patients in which ease of use is of the highest importance. Others who use Trizivir tend to combine it with a fourth drug to overcome any possible weakness from using three of the same type of drug. Still others question the wisdom of this approach as it adds the cost of a fourth drug and eliminates some of the simplicity achieved by Trizivir. They argue that there are a number of three drug combinations that can work just as well as a mix of Trizivir and a fourth drug, but for less money and with greater simplicity.—Martin Delaney

Combo Drug

BRAND NAME: **Trizivir**

COMMON NAME: **abacavir sulfate, zidovudine, and lamivudine**

Combo Drug

BRAND NAME: **Truvada**

COMMON NAME: **emtricitabine and tenofovir DF**

CLASS: fixed dose combination—nucleoside/nucleotide analogs (also called nucleoside or nucleotide reverse transcriptase inhibitors, NRTIs or nukes)

STANDARD DOSE: One tablet (300 mg Viread and 200 mg Emtriva) once a day, no food restrictions (may be taken with or without food). Dosing frequency needs to be adjusted for people with decreased kidney function. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $934.50 / month

MANUFACTURER CONTACT: Gilead Sciences, www.gilead.com, 1 (800) GILEAD5 (445–3235)

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: See the drugs contained in Truvada: Viread and Emtriva. Overall, fairly well tolerated, however, individuals may experience the following: nausea, headache, dizziness, diarrhea, rash, vomiting, abdominal distension/pain and gas.

POTENTIAL DRUG INTERACTIONS: See the drugs contained in Truvada (Viread and Emtriva). Do not take with Emtriva, Viread, Atripla, Epivir, Combivir, 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 (ddI) are increased by 44–60% when given at the same time as Viread. Therefore, a dose reduction to 250 mg for Videx is recommended for people who weigh more than 60 kg (132 pounds) and to 200 mg for those who weigh less than this. See Tips. Viread decreases the concentration levels of Reyataz. In addition, Reyataz (and Kaletra) increases Viread concentrations. The reasons for these interactions are not fully understood. Higher Viread concentrations could increase the risk of Viread-associated adverse events, including kidney disorders. The FDA suggests that 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). Reyataz without Norvir should not be taken with Viread.

TIPS: Remember, Truvada is two drugs in one pill, so see the pages for those drugs, Emtriva and Viread. Currently, U.S. HIV treatment guidelines recommend Truvada over Epzicom as a preferred agent for the NRTI component of an HIV regimen. The combination of Viread with either Epivir or Emtriva has shown potent virologic suppression with Sustiva and was not worse than Combivir. The kidney toxicity must be monitored before and during treatment with Truvada. And Truvada may not be a good option for patients with underlying kidney problems. Please see package insert for more complete potential side effects and interactions.

Doctor

Truvada is a safe, effective, and well tolerated nuke backbone, for the reasons discussed under "tenofovir" and "emtricitabine." Truvada would generally be combined with PIs; if you're taking this backbone with efavirenz, you'd use Atripla. The only real downside is the potential for kidney toxicity, though this is quite uncommon in people with normal kidney function (see "Viread").—Joel Gallant, M.D.

Activist

Truvada was the first fixed dose combination from Gilead Sciences. It combined two of the company's highly successful products, Viread/tenofovir and Emtriva/FTC. It has quickly become a mainstay of treatment. Viread appears to be the most potent and perhaps the least toxic of the nucleoside/nucleotide drugs, and Emtriva is believed to be slightly superior to Epivir. Thus, Truvada has quickly overcome the market lead once enjoyed by Combivir. Truvada in turn has been combined in a single pill with a third drug, Sustiva, to create a highly potent complete combination that requires only one pill once a day. Though there are lingering concerns about potential kidney toxicity and possible bone toxicity from the Viread/tenofovir component of Truvada, it hasn't shown up to a significant degree in any clinical studies. Individual physicians have reported cases but not enough yet to warrant any major concerns. Overall, Truvada is widely used and highly regarded by patients and physicians alike.—Martin Delaney

CLASS: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)

STANDARD DOSE: One 400 mg enteric coated (Videx EC) delayed-release capsule once a day, with adjustments for weight and when combined with Viread, Truvada, or Atripla. (Also available in 125 mg, 200 mg and 250 mg caps.) Videx is also available as a buffered powder for oral solution. Take Videx and Videx EC strictly on an empty stomach (unless taking with Viread), one hour before or two hours after food or drink, except water. A reduced dose may be needed for people with kidney problems. Take missed dose as soon as possible, but do not double up on your next dose. Generic Videx EC is available.

AWP: $367.93 for Videx EC (generic enteric-coated $344.92) / month

MANUFACTURER CONTACT: Bristol-Myers Squibb, www.bmsvirology.com, 1 (800) 272–4878

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet) may go away once ddI is stopped, but can be painful and permanently debilitating if not treated in time and occurs more frequently when used with Zerit. Upset stomach, diarrhea, headache, and more rarely pancreatitis (inflammation of the pancreas) have also been reported. Other toxicities include eye changes and optic neuritis. Have periodic eye exams by someone who is aware you are HIV-positive. Increased uric acid levels (indicating a number of disorders, including kidney damage and metabolic diseases), and insomnia are other potential side effects. Rare but potentially fatal toxicity with all NRTIs is pancreatitis, enlarged fatty liver, and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in patients taking NRTIs but is more common and more severe in women, people who are obese, and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distension, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver. People with a history of peripheral neuropathy, pancreatitis or heavy alcohol use should avoid ddI. Pancreatitis 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 immediately. Body fat redistribution/accumulation has also been reported with ddI.

POTENTIAL DRUG INTERACTIONS: The levels of ddI are increased by 44–60% when given at the same time as Viread, therefore a dose reduction to 250 mg for Videx is recommended if you weigh more than 60 kg (132 pounds). See Viread page. The combined use of ddI and zidovudine or hydroxyurea may increase risk of peripheral neuropathy. Combining ddI with Zerit or with hydroxyurea, alcohol, ganciclovir, valganciclovir, or intravenous (not inhaled) pentamidine may increase risk of pancreatitis. Combining ddI with Zerit may increase the risk of lactic acidosis. Also, ganciclovir and ribavirin substantially increase ddI levels, and are generally recommended not to be taken together. Didanosine oral solution should be taken on an empty stomach two hours apart from 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, 373 calories). The dose of ddI may need to be increased when taken with methadone.

TIPS: Study indicates Videx EC (compared to Videx) may have lower risk of peripheral neuropathy. Either drug taken with Zerit increases the risk of facial wasting, pancreatitis, or lactic acidosis. Swallow the capsules whole. The capsules eliminate the bad taste and texture of the tablets and the enteric coating reduces diarrhea. Absorption can be decreased by as much as 50% when taken with food, so take on an empty stomach. If you have reduced kidney function, you may require a lower dose. Notify your doctor immediately if peripheral neuropathy is suspected. Please see package insert for more complete potential side effects and interactions.

Doctor

In the pre-HAART era, Videx was the drug we often went to when Retrovir failed. It wasn't fun to take—you had to chew it or drink it or mix it with antacids twice a day. It tasted awful, and it caused diarrhea. The enteric coated (EC) formulation turned Videx into a simple pill like all the rest, but it still has its problems. Like Zerit, it can cause neuropathy. It can also cause pancreatitis, a potentially life-threatening inflammation of the pancreas. It may cause mitochondrial toxicity, too, though it's hard to know for sure because it's been studied mostly with two other drugs that cause the same problem: d4T and AZT. I use ddI occasionally—usually in people whose virus is resistant to other nukes. It should never be combined with Zerit, and if it's taken with Viread, Truvada, or Atripla, it should be given at a lower dose.—Joel Gallant, M.D.

Activist

Videx/ddI, like AZT, is one of the oldest drugs developed for HIV. Early versions of the drug were large pills that were difficult to swallow or drink after being dissolved in water. A later, much improved enteric-coated version called Videx EC overcame these problems, though the underlying side effects of the drug remained. Videx was the first drug widely distributed in an expanded access program, under which it was given to more than 17,000 people in the U.S. alone who had already developed resistance to AZT. It was the only alternative in those days. But the widespread distribution quickly uncovered two major side effects in the form of pancreatitis and peripheral neuropathy. Research in later years found these problems to be a likely consequence of mitochondrial toxicity, a problem shared with any of the "d" drugs (ddI, ddC, d4T). These are serious lifelong problems and pancreatitis can be fatal. To be fair, such problems are most likely to occur in people with very advanced disease. Therefore, Videx is probably not a good choice under that circumstance. A recent laboratory study concluded that Videx/ddI was perhaps the worst cause of mitochondrial toxicity, followed by AZT. Problems like this are the reasons that some researchers are urging the retirement of the older nucleoside analogue drugs. The main use today for Videx is in people who have run out of other options due to the development of resistance.—Martin Delaney

BRAND NAME: **Videx & Videx EC**

COMMON NAME: **didanosine or ddI**

BRAND NAME: **Viread**

COMMON NAME: **tenofovir disoproxil fumarate (TDF)**

CLASS: nucleotide analog (also called nucleotide reverse transcriptase inhibitor—part of the nucleosides—NtRTI, or nuke)

STANDARD DOSE: One 300 mg tablet once a day, with no food restrictions (with or without food). Dosing frequency needs to be adjusted for people with decreased kidney function. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $578.87 / month

MANUFACTURER CONTACT: Gilead Sciences, Inc., www.viread.com, 1 (800) GILEAD5 (445–3235)

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

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. Viread has some efficacy against hepatitis B, and people may see a flare-up of their hepatitis B if they stop Viread. In some studies, laboratory tests showed changes in the bones. It is not known whether long-term use of Viread will cause damage to the bones. Less common side effects of Viread occurring with undetermined incidence include kidney toxicities and low blood phosphate. See zidovudine (AZT) page for rare but potentially fatal toxicity with all NRTIs as a drug class.

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: The levels of Videx EC and Videx are increased by 44–60% when given at the same time as Viread. Therefore, a dose reduction to 250 mg for Videx is recommended for people who weigh more than 60 kg (132 pounds) and to 200 mg for those who weigh less than this. See tips. Viread decreases the concentration levels 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). Reyataz without Norvir should not be taken with Viread. Do not take with Truvada or Atripla, since Viread is in these medications.

TIPS: Viread along with Emtriva (also available as Truvada and in Atripla) are considered a preferred NRTI combination by U.S. HIV treatment guidelines. The body clears 70–80% of Viread through the kidney and dosing adjustment is recommended for those with impaired kidney function. Serious kidney problems have been rare and the majority 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 in people with advanced HIV disease, even in people 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.

Bad news in combination with Videx in a small study of treatment-naïve individuals—barely raising T-cells in people who are undetectable, failure to reach undetectable in people who started with less than 200 T-cells and more than 100,000 viral load.

Like Epivir and Emtriva, Viread has activity against hepatitis B, which may flare up when Viread is discontinued. These patients should be closely followed by their physician. While data is limited, Viread may have prolonged activity against hepatitis B even when resistant to Epivir. Viread selects for the K65R mutation (as do Ziagen and Videx). This mutation can reduce susceptibility to other nukes. The activity of Viread can be reduced in patients who have acquired resistance to other nukes. The complex interaction of nuke resistance and Viread susceptibility is an area of research. Further research needs to be done in this area. Available in a combination pill with Emtriva called Truvada and it is also combined with Sustiva and Emtriva in a pill called Atripla. Please see package insert for more complete potential side effects and interactions.

Doctor

Tenofovir, usually combined with FTC, has become a favorite nuke for first-line therapy. Studies have shown that it's safer than d4T and is less toxic, more effective, and less prone to resistance than AZT. It's easy to take and well tolerated: other than gas, it has few side effects. The only down-side is the possibility of kidney damage, but that's very unlikely in people who have healthy kidneys to start with. Kidney function should be monitored if you're on Viread, Truvada, or Atripla (with the same tests that would be done anyway). Be careful about taking other drugs that can damage the kidneys. For example, avoid taking a lot of ibuprofen or other over-the-counter non-steroidal anti-inflammatory drugs.—Joel Gallant, M.D.

Activist

Viread was the first highly successful product of Gilead Sciences. It is generally believed to be the most potent of the nucleoside/nucleotide class and also the least toxic. The drug is not recommended though for people with a history of kidney disease and it doesn't combine well with a few other antivirals. But overall, it has been a highly successful drug both for patients and for the company. It is under study today for possible use as a preventive therapy, in which the drug is given to people who are at risk of HIV but are not yet infected. Some people fear that the drug still might cause kidney problems in people without a prior history of this, but clinical trial data does not bear this out. A number of physicians report individual cases of kidney disease but not enough yet to suggest a major problem. The biggest problem Gilead has faced with Viread has been in learning how to get it approved for use quickly in developing nations, where there is great interest in the drug. The company has stumbled and made some poor choices in this effort and this has caused a bit of conflict with activists working on behalf of international access to treatments.—Martin Delaney

Nucleoside Reverse Transcriptase Inhibitor

Brand Name: **Zerit**

Common Name: **stavudine or d4T**

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)

Standard dose: One 40 mg capsule twice-a-day for people weighing 132 pounds (60 kg) or more, or one 30 mg capsule twice-a-day for people weighing less; no food restrictions (may be taken with or without food). 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 may be reduced in people with kidney problems. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $410.30 / month for 40 mg

Manufacturer contact: Bristol-Myers Squibb, www.bmsvirology.com, 1 (800) 272–4878

AIDSInfo:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

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. Additive lipoatrophy (facial wasting) and mitochondrial toxicities when combined with Videx. Caregivers of young children should be instructed regarding noticing and reporting peripheral neuropathy. Adverse reactions and serious laboratory abnormalities in children were similar in type and frequency to those seen in adults. Other side effects include headache, chills/fever, malaise (general ill feeling), insomnia, anxiety, depression, rash, upset stomach (nausea and vomiting), diarrhea and abdominal pain. Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly with steatosis (enlarged, fatty liver) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in patients taking NRTIs but is more common and more severe in women, people who are obese, and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. Pregnant women should particularly avoid the combination of Zerit and Videx due to the risk of lactic acidosis. People with lactic acidosis may experience persistent fatigue, abdominal pain or distension, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver. People with a history of peripheral neuropathy, pancreatitis or heavy alcohol use should avoid Zerit. Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Stop taking Zerit immediately if exeriencing symptoms of pancreatitis and seek immediate medical attention. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Lipoatrophy (fat loss) in the face and limbs (arms and legs) and, to a lesser degree, lipohypertrophy (such as "buffalo hump" and increase in abdominal girth) has been associated with Zerit. Zerit and zidovudine are the HIV drugs (the thymidine analogs) 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. Zidovudine 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: Contact your healthcare provider immediately if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your healthcare 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 and many leading HIV advocates are adamant that it should be avoided for this reason. Please see package insert for more complete potential side effects and interactions.

Doctor

It's strange to think that when Zerit first came out, it was viewed as the less toxic alternative to its chief competitor, AZT. How things have changed! Now we know it's the nuke most likely to cause mitochondrial toxicity, which includes lactic acidosis, hepatic steatosis (fatty liver), and the dreaded lipoatrophy. It's also the most common cause of peripheral neuropathy—nerve damage in the feet and legs that causes pain and numbness. d4T is still widely used in developing countries because it's cheap and generic, but people there are now experiencing all the same toxicities that people here experienced before we had better alternatives. There are few reasons to use this drug anymore.—Joel Gallant, M.D.

Activist

Zerit has had a long and troubled history. In its early years, it was viewed with great hope as the long awaited superior replacement for AZT, ddI and ddC. Clinical studies though dragged on longer than expected when it was found that the dose originally studied was too high and had to be adjusted for patient weight. Once this hurdle was overcome and dosing properly understood, Zerit became the favorite of the nucleoside class. It had none of the initial nausea and headaches of AZT and didn't seem to produce much of the pancreatitis and neuropathy caused by ddI. It had a low pill burden and was easy to take. Later, research led to the conclusion that lipodystrophy (fat accumulation) may mostly be caused by protease inhibitors, but lipoatrophy (loss of limb and facial fat) was caused by the nucleoside drugs, and in particular by Zerit. The mechanism was a form of mitochondrial toxicity (mitochondria are energy sources of cells). Scientists learned that mitochondrial toxicity, which could cause lipoatrophy, nerve damage, pancreatitis and even death, was related primarily to drugs that were either thymidine nucleoside analogues like AZT and Zerit, and the "dd" (didioxy…") drugs like ddI and ddC, and Zerit. Thus, Zerit had both the elements responsible for this class of toxicity. Arguments continue to this day about which of the nucleosides cause the greatest degree of these problems and there is conflicting data. Almost overnight, it went from being a key element in nearly all clinical studies to a drug that simply was not used at all.—Martin Delaney

BRAND NAME: **Ziagen**

COMMON NAME: **abacavir sulfate (ABC)**

CLASS: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)

STANDARD DOSE: Two 300 mg tablets once-a-day (or one 300 mg tablet twice-a-day), no food restrictions (may be taken with or without food). A strawberry/banana flavored liquid is available. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $519.92 / month

MANUFACTURER CONTACT: GlaxoSmithKline, www.treathiv.com, 1 (888) 825–5249

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Approximately 8% of people taking abacavir experienced hypersensitivity reaction (HSR, an allergic-like reaction) during clinical trials. People who think they are experiencing HSR must be evaluated by an experienced HIV provider as soon as possible before they stop taking abacavir. Be very careful, especially in the first two months of treatment. Symptoms worsen with every dose, but very slowly. If treatment is stopped because of this serious reaction, they can never take abacavir, Epzicom or Trizivir again (called "re-challenging") because of life-threatening and potentially 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). This reaction usually occurs during the second week of treatment, but may take as long as six weeks to appear, but can occur anytime during treatment. It gets progressively worse and resolves quickly (24–48 hours) after permanent discontinuation. Symptoms usually, but not always, include some combination of sudden fever, muscle ache, severe nausea, vomiting or abdominal pain, severe tiredness, respiratory symptoms (cough, difficulty breathing and sore throat) and possibly mild rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. Always keep the warning card with you. HSR might be confused with flu during flu season, but remember that it worsens with every dose. See Epzicom tips. Check with your doctor if you have any side effects after taking this medicine—don't just stop! A blood test for HLA-B*5701 can identify patients at high risk for this reaction. More common side effects include nausea, vomiting, diarrhea, fatigue, headache, fever, rash, and anorexia (loss of appetite). Rare but potentially fatal toxicity with all NRTIs is hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in patients taking NRTIs but is more severe in women, people who are obese, and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. Symptoms include persistent fatigue, abdominal pain or distension, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis).

POTENTIAL DRUG INTERACTIONS: Excessive alcohol increases abacavir levels and may increase side effects. Dose adjustment needed in people with moderate liver disease. Avoid Ziagen in people with severe liver disease. Do not take with Epzicom or Trizivir, since Ziagen is already in these medications.

TIPS: This is a potent NRTI, but due to the potential hypersensitivity reaction (HSR) U.S. HIV treatment guidelines do not recommend Ziagen as first-line treatment. Inexpensive screening, however, can now virtually eliminate the risk of HSR! Healthcare providers should visit www.hlab5701survey.com to learn more and get free tests. Don't be afraid of genetic testing—it's only looking for one tiny part of your genes. Regardless of the results, it is important to monitor for the potential for this reaction. If HSR is suspected or cannot be ruled out, abacavir products should be discontinued. The test should never be used to diagnose HSR. It is important to remember that HSR occurs in 5–8% of people and is not fatal unless ignored, and to communicate any and all symptoms to your healthcare provider. Do not stop Ziagen until you have discussed this with your healthcare provider. You don't want to burn through a potent and tolerable HIV drug. The manufacturer recommends that people with symptoms of acute respiratory disease consider HSR even if other diagnosis such as pneumonia, bronchitis or flu is possible. An analysis of 8,000 patients found a reduced risk of HSR in blacks and in men. Please see package insert for more complete potential side effects and interactions.

Doctor

Abacavir has always been a great nuke—potent, easy, and well tolerated—but it's also been a pain in the ass. A small fraction of people who took it developed the abacavir hypersensitivity reaction (HSR), a flu-like reaction that got steadily worse and that could even be fatal in people who developed HSR, stopped the drug, and then took it again. When I prescribed the drug, I had to spend about five minutes talking to patients about HSR, and then another 10 minutes on the phone the next day, trying to convince them to take it after they read about the "RISK OF DEATH!" in the card they got from the pharmacist. Things are much better now: You can virtually eliminate the risk of HSR by ordering a HLA-B*5701 blood test first. If it's positive, *don't take abacavir* (in any of its many forms.) If it's negative, you should still be aware of HSR, but it's unlikely to happen. Ziagen doesn't have any known long-term toxicity. The unanswered question is how it compares to Viread. Several head-to-head trials comparing Truvada and Epzicom are in progress.—Joel Gallant, M.D.

Activist

Ziagen came through development with high hopes as a more potent and generally less toxic addition to the nucleoside class. Its otherwise good reputation was tarnished though by an occasional problem called hypersensitivity reaction, which is another way of saying a severe allergic reaction. In the worst cases, the reaction could be fatal, and it wasn't always easy to distinguish the onset of the problem from a simple rash. In the case of Ziagen, rechallenging people was the surest route to a severe or fatal reaction. Over time, most physicians have learned how to recognize and deal with this reaction before it becomes serious. More importantly, there is now a genetic test that a person can take which predicts who will and who will not have the reaction. Even at worst, without pre-testing, the problem is likely to occur in less than 3% of the population. The unfortunate thing is that this largely managed problem hangs like a cloud over the drug and still discourages some doctors and patients from considering it. The truth is that when properly used, Ziagen is a better and safer choice than any of the older nucleoside analogue drugs and offers robust competition to Viread as the top of the field.—Martin Delaney

Non-Nucleoside Reverse Transcriptase Inhibitor

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)
Standard dose: Two 100 mg tablets twice a day
AWP: Not available at press time
Manufacturer contact: Tibotec Therapeutics, 1 (877) REACH-TT (732-2488), www.tibotectherapeutics.com
AIDSInfo:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov
Potential side effects and toxicity: The most common side effects seen in the Phase 3 DUET studies were rash (17%), diarrhea (15%), nausea (14%), and headache (9%). The rashes seen with etravirine were generally mild to moderate and resolved with continued dosing.
Potential drug interactions: Intelence should not be used with unboosted (without Norvir) PIs (Intelence lowers their levels), Aptivus (Intelence level is lowered 76% with Aptivus), or with Sustiva, Viramune or full-dose (600 mg twice daily) Norvir (Intelence levels are lowered with each of these). Intelence has been studied and can be used without dose adjustment with the boosted protease inhibitors Prezista/Norvir and Invirase/Norvir. Cannot be taken with Reyataz/Norvir, Lexiva/Norvir, or Aptivus/Norvir. Kaletra increases Intelence blood levels, use together with caution. Intelence may be given without dose adjustment with Isentress and the experimental integrase inhibitor elvitegravir, but does require dose adjustment with Selzentry (600 mg twice daily Selzentry). In people with failed therapy with other non-nukes, Intelence should not be taken only with nukes (including Viread). No interaction was found with the acid suppressants ranitidine (Zantac and others) or Prilosec (omeprazole) when given with Intelence. There was also no interaction with methadone and Intelence.
Tips: Received accelerated approval by the FDA as *Positively Aware* went to press. (Was not yet approved when pull-out chart was printed.) Intelence is a badly needed drug in the non-nuke class. The current non-nukes can develop resistance quickly, and with only one mutation in the virus. The second-generation 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 for Sustiva failure (people with the HIV mutation K103N). Sustiva and Viramune are known for potency and tolerability compared to the protease inhibitors, although they have the potential for very negative side effects. Remember also that Sustiva should not be taken during pregnancy and that Viramune may lead to liver damage or life-threatening rash. Intelence is likewise generally tolerable. Diarrhea is a commonly reported side effect in studies, but the incidence is not much higher than the comparative arms. 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. In another early study in people with NNRTI resistance, Intelence substituted for 7 days for the failing NNRTI led to about a 1 log drop (90% reduction) in viral load. One Phase 2 study was stopped, however, when Intelence didn't perform as well as the protease inhibitors in the comparator group of people, but in this study Intelence was not given with other active drugs in the regimen. In a Phase 2b study presented at the 2006 International AIDS Society meeting, 199 individuals with documented NNRTI resistance were randomized to receive either Intelence or another type of drug regimen (a comparator). The viral load reduction in people receiving an Intelence regimen was significantly greater than in the comparator group with optimized therapy. The DUET studies recently published demonstrated good activity when combined with Prezista in treatment-experienced people. In the recent Phase 3 DUET studies in treatment-experienced individuals with NNRTI resistance, a significantly greater number (59%) treated with Intelence than placebo (41%) reached an undetectable (less than 50 copies) viral load. These are encouraging results. It is important to remember that as the clinical studies are being completed, we will find out more information about this new drug. Tibotec is also developing another non-nuke, TMC-278, which may have pharmacologic advantages over 125, including the ability to dose once a day.

Doctor

Etravirine was available through an early access program (EAP), and was approved early in 2008. It's a "second generation NNRTI," which means that it can work when other NNRTIs have failed. The DUET studies showed that etravirine was more effective than placebo (in combination with other drugs) in people with resistance to other drugs, including NNRTIs. However, if you have lots of NNRTI mutations (and specifically three or more etravirine mutations), it won't be as effective. That's why it's important not to keep taking Sustiva or Viramune if they're not working, because you'll continue to collect drug mutations that could lead to cross-resistance to etravirine.—Joel Gallant, M.D.

Activist

Intelence is a new player in the non-nucleoside class. It received FDA approval in January of 2008. It offers one major advantage over other drugs in this class—it can still work after resistance develops to any of the others. In short, Intelence restores the use of this class for people who had previously developed resistance to it. Intelence has a good side effect profile, showing only a small amount of rash, diarrhea, and headache. While it has been primarily tested by the manufacturer, Tibotec Therapeutics, in people who had prior resistance to Sustiva or Viramune, there is no reason not to expect it to perform well as first or second line therapy. It is not a once-a-day drug, which some consider a competitive disadvantage relative to Sustiva, but once daily dosing may be an overrated benefit. Few people with HIV actually take drugs only once a day, even if their primary HIV regimen is a once-daily drug. Tibotec has a second drug of this type well along in clinical studies.—Martin Delaney

Brand Name: **Intelence**

Common Name: **etravirine or TMC-125**

BRAND NAME:
Rescriptor

COMMON NAME:
delavirdine (DLV)

CLASS: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)

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; no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $303.70 / month for 200 mg

MANUFACTURER CONTACT: Pharmacia and Upjohn Company, a Pfizer company, www.pfizer.com, 1-800-879-3477 (TRY-FIRST)

AIDSINFO:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Most common side effects include headache, nausea, vomiting, diarrhea, fatigue, elevated liver enzymes, 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 eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or general malaise (general ill feeling), you may need to stop the medications so seek medical attention immediately. Body fat accumulation or redistribution may occur.

POTENTIAL DRUG INTERACTIONS: You cannot take Rescriptor with Versed (midazolam), Halcion (triazolam) and Xanax (alprazolam), Orap (pimozide), ergot alkaloids, used for migraine headaches (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), Lescol (fluvastatin), Crestor (rosuvastatin), and Pravachol (pravastatin, the one with less frequency of problems and interactions according to study data). 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 healthcare provider if you have a history of heart or blood pressure problems. Potential toxicity when given with Biaxin (clarithromycin), dapsone, Mycobutin (rifabutin), Procardia or Adalat (nifedipine), Norvasc (amlodipine), Plendil (felodipine), Coumadin (warfarin), and quinidine. Tegretol (carbamazepine, an anti-seizure medication used to treat peripheral neuropathy), phenobarbital, and Dilantin (phenytoin). Mycobutin, and rifampin (used to treat tuberculosis) are drugs that decrease Rescriptor levels. Rescriptor is not recommended with either rifampin or Mycobutin. Rescriptor increases levels of Crixivan, Lexiva, Invirase, Kaletra, Norvir, Reyataz, Viracept, immunosuppressants, birth control pills (ethinyl estradiol), and methadone, so caution is advised if using together. Cialis, Levitra, and Viagra levels are increased by Rescriptor; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 hours, or 25 mg Viagra per 48 hours. Also, increased levels of trazodone (Desyrel) can occur with Rescriptor. A lower dose of trazodone is recommended. 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.

TIPS: Research demonstrates 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. Please see package insert for more complete potential side effects and interactions.

Doctor

Rescriptor is rarely used these days. It's dosed three times a day, hasn't been as extensively studied as Sustiva or Viramune, and may be less effective. There are some people with unusual NNRTI mutations that cause resistance to Sustiva and Viramune but not to Rescriptor. No one has ever studied using Rescriptor for that purpose, but I have one patient who's taking it because of her funny resistance mutations, and she's doing great. For her sake, I hope the drug sticks around.—Joel Gallant, M.D.

Activist

Rescriptor, which is so uncommonly used that almost no one remembers its generic name (I don't), is from the small class of drugs known as non-nucleoside RT inhibitors. It never achieved the success of the others in this class, Sustiva and Viramune. This is due to the fact that it is more difficult to use because it takes more pills to achieve the dose, generally lower efficacy and generally higher side effects. So why is it still available? Hard to say. The drug was part of a package deal that came to Pfizer when it purchased a smaller drug company. There are some physicians who use Rescriptor as a booster for indinavir, another drug that is not widely used. Indinavir requires some kind of booster and the choices are either Norvir or Rescriptor. Docs who passionately dislike Norvir, and use indinavir, sometimes boost it with Rescriptor. Given all the other well proven drugs available today, the logic of this approach escapes most people.—Martin Delaney

CLASS: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)

STANDARD DOSE: One 600 mg tablet, once a day, typically at bedtime; on an empty stomach or with a light, low-fat snack. Also available in smaller 50 mg, 100 mg and 200 mg capsules. Dose can be split up. Approved for children 3 years and older. Strawberry/mint flavored solution available to children under expanded access program. Take missed dose as soon as possible, but do not double up on next dose.

AWP: $531.04 / month for thirty 600 mg tablets

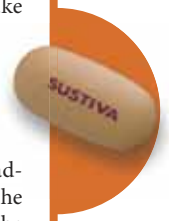
MANUFACTURER CONTACT: Bristol-Myers Squibb, www.sustiva.com; 1 (800) 334–4486

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

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 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: You cannot take the following medications with Sustiva: midazolam, triazolam, or ergot medications (Wigraine, Methergine, and Cafergot), or Vfend, St. John's wort, and 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 should also be "boosted" with Norvir (Reyataz 300 mg/Norvir 100 mg once daily) when taken with Sustiva. Sustiva and Invirase should not be used in combination. With once-daily Lexiva, boost with 300 mg Norvir. Rifampin decreases Sustiva concentrations, so it should be avoided. 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 diltiazem. Dose adjustment may be needed when co-administering these drugs with Sustiva. Do not take with Atripla, since Sustiva is already in Atripla.

TIPS: Sustiva taken at bedtime helps reduce CNS symptoms, but it can be taken at any time. Avoid driving or operating heavy machinery for a few hours after dose. High-fat food and alcohol could up the risk of side effects; this is why taking it on an empty stomach is recommended. Some people adjust to Sustiva when taking Ativan or Ambien to sleep for the first few weeks, but either may make you even more groggy the next morning. Women who can become pregnant need to use appropriate birth control, as Sustiva can affect the effectiveness of the Pill (see Interactions above) and increase the risk of birth defects. Please see package insert for more complete potential side effects and interactions.



Doctor

Efavirenz is now not only the "gold standard" NNRTI; it's simply the "gold standard"… period. In trial after trial, no drug has ever done better at suppressing viral load and keeping it suppressed. It works at high viral loads and at low CD4 counts, has little long-term toxicity, and is the key component of the first one-pill, once-a-day combination, Atripla. This is the drug I use for first-line therapy unless I can think of a reason not to. But there *are* reasons not to use efavirenz: It can cause birth defects, so women who want to get pregnant or who aren't preventing pregnancy should avoid it. If your baseline genotype shows NNRTI mutations, you should take something else. It sticks around for a long time in the blood, so it's forgiving of the occasional late or skipped dose, but this is *not* a drug for people who are prone to stopping therapy altogether: resistance occurs easily as drug levels begin to fall. Finally, it has some early side effects that can be a problem for some people. Vivid dreams, dizziness, and mental "fogginess" are common during the first few days—sometimes weeks—of therapy, and for a small fraction, those side effects are deal breakers. My advice when starting Sustiva or Atripla: (1) Start it on a weekend, when you have a few days (and especially mornings) with nothing important to do; (2) Get out of bed slowly; (3) Read or watch something funny…or sexy…before you go to bed, not something scary—you may have wild dreams, so you might as well enjoy them!; (4) If you're dreaming too much and not feeling rested the next day, talk to your doctor about using a sleeping pill until things get better; (5) Remember, the side effects tend to improve with each dose. If you've been on Sustiva or Atripla for 3 to 4 weeks and still don't like the way it makes you feel, it's probably time for a switch. Sustiva can also cause a rash, usually within the first few weeks of treatment. The rash can be itchy and annoying, but it usually goes away on its own and is rarely a reason to stop the drug.—Joel Gallant, M.D.

Activist

Sustiva is the big shot of the non-nucleoside field. It's a very potent drug with a very long half life in the blood, which makes it tolerate the occasional skipped dose better than most drugs. But it takes only a single mutation for HIV to develop resistance, and when resistance occurs, it also knocks out the other drugs of this class. A new drug (Intelence) has finally solved that problem. For those who don't have mental disturbances, Sustiva has proven to be an excellent drug with virtually no other continuing or long term side effects. —Martin Delaney

BRAND NAME: **Sustiva**

COMMON NAME: **efavirenz (EFV)**

Non-Nucleoside Reverse Transcriptase Inhibitor

Brand Name: **Viramune**

Common Name: **nevirapine (NVP)**

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI, or non-nuke)

Standard dose: One 200 mg tablet daily for two weeks, then full dose of one 200 mg tablet twice daily, no food restrictions, may be taken with or without food; frequently prescribed as two 200 mg tablets once a day, although once-daily dosing is not FDA-approved. Take missed dose as soon as possible but do not double up on your next dose. For dialysis patients, an additional dose of 200 mg is required after each dialysis.

AWP: $463.85 / month

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

AIDSInfo:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

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 healthcare provider immediately. If you experience blistering, mouth sores, conjunctivitis (redness or inflammation of eye, or pink eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or general malaise (general ill feeling), you may need to stop all medications, so seek medical attention immediately. Do not increase dose if rash develops during dose escalation or if you develop any rash accompanied by the above listed conditions. An increase in liver enzyme levels has been observed and in rare instances the development of hepatitis. May need to stop taking nevirapine until liver function returns to normal. Permanently discontinue if abnormalities return. Although rare, severe and life-threatening hepatotoxicity (liver damage), including 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. The package insert says Viramune should not be started in these groups unless the benefit outweighs the risk. But the liver damage can happen to anybody. 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: Caution should be used with midazolam, triazolam, fluconazole, or ergot medications, used for migraine headaches (Wigraine, Methergine, and Cafergot), St. John's wort, Cordarone, lidocaine or disopyramide, carbamazepine, ethosuxomide, or clonazepam, calcium channel blockers (Procardia, diltiazem, verapamil), immunosuppressants, or the blood thinner Coumadin (warfarin). Do not use with Biaxin (clarithromycin) or Nizoral (ketoconazole). Viramune decreases methadone levels; dosing 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. Kaletra should be increased to three tablets twice-a-day in people who previously took HIV drugs. Viramune interacts with rifampin, requiring dose adjustment, and caution is advised with Mycobutin. The effectiveness of birth control pills may be decreased; women and their male partners should consider the use of alternative contraception methods with barrier. 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 seven days, you will need to start at the lower dose for two weeks and then increase back up to twice-daily dosing. 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 last year, 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, the first NNRTI, is now considered to be an "alternative" to Sustiva. Even though it's been around longer, it hasn't been studied as extensively, so we can't say whether it's just as effective. It can also be more toxic: Rashes from Viramune can be more severe (even life threatening) than with Sustiva, and there is also a risk of serious liver damage. These toxicities tend to occur early—within the first few weeks of therapy—and are more common in women and people with high CD4 counts. Women starting therapy with CD4 counts above 250 and men starting with counts above 400 should not start Viramune. Take just one pill once a day for the first two weeks, and then, if your liver tests are okay and you have no rash, increase to the full dose (one pill twice a day). Once you've made it through the first few weeks, Viramune is a very safe and well tolerated drug.—Joel Gallant, M.D.

Activist

Viramune was the first drug approved in the non-nucleoside class. It has none of the mental/emotional side effects of Sustiva but shares its long half life and generally high potency. Its most common side effect is a mild to moderate rash, which is usually easily treatable. The bigger risk with Viramune is liver toxicity, particularly for women with high CD4+ counts. Why this is the case no one knows. It just is. Viramune is also widely used in the developing world for prevention of mother-to-child transmission. A single dose can block most such transmission, although this use has also shown that some women can develop resistance to the drug after that one dose. All things considered, Viramune is probably one of the more underrated HIV treatments. There is no convincing data showing it to be inferior to Sustiva, and overall it appears to be somewhat less toxic. Yet somehow it doesn't have quite the same "buzz" about it as Sustiva and is nowhere near as widely used. A number of people think this is a mistake and that wide use of Viramune would likely be a good thing.—Martin Delaney

Dual-Class Fixed Dose Combination

Class: Dual-class fixed dose combination; single dose regimen—nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTI or nukes) and non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)

Standard dose: One tablet ([600 mg] Sustiva and Truvada [200 mg Emtriva, 300 mg Viread]), once-a-day; on an empty stomach or with a light, low-fat snack. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $1,465.54 / month

Manufacturer contact: Bristol-Myers Squibb, www.atripla.com, 1 (800) 334–4486 and Gilead Sciences, www.gilead.com, 1 (800) GILEAD5 (445–3235)

AIDSInfo: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

Potential side effects and toxicity: Includes nausea, diarrhea, rash. See the drugs contained in Atripla: Sustiva, Emtriva, and Viread. Dose cannot be adjusted for people with kidney problems.

Potential drug interactions: See the drugs contained in Atripla: Sustiva, Emtriva, and Viread. Do not take Sustiva, Emtriva, Truvada, Viread, Epivir, Epzicom, Combivir, or Trizivir, while taking Atripla, since these medications are already in Atripla or have equivalent medications. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; report symptoms of illness, such as shingles and TB, to health care provider.

Tips: Where to begin to sing the praises of Atripla? Atripla is a complete HIV treatment by itself—no other pills needed. And this is only one pill, once a day. It's a first in HIV. A great benefit: the single med cuts the number of insurance co-pays. The medicines in Atripla can be very tolerable, or not, depending on the person taking them. It is well-tolerated in most people. Atripla, however, is not for everyone. Most treatment-experienced people, those who've already been on HIV therapy, may not be able to use it due to their having developed drug resistance, when medications may no longer work against the virus. Drug resistance most commonly occurs when people don't take their HIV medicine as prescribed, but you may also be infected with a drug-resistant virus against which some of the medications in Atripla will not work. Because it is one dose once a day, it is important not to miss a dose. The separate components of Atripla have their various considerations: Sustiva cannot be taken during pregnancy, and use of Viread must be monitored in people with underlying kidney problems. In this combination product, the Viread dose cannot be adjusted. Therefore, Atripla should not be used in people with severe kidney problems. Please see package insert for more complete potential side effects and interactions. See the drugs contained in Atripla: Sustiva, Emtriva, and Viread.

Doctor

The approval of Atripla was a landmark in the history of antiretroviral therapy, since we'd finally achieved a one pill, once a day regimen. We also did it without any compromise, since this combination has been a real winner in clinical trials. However, Atripla is not an appropriate choice for everyone. I discussed some of these issues in the Sustiva section. I also avoid Atripla in patients with kidney problems, because it contains tenofovir. Remember also that Atripla is a first-line regimen; it's not intended for people who already have drug resistance.—Joel Gallant, M.D.

Activist

Atripla is the most widely used 3-drug fixed dose combination, combining Sustiva, Viread and Emtriva in a single pill taken once daily. For many it is the holy grail of HIV therapy, a powerful easy to use combination in a single pill. This works well in a great number of situations and it is close to being the most widely used initial treatment. One major limitation that concerns a fair number of people is that it is based on the use of Sustiva, which is fine if you don't have the traditional Sustiva side effects of nervous system disturbances. If you do, it's a difficult choice. Another issue is that Sustiva is strongly discouraged for women who might become pregnant. Almost everyone likes the idea of the single drug/once daily regimen. What Atripla's success really means is that drugs should be combined in this way whenever possible for the sake of simplicity. To achieve this, manufacturers will have to do what Gilead and Bristol-Myers Squibb did to create Atripla, namely cooperate. It is very unusual for competing companies to combine their products in this way, but Atripla shows that it works and benefits both the competitors and the patients. —Martin Delaney

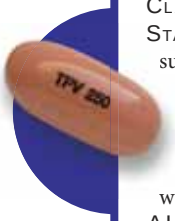
Combo Drug

Brand Name: **Atripla**

Common Name: **efavirenz, emtricitabine, and tenofovir DF**

BRAND NAME:
Aptivus

COMMON NAME:
tipranavir (TPV)



CLASS: HIV protease inhibitor (PI)

STANDARD DOSE: Two 250 mg capsules with two 100 mg capsules of Norvir, both twice daily. Must be taken with Norvir. Take with food. Take missed dose as soon as possible but do not double up on your next dose.

AWP: $1,072.80 / month for Aptivus only

MANUFACTURER CONTACT: Boehringer-Ingelheim, www.aptivus.com, 1 (800) 274–8651

AIDSINFO:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

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, have occurred with Aptivus. If a rash occurs, Aptivus should be discontinued. Other side effects include headaches, dry mouth, and dizziness. Reports of liver problems in people taking it who also have hepatitis. Be sure to know your hepatitis status if you are about to or are taking this drug! During clinical studies, bleeding in the brain occurred in people taking Aptivus/Norvir who had medical conditions or were receiving other medications that may have increased the risk of this. Use with caution by people who may be at risk of increased bleeding from trauma, surgery or other medical conditions, or who are receiving medications known to increase the risk of bleeding such as antiplatelet drugs or anticoagulants. Aptivus has a "sulfa" component to it, so it should be used cautiously in patients with "sulfa" allergies. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; report symptoms of illness, such as shingles and TB, to health care provider.

As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) 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 sometimes the upper back), onset of new cases or worsening of diabetes (see your doctor promptly), and increased bleeding in hemophiliacs. See Norvir for more details on potential side effects.

POTENTIAL DRUG INTERACTIONS: Aptivus/Norvir interacts with many other drugs, so it is important to tell your healthcare professional of the medications you are taking. See the package insert. Do not take with Tambocor, Rythmol, Cordarone, quinidine, Versed, Halcion, rifampin, pimozide, ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), or the herb St. John's wort. Do not use simvastatin, Vytorin or lovastatin for the treatment of high lipids. It also increases the concentrations of Lipitor and Crestor, and the lowest possible dose should be used in combination with Aptivus. Other lipid lowering alternatives are Lescol and pravastatin, but they should be used with caution due to potential for liver toxicity. Increased levels of the inhaled and nasal sprays with fluticasone (found in Advair, Flonase, Flovent), can occur with Aptivus/Norvir and therefore should be used with caution. Aptivus can lower blood levels of Ziagen, Videx, and zidovudine. The clinical significance of this interaction is not known. No significant changes were seen when combining Aptivus with Sustiva or Viramune. Should not be given with other protease inhibitors because it greatly lowers their blood levels. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Norvir may decrease levels of methadone, but withdrawal rarely occurs. Methadone doses may need to be increased. Trazodone concentrations may increase; a lower dose of trazodone is recommended. The blood pressure medications called calcium channel blockers should be 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 must be exercised when using Sporanax or fluconazole. Rifabutin requires a reduced dose. Norvir and Aptivus capsules contain alcohol (but should not be enough to trigger relapse), so be cautious with disulfiram or Flagyl (metronidazole).

TIPS: Received full FDA approval last year, based on 48 week data. Nevertheless, due to its resistance profile and its drug interactions, Aptivus is less popular than the other new PI, Prezista. Take with food to minimize stomach problems. Do not take at the same time as antacids. Aptivus did its best when used with Fuzeon. Aptivus is only for experienced patients. Aptivus is expected to do less well for people with combinations of certain protease-related mutations. See package insert or www.aptivus.com for a list of mutations. 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 much of the GI side effects as you might expect. The capsules should be refrigerated prior to opening. Once the bottle is opened, Aptivus can be stored at temperatures less than 77°F and must be used within 60 days. Please see package insert for more complete potential side effects and interactions.

Doctor

Aptivus was the first of what are sometimes called "second generation PIs," meaning that they work when resistance has developed to other PIs. The RESIST trials showed that Aptivus was more effective than other PIs in people with a lot of drug resistance. However, Aptivus never made a big splash, in part because of Prezista, which followed right behind, was better tolerated, less toxic, and more likely to be active against resistant virus. If you have a lot of PI mutations, you may be resistant to both drugs or to neither, but if you're only resistant to one, more often than not it's Aptivus. However, I've seen a few patients whose resistance tests show susceptibility *only* to Aptivus, which points out how important it is to do resistance testing before choosing drugs. Aptivus must be taken with two capsules of Norvir twice a day, and it's more likely to increase lipids or cause liver toxicity than other PIs.—Joel Gallant, M.D.

Activist

Aptivus requires twice the normal dose of ritonavir, which adds substantially to the overall cost of using the drug, as well as making it cumbersome to use. Its value nearly disappeared when Prezista, and then Isentress, became available. Perhaps the only reason the drug is still on the market is that a small percentage (about 10%) of people who are resistant to all other protease inhibitors, and resistant to Prezista, still show some sensitivity to Aptivus. No one disputes the value of having a "last chance" drug available, even if it is needed only rarely. —Martin Delaney

CLASS: HIV protease inhibitor (PI)

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 combination doses taken with food, and with plenty of water to avoid kidney sludge or stones). Take missed dose as soon as possible, but 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

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Headache, fatigue or weakness, malaise (general ill feeling), 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, and liver toxicity. Itchy/dry skin, ingrown toe nails and hair loss are unique to Crixivan. Kidney stones, which may lead to more serious problems, can also occur. If pain develops in the middle to lower stomach or the back, or if there is blood in the urine call your healthcare provider immediately. An increase in bilirubin (a test of liver function) has been reported, but it is not associated with liver problems. It may sometimes cause yellowing of the skin or eyes. As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) 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 sometimes the 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; report symptoms of illness, such as shingles and TB, to health care provider.

POTENTIAL DRUG INTERACTIONS: Do not take with Tambocor (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 simvastatin, Vytorin, or lovastatin; lipid-lowering alternatives are Lipitor, Lescol, and pravastatin, but they should be used with caution due to potential for liver toxicity.

Not recommended in combination with Reyataz. Reduce Crixivan to 600 mg every eight hours when taken with Rescriptor. Reduce Crixivan to 600 mg every eight hours when taken with itraconazole (200 mg twice-a-day) or ketoconazole (200 mg once-a-day). The dose of Mycobutin should be reduced by 50% and increase Crixivan dose to 1,000 mg every eight hours when taken together.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 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). Tegretol (carbamazepine), Dilantin (phenytoin), or phenobarbital may decrease Crixivan, so alternate seizure medications should be used. Crixivan may decrease levels of methadone but withdrawal rarely occurs and methadone doses may need to be increased. Also, increased levels of trazodone (Desyrel) 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 a kidney stone. 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 decreases Crixivan blood levels. Store in original container and keep dry. Please see package insert for more complete potential side effects and interactions.

Doctor

In the early years of the HAART era, when people mentioned "The Cocktail," they were often referring to a combination of Combivir and Crixivan, a regimen that saved countless lives in the late '90's. Today, that "cocktail" is as out of fashion as the Harvey Wallbanger. Looking back, I find it incredible that so many people could take it correctly, but those were desperate times. If you did things right, you took five rigidly-timed doses per day: one capsule of Combivir twice a day, usually with food to decrease side effects, and two capsules of Crixivan every eight hours on an empty stomach, at least a half hour before and two hours after eating. You also had to drink water all day to avoid kidney stones. The compulsive folks who were able to do this right did well, but they were slaves to the clock. Crixivan also caused dry skin, ingrown toenails, chapped lips, hair loss, diabetes, and even rare cases of kidney failure. Crixivan is seldom used anymore, and when it is, it's boosted with Norvir, which simplifies the dosing schedule but doesn't eliminate the side effects. Since it's rare to have a virus that's susceptible *only* to Crixivan, I don't come across many reasons to use this drug anymore, though I'm grateful for all the lives it saved.—Joel Gallant, M.D.

Activist

For the first year or so of the protease inhibitor era, Crixivan was the drug of choice, despite being very difficult to use. The two alternatives had even worse problems. Crixivan had to be taken three times a day, eight hours apart, without food, and with several glasses of water. Even when used with care, the drug often resulted in kidney stones. Once Viracept came along with simpler dosing and a side effect profile largely limited to diarrhea, sales of Crixivan collapsed and never recovered. Despite this, the drug is still used by a small number of people today, largely because it worked well for them and their doctors discouraged them from changing. Merck demonstrated a great sense of civic responsibility in the pricing of Crixivan, charging a price that was more than $2,000 per year below that of competing PIs. Unfortunately, the company got little credit or acknowledgement for this and therefore didn't repeat the act the next time they got a drug approved, nor did any other company follow Merck's lead.—Martin Delaney

BRAND NAME: **Crixivan**

COMMON NAME: **indinavir sulfate (IDV)**

BRAND NAME: **Invirase**

COMMON NAME: **saquinavir (SQV)**

CLASS: HIV protease inhibitor (PI)

STANDARD DOSE: Two 500 mg film-coated tablets + Norvir 100 mg two times a day with food, or within two hours after a meal. Must be taken with Norvir. Take a missed dose as soon as possible, but do not double up on your next dose. The 200 mg hard-gel capsules are still available.

AWP: $789.70 / month for 500 mg and $649.26 / month for 200 mg

MANUFACTURER CONTACT: Roche Pharmaceuticals, www.rocheusa.com, 1 (800) 562-6367

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Most common are stomach related: diarrhea, abdominal discomfort and nausea. As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) 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 sometimes the 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; report symptoms of illness, such as shingles and TB, to health care provider.

POTENTIAL DRUG INTERACTIONS: Do not take with Tambocor (flecainide), Rythmol (propafenone), Biaxin (clarithromycin), dexamethasone, Cordarone (amiodarone), Versed (midazolam), Halcion (triazolam), Rifadin (rifampin), Orap (pimozide), Lanoxin (digoxin), ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), quindine, garlic supplements, or the herb St. John's wort. Do not use Crestor (rosuvastatin), Zocor (simvastatin), Vytorin, or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol (fluvastatin), and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Data show that when rifampin is given with saquinavir/ritonavir, there is significant liver toxicity in 40% of patients. The combination should be avoided. Methadone doses may need to be increased. Increases levels of fluticasone (active component of Advair, Flonase, Flovent) and trazodone.

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

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 hours, or 25 mg Viagra per 48 hours.

TIPS: Invirase, the first HIV protease inhibitor out on the market, made a comeback over the past two years, due to study results indicating strong efficacy with fewer side effects when taken with a mini-dose of Norvir, as compared to Fortovase/Norvir. It has the considerable advantage of less diarrhea, vomiting and abdominal distension compared with Fortovase (a different formulation of saquinavir, now discontinued) plus Norvir. Invirase/Norvir has demonstrated safety, but the efficacy according to U.S. HIV treatment guidelines is inferior to Kaletra in patients new to HIV treatment. Must be taken with food. There is also some research supporting Invirase 1,000 mg + Kaletra standard dose twice-a-day in people with limited treatment options. Please see package insert for more complete potential side effects and interactions.

Doctor

Saquinavir is a PI that has had many lives. It was the first approved PI in its Invirase form, but it quickly fell out of favor because it was barely absorbed. Then came Fortovase, a soft-gel capsule formulation of saquinavir that actually made it into the bloodstream. Fortovase was later the first PI to be combined with Norvir, and the combination was effective…but not much fun to take because of the high doses of Norvir that were used. We then found out that Invirase, which came close to being taken off the market, was absorbed well when combined with Norvir and had fewer side effects than Fortovase. Fortovase promptly disappeared, and Invirase made a modest comeback, especially with the development of a 500 mg tablet. When Invirase is used now, it must always be boosted with a low-dose of Norvir. It's generally well tolerated, and a recent study found that it was as effective as Kaletra. However, because you still have to take three pills twice a day at current dose and there's no clear advantage over other PIs, it's still not widely used. Ongoing studies, including studies of once-daily doses using less Norvir, may change that, but for now it's generally viewed as an alternative to the standard PIs.—Joel Gallant, M.D.

Activist

Invirase was the first protease inhibitor approved by the FDA, in 1995. Only around 4% of the drug a person took would become active in the blood. As a consequence of this poor bioavailability, a large percentage of the people who used Invirase failed quickly on the drug. More importantly, because they were receiving the equivalent of only a partial and inadequate dose of the drug, it quickly selected for resistant mutations, thus knocking out the whole class of the new wonder drugs within a matter of months. Activists fought bitterly with the manufacturer, Hoffman La Roche, about this since the company steadfastly defended the drug and aggressively marketed it, despite the warnings by many researchers and physicians. Many people who were familiar with this early era of protease inhibitors still believe that a significant number of people lost the opportunity to benefit from protease inhibitors because of this and subsequently died. Over time, Roche quietly acknowledged the problem and worked hard to come up with a formulation (Fortovase) that overcame this problem. Roche was close to taking Invirase off the market, but instead they ended up discontinuing Fortovase, which they had worked so hard to create. In yet another irony, in one of the earliest publications about Invirase, a research group in Boston had combined Invirase with full dose Norvir in a simple 2-drug combination and showed results equal to or better than most 3-drug combinations which included protease inhibitors. This early study was a very advanced concept at its time and a harbinger of things to come. Today, Invirase with a low dose Norvir booster is enjoying a new popularity as a potent and relatively non-toxic treatment. When Invirase goes off patent in 2010 and generic versions become available, there is talk that some payers might even require the use of generic Invirase as the first choice among protease inhibitors as a cost-savings move.—Martin Delaney

Protease Inhibitor

Class: HIV protease inhibitor (PI)

Standard dose: Two 200/50 mg tablets twice a day or four 200/50 mg tablets once daily for first time therapy (no once-daily dose if taken with Sustiva or Viramune). Three tablets twice a day may be considered for treatment experienced or those taking it with Sustiva or Viramune. Half-strength film-coated tablet now available: 100 mg lopinaivr and 25 mg ritonavir. Take with or without food, preferably with food to lessen side effects; liquid formula available. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $794.99 / month

Manufacturer contact: Abbott Laboratories, www.kaletra.com, 1 (800) 222–6885

AIDSInfo: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

Potential side effects and toxicity: Diarrhea is the most common. Rash, nausea, vomiting, stomach pain, headache, muscle weakness, increased cholesterol and triglycerides (fats in the blood), and liver function tests, a sign of liver damage—this may be more common in people with hepatitis B or C. As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) 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 sometimes the 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; report symptoms of illness, such as shingles and TB, to health care provider.

Potential drug interactions: Interacts with many—tell your provider all the drugs you are taking. Do not take with Tambocor, Rythmol, Cordarone, Versed, Halcion, Uroxatral, 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 Zocor, Vytorin or Mevacor; lipid-lowering alternatives are Lipitor, Lescol, and pravastatin, but they should be used with caution due to potential for liver toxicity. Oral solution contains alcohol, so do not use with Antabuse or Flagyl (metronidazole). Avoid certain calcium channel blockers.

Dosage of methadone may need to be increased when taken with Kaletra. Increase Kaletra dose to three tablets twice-a-day with food recommended when using with Sustiva or Viramune in people who previously took HIV drugs, especially protease inhibitors. Not recommended to be taken with Lexiva. Kaletra may lower levels of zidovudine (Retrovir) and Ziagen. Videx should be given an hour before or two hours after Kaletra, if Kaletra is taken with food. Mycobutin (rifabutin) dosage should be reduced to 150 mg every other day (or 150 mg three times per week) when used with Kaletra. Phenobarbital, phenytoin or carbamazepine may lower blood levels of Kaletra. Reduces effectiveness of birth control pills; use alternative contraceptive. Mepron levels may be reduced with Kaletra. Avoid Sporanox doses greater than 200 mg per day with Kaletra. People with kidney impairment may require lower Biaxin doses with Kaletra. Immunosuppresants require close monitoring with Kaletra. Kaletra may alter Coumadin levels. Steroids, especially Decadron, may decrease levels of Kaletra. Increases levels of fluticasone (active component of Advair, Flonase, Flovent) and trazodone. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 hours, or 25 mg Viagra per 48 hours.

Tips: Kaletra twice daily was the first protease inhibitor recommended by U.S. treatment guidelines for first-time therapy. The newer formulation doesn't require refrigeration (especially important for resource-poor countries) and has fewer food restrictions. Great viral load results out to 7 years in people on their first HIV regimen. Good results also seen in heavily treatment-experienced adults, when compared to Reyataz, even those with protease inhibitor resistance. Use Kaletra with caution in people with mild to moderate liver impairment. The taste may be unappealing due to Norvir. Four tablets once daily can increase side effects, especially diarrhea. Solution (40% alcohol with peppermint taste) should be stored in the refrigerator, but is stable for up to 60 days at room temperature (77 F˚). However, avoid extreme heat and bright light. New healthcare letter on pediatric dosing following a death from overdose: carefully follow instructions. Lower blood concentrations during the third trimester of pregnancy have been observed. This may require dose adjustment. Avoid the oral solution during pregnancy. Please see package insert for more complete potential side effects and interactions.

Doctor

Kaletra is the only PI that contains a boosting dose of Norvir within the same tablet as the active PI (lopinavir). That's probably its strongest advantage over other PIs, because it means fewer prescriptions, fewer co-pays, and no concerns about refrigeration or running out of one before the other. The new tablet formulation has also reduced the pill burden to 4 per day and has made it easier on the stomach. Kaletra is also the most extensively studied of the boosted PIs, and has been the "gold standard" in that class for a long time. It's effective at high viral loads and low CD4 counts, and can be taken with or without food, once or twice a day, though twice daily dosing may be a little more effective. Now that Viracept has been taken off the list, Kaletra is the only PI recommended for pregnant women. However, Kaletra has lost its "king of the world" status in the last few years. Other PIs appear to be as effective (Reyataz, Lexiva, and Invirase) or maybe even better (Prezista), and some, such as Reyataz and Prezista, may have fewer side effects (diarrhea and lipid elevation). Sustiva also outperformed Kaletra in a recent trial, though it wasn't a complete win: Kaletra increased CD4 counts more than Sustiva, and although Kaletra was more likely to fail, there was a lot less resistance with Kaletra failure than with Sustiva failure.—Joel Gallant, M.D.

Activist

Kaletra has created a strong marketing advantage for Abbott Labs. Everyone else requires the patient to order Norvir separately, often at highly inflated prices. Kaletra has proven to be extremely durable (lasts a long time without failure or resistance), can be dosed once daily and has even performed quite well in studies as a single drug regimen. While not as successful as the best 3-drug regimens, it works well and for a long time in many patients as monotherapy. This has given researchers and patients alike legitimate hope that treatment can someday be simplified. Additional studies of simplified regimens are underway.—Martin Delaney

Brand Name: **Kaletra**

Common Name: **lopinavir/ritonavir (LPV/r)**

BRAND NAME: **Lexiva**

COMMON NAME: **fos-amprenavir calcium (FPV)**

CLASS: HIV protease inhibitor (PI)

STANDARD DOSE: Once-a-day—two 700 mg tablets with either one 100 or two 100 mg Norvir. Twice-a-day: either two 700 mg tablets (without Norvir) or one 700 mg tablet with 100 mg Norvir. PI-experienced patients should use Lexiva twice daily with Norvir. A grape-bubblegum-peppermint-flavored oral suspension is also available. No food restrictions (may be taken with or without food) with any dosing. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $734.56 / month for tablets and $112.55 for oral suspension (50 mg/mL)

MANUFACTURER CONTACT: GlaxoSmithKline, www.lexiva.com, 1 (888) 825–5249

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Because Lexiva has a "sulfa" part, it should be used with caution in patients with allergies to sulfa drugs. The most common moderate to severe side effects 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 follow-up and monitoring. 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, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) 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 sometimes the 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; report symptoms of illness, such as shingles and TB, to 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. There is insufficent information on combining Lexiva and Kaletra, or the two of them with Sustiva—consider monitoring drug blood concentrations if used. Do not take with Tambocor, 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 (hypericum perforatum). Do not use Zocor (simvastatin), Vytorin, or Mevacor (lovastatin). Lexiva can raise levels of Lipitor (atorvastatin) Crestor (rosuvastatin); if used in combination, the lowest possible dose of Lipitor or Crestor should be used. Lipid-lowering alternatives are Lescol (fluvastatin) and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Also avoid certain calcium channel blockers, used for heart disease. Lexiva can lower methadone concentrations. A dose adjustment of Mycobutin (rifabutin) will be needed when used in combination with Lexiva. Steroids, especially 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. The effectiveness of birth control pills may be decreased when taking Lexiva; women and their male partners should consider the use of alternative contraception methods with barrier.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 hours, or 25 mg Viagra per 48 hours.

TIPS: Lexiva is one of the three protease inhibitors recommended for people on antiviral therapy for the first time by the U.S. HIV treatment guidelines. It can be taken once daily in treatment naïve patients. The lower dose of Norvir may have less increase of 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 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.

Doctor

Lexiva turns into amprenavir after it gets absorbed. Amprenavir used to be available as Agenerase, which came in big, suppository-sized capsules. You had to take a lot of them, and they caused nausea, diarrhea, and other unpleasantness. The switch to Lexiva was a big improvement. With or without Norvir, the dose has been four pills per day, which can be taken with or without food either once a day (with Norvir) or twice a day (with or without Norvir). The FDA also just approved a once-daily dose of Lexiva with a lower dose of Norvir, which may lower the effect on lipids and decrease GI side effects. However, if you have PI resistance, you should take Norvir-boosted Lexiva twice a day. Failure of unboosted Lexiva could lead to mutations that can cause cross-resistance to Prezista, but that's not a problem if you boost Lexiva with Norvir.—Joel Gallant, M.D.

Activist

Lexiva (fos-amprenavir) is an improved version of an earlier protease inhibitor from GlaxoSmithKline called Agenerase. Agenerase was poorly absorbed and required a large number of pills taken daily. Lexiva solved that problem and can be used with and without a Norvir booster. Generally speaking, Lexiva doesn't require boosting when used as one's first protease inhibitor but does require the booster if a patient has had prior experience with protease inhibitors. When boosted, Lexiva can work against some forms of protease resistant virus and is generally well tolerated. Given its high potency, relative ease of use and low toxicity, it is a mystery why it is not more widely used. It deserves to play a larger role in treatment-experienced patients. —Martin Delaney

CLASS: HIV protease inhibitor (PI)

STANDARD DOSE: Almost never used at its approved dose (a lead-in dosing, then six 100 mg soft gelatin capsules twice-a-day, preferably with food—dose escalation is important to avoid side effects). 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. Take a missed dose as soon as possible, but 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 / month for 30 capsules

MANUFACTURER CONTACT: Abbott Laboratories, www.norvir.com, 1 (800) 222–6885

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Most common side effects include weakness, stomach pain, upset stomach (nausea, diarrhea, and vomiting), tingling/numbness around the mouth, hands or feet, loss of appetite, taste disturbance, weight loss, headache, dizziness, pancreatitis (see nukes), and alcohol intolerance.

As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) 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 sometimes the 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; report symptoms of illness, such as shingles and TB, to health care provider.

Other potential side effects are liver problems, such as 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: Ritonavir interacts with many other drugs. See the manufacturer package insert for the most complete list. Do not take with Tambocor, Rythmol, Cordarone, Versed (midazolam), Halcion (triazolam), Uroxatral, Rifadin (rifampin), Orap (pimozide), ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), Antabuse (disulfiram) or Flagyl (metronidazole), garlic supplements, or the herb St. John's wort. Do not use Zocor or Mevacor; lipid-lowering alternatives are Lipitor, Lescol (fluvastatin), and Pravachol, but they should be used with caution due to potential for liver toxicity. Increases levels of fluticasone (active component of Advair, Flonase, Flovent) and trazodone (Desyrel).

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 hours, or 25 mg Viagra per 48 hours.

The effectiveness of birth control pills may be decreased when taking Norvir; women and their male partners should consider the use of alternative contraception methods with barrier.

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 percent. Rifampin decreases Norvir levels by 35 percent. Contains alcohol (but should not be enough to trigger relapse), so be cautious with Antabuse (disulfiram) or Flagyl (metronidazole)—greatly hastens intoxication.

TIPS: The real strength of Norvir is in combination with other PIs (used as a boosting agent), allowing for a lower dose of both and in many cases decreasing the frequency of doses. Stomach side effects are reduced by taking Norvir with high fat foods (such as peanut butter or avocado)—however, be careful because some other HIV medicines should not be taken with high fat foods. You can mix liquid solution in ice cream, milk or pudding to hide the taste. The capsules contain castor oil and have bitter taste. Chocolate masks the bitter taste. Blood concentration increases in people with hepatic (liver) impairment. Please see package insert for more complete potential side effects and interactions.

Doctor

Norvir didn't have an auspicious beginning. You had to gradually work your way up to the full dose of 6 capsules twice a day because the side effects were so awful, but even with "dose escalation," the side effects were *still* awful: nausea, diarrhea, fatigue, tingling sensations, and general misery were pretty typical. We came up with all sorts of strategies to reduce the misery. I remember telling my patients about the importance of the "Three F's": food, fat, and fiber. (The drug was raising my patients' cholesterol and triglycerides, and I was telling them to *eat more fat*…in Baltimore, where there's no shortage of fat in the diet!) It was also a drug that had the longest list of drug interactions anyone had ever seen. In the end, though, it was the drug interactions that rescued Norvir from oblivion. It turned out that much lower and more tolerable doses of Norvir could be used to increase the drug levels of the other PIs, which made them stronger and less prone to resistance and allowed them to be taken less often or with fewer pills. That's the only legitimate use for Norvir now, and it's an important one. The only reason *not* to take Norvir if you're on a PI is if you're what I call a "ritonophobe": one of those rare people who can't tolerate even a single capsule. That doesn't apply to Invirase, Prezista or Aptivus, which *must* be boosted. And if you're still taking 600 mg twice a day, consider getting a second opinion!

The instructions on your bottle of Norvir will mention the need for refrigeration, but that's more important for storage by the pharmacist than it is for you. A month's supply doesn't *have* to be refrigerated; it can be kept at standard room temperature, but it shouldn't be allowed to get too hot.—Joel Gallant, M.D.

Activist

Within the first year of sales, it became clear that there was little or no use for full dose Norvir. An easier to tolerate pill version was launched in a few years, but liver and cholesterol problems also surfaced with annoying frequency. Over time, the use of the drug as a booster took prominence. Still, not everyone agrees that using Norvir as a booster is an acceptable thing. They argue that Norvir boosts many other drugs by suppressing a powerful and natural function of the liver that is intended to protect the body from a variety of harmful substances. Moreover, it creates a large and sometimes difficult to manage number of interactions with other drugs that are also affected by the action of Norvir.—Martin Delaney

BRAND NAME: **Norvir**

COMMON NAME: **ritonavir (RTV)**

BRAND NAME: **Prezista**

COMMON NAME: **darunavir (DRV, formerly TMC-114)**

CLASS: HIV protease inhibitor (PI)

STANDARD DOSE: 600 mg (two 300 mg tablets) with 100 mg Norvir, twice daily, with food. Take missed dose as soon as possible, but if more than 6 hours late, do not double up on your next dose; take the next dose on schedule.

AWP: $900 / month

MANUFACTURER CONTACT: Tibotec Therapeutics, www.prezista.com, 1 (877) REACH-TT (732-2488)

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Prezista may cause mild to moderate rash, but the most common side effects include diarrhea, nausea, headache, and common cold. Severe rash, while rare, can be life-threatening; notify your healthcare provider immediately. If you experience blistering, mouth sores, conjunctivitis (redness or inflammation of eye, or pink eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or general malaise (general ill feeling), you may need to stop all medications, so seek medical attention immediately. Prezista contains a "sulfa" part to it and should be used cautiously by people with "sulfa" allergies. Overall, the rate of adverse effects were similar between Prezista and the comparator group studied, with diarrhea being the most common side effect, seen less in the Prezista groups.

As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz), 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 sometimes the 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; report symptoms of illness, such as shingles and TB, to health care provider.

POTENTIAL DRUG INTERACTIONS: Do not take with midazolam, triazolam, ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), or the herb St. John's wort. Medications used for seizures such as Tegretol (carbamazepine), Dilantin (phenytoin), or phenobarbital may decrease Prezista/Norvir levels and alternate seizure medications should be used. A reduced dose of rifabutin is recommended. Do not use Zocor, Vytorin, Mevacor, or Pravachol; lipid-lowering alternatives such as Lipitor can be used with caution due to potential for liver toxicity. The antifungal drugs such as itraconazole and ketoconazole may increase levels of Prezista, so caution must be exercised when used together (maximum dose is 200 mg a day for the antifungals). Vfend is not recommended. Prezista/Norvir may decrease Zoloft and Paxil, but no dosing changes are recommended. Kaletra and Invirase lower Prezista levels and Prezista can decrease methadone levels and increase Biaxin levels, but the clinical significance of these interactions is unknown.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 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 they should be monitored for side effects. A lower dose of trazodone 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, Cutivate, Flonase, and Flovent) can occur and therefore should be used with caution. Effectiveness of birth control pills may decrease, consider the use of alternative or additional contraception. Other interactions include Vascor, Lidoderm, Cordarone, Lanoxin, Carbatrol, Rifadin, Rifater, Rifamate, Plendil, Adalat, Cardene, Decadron, Crestor, and Neoral.

TIPS: Prezista is approved for people who are treatment-experienced. Tibotec received community kudos for not pricing Prezista higher than other new PIs. In clinical trials of highly treatment-experienced people, 45% of patients taking Prezista achieved undetectable viral loads (less than 50 copies) when compared to control arm, of which only 12% achieved this. Similar results were found at 48 and 96 weeks. Also, in all these studies there was a significant increase in CD4 T-cell counts in patients taking Prezista. In a recent trial it demonstrated superior viral load responses when compared to Kaletra. Limited information is available in treatment-naïve patients but the dose studied is not commercially available. Please see package insert for more complete potential side effects and interactions.

Doctor

Prezista, the most recently approved PI, is a rising star. It was approved based on the POWER studies, which demonstrated its effectiveness in people with lots of drug resistance, including resistance to PIs. Then came the TITAN study, which found that in people with less extensive drug resistance, it was better than Kaletra overall, and maybe even in those whose virus was still susceptible to Kaletra on resistance tests. Finally, the recent ARTEMIS study found that a lower, once-daily dose of Prezista was at least as effective as Kaletra in people starting therapy for the first time, and *more* effective in those with high baseline viral loads. Prezista also caused less lipid elevation and diarrhea than Kaletra, though most people were using the older capsule formulation of Kaletra, which may cause more diarrhea. The dose used in that study (800 mg of Prezista plus 100 mg of Norvir once a day) is not available yet—the closest you could get would be to take three 300 mg tablets of Prezista with 100 mg of Norvir), but the manufacturer is working on a new formulation. Prezista is the new gold standard PI for people with just about any degree of PI resistance, and it's beginning to look promising as a first PI, as well.—Joel Gallant, M.D.

Activist

Prezista, unlike Aptivus, is easy to use, requires only a small amount of Norvir booster and is genuinely well tolerated. It was initially tested in advanced stage patients with a long history of resistance to multiple classes of drugs. It proved highly effective and durable in this population and appeared to add little toxicity of its own. Later studies demonstrated superiority to a Kaletra regimen in some patient populations. Today, Prezista is widely considered the best or at least among the best of all protease inhibitors. Prezista is difficult to write about from an activist perspective because the drug works very well and the manufacturer has exhibited excellent behavior in its relations with the community.—Martin Delaney

CLASS: HIV protease inhibitor (PI)

STANDARD DOSE: One 300 mg capsule plus 100 mg Norvir, once daily (this dose must be used if taking Viread or Truvada), or two 200 mg capsules, once daily; take with food. Also available in 100 mg and 150 mg capsules. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $927.14 / month 150 mg, 200 mg, or 300 mg capsules

MANUFACTURER CONTACT: Bristol-Myers Squibb, www.reyataz.com, 1 (800) 272–4878

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Dizziness and lightheadedness. Elevated levels of unconjugated bilirubin (produced by the liver) were reported in studies. This may result in cases of jaundice (yellowing of the skin or eyes), reported in 7–9% of individuals taking Reyataz. However, no evidence of liver problems was reported. These symptoms may go away after about two weeks or after you stop taking Reyataz. Other side effects include rash, kidney stones, and elevated liver function tests, a sign of liver damage; this may be more common in people with hepatitis B or C.

As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) which may be associated with an increased risk of heart disease. However, if Reyataz is boosted with Norvir these same changes in cholesterol and triglycerides may occur. 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 sometimes the upper back), changes in heart rhythm, 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; report symptoms of illness, such as shingles and TB, to health care provider.

POTENTIAL DRUG INTERACTIONS: Treatment-experienced people cannot take with proton pump inhibitors (PPIs—long-acting medicine for acid reflux). Treatment-naïve people can take no more than 20 mg a day of the PPI Prilosec-OTC (or the equivalent thereof) 12 hours before their Reyataz/Norvir. Pepcid may be taken (no more than 20 mg a day if treatment-experienced or 40 mg a day if treatment-naïve, or equivalent doses) at the same time as Reyataz/Norvir (before the antacid has started to work) or at least 10 hours later. If taking with Viread or Truvada *and* Pepcid, you must take them with 400 mg Reyataz /100 mg Norvir. 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 (Rolaids, Tums, and Mylanta). Do not take with rifampin, Camptosar (irinotecan), Versed, Halcion, ergot derivatives (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), pimozide, Crixivan, or St. John's wort. Do not use simvastatin, Vytorin, or lovastatin; lipid-lowering alternatives are Lipitor, Lescol, and pravastatin, but they should be used with caution due to potential for liver toxicity.

Must be taken two hours apart from Videx, due to Videx's buffer, and must take Videx EC an hour before or two hours after Reyataz (unless taking Videx EC with Viread). Boost with Norvir (100 mg) when taking in combination with Sustiva. Viread decreases the concentration levels of Reyataz. In addition, Reyataz increases Viread concentrations, which could increase Viread-associated adverse events, including kidney disorders. The FDA suggests those receiving Reyataz and Viread should be monitored for Viread-associated adverse events. The heart medications Tambocor, Rythmol, Cordarone, quinidine, and lidocaine should be used cautiously. Monitoring may be required when used with Coumadin or immunosuppressants. 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 decrease, consider the use of alternative or additional contraception. Use caution when using itraconazole or ketoconazole. Vfend is not recommended. Reduce dose and frequency of rifabutin to 150 mg once a day.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours, 2.5 mg Levitra per 24 hours, or 25 mg Viagra per 48 hours. Medications used for seizures such as carbamazepine, Dilantin (phenytoin), or phenobarbital may decrease Reyataz levels and alternate seizure medications should be used. The blood pressure medications called calcium channel blockers should be monitored for side effects because Reyataz may increase levels of these medications. Also increased levels of trazodone can occur with Reyataz. A lower dose of trazodone is recommended.

TIPS: Reyataz/Norvir is now one of the three protease inhibitors recommended by the U.S. HIV treatment guidelines for people on antiviral therapy for the first time. May be an option for patients with cholesterol problems. Needs an acidic environment, so take it with food. Please see package insert for more complete potential side effects and interactions.

Doctor

Atazanavir is now the easiest and best tolerated of the PIs. Whether it's given boosted or unboosted, the dose is just two pills per day. It's easy on the tummy and doesn't raise lipids or cause insulin resistance as much as some other PIs do. Its biggest drawback is that it needs stomach acid to get absorbed, which is a problem if you're taking medications that lower stomach acid to treat heartburn, ulcers, or reflux. If you're taking Reyataz with a proton pump inhibitor (Prilosec, Nexium, Protonix, Prevacid and Aciphex), antacids or H2 blockers (Tagamet, Zantac, Pepcid, etc.), you have to separate the doses carefully. The other problem is jaundice—a small fraction of people who take Reyataz will develop yellow eyes or skin. This is a completely harmless side effect, but it's probably not the "look" you were going for. When that happens, it usually requires a switch to a different drug. There have been recent reports of kidney stones with Reyataz, though this is far less common than with Crixivan.—Joel Gallant, M.D.

Activist

Reyataz offers some advantages over earlier drugs. It is not completely cross resistant with other drugs of this class, meaning it can work despite the presence of some resistance mutations. Perhaps more importantly, it was the first protease inhibitor that seems to cause less disturbance of cholesterol processing by the body. It can, however, cause a type of liver problem that results in jaundice (yellowing of the skin or eyes), though this is seen in less than 10% of users. The problem corrects itself quickly when a person is taken off the drug. —Martin Delaney

BRAND NAME: **Reyataz**

COMMON NAME: **atazanavir sulfate (ATV)**

BRAND NAME: **Viracept**

COMMON NAME: **nelfinavir (NFV)**

CLASS: HIV protease inhibitor (PI)

STANDARD DOSE: 1,200 mg taken as either two 625 mg tablets or five 250 mg tablets twice-a-day with food. Take a missed dose as soon as possible, but do not double up on your next dose. Viracept Oral Powder also available for children and individuals unable to swallow tablets.

AWP: $726.40 / month for 625 mg

MANUFACTURER CONTACT: Agouron Pharamaceuticals, a Pfizer company, www.viracept.com, 1-800-879-3477 (TRY-FIRST)

AIDSINFO:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Most common include: diarrhea (30–40% of patients), stomach discomfort, nausea, gas, weakness, and rash. As seen with other protease inhibitors, there can be increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz) 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 sometimes the 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; report symptoms of illness, such as shingles and TB, to health care provider.

POTENTIAL DRUG INTERACTIONS: In general, less severe interactions compared to other drugs in this class. Do not take with Versed (midazolam), Cordarone (amiodarone), Halcion (triazolam), Rifadin (rifampin), Prilosec (omeprazole), ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form), garlic supplements, or the herb St. John's wort (hypericum perforatum). Do not use Zocor (simvastatin), Vytorin or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol (fluvastatin), and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Viracept may decrease methadone levels but withdrawal rarely occurs; methadone doses may need to be increased.

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. Invirase levels increase three-to-five-fold and Crixivan increases 50% (see Crixivan for potential drug interactions), so dose adjustments may be needed. 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 per 72 hours, 2.5 mg Levitra per 24 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; women and their male partners should consider the use of alternative or additional contraception methods. Also, increased levels of trazodone (Desyrel) can occur. A lower dose of trazodone is recommended.

TIPS: Do not leave pharmacy without anti-diarrhea meds such as Immodium, 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. Ethyl methanesulfonate (EMS) is a process-related impurity in Viracept. In June 2007, excess levels of EMS detected in Viracept caused recall of the product in Europe. So far EMS has not been detected at high levels in the U.S. Exposure to EMS can potentially increase the risk of cancer in adults. As a precaution, the maker of Viracept is not recommending to start Viracept in pediatric patients and pregnant women.

People using Viracept can crush adult tablets or dissolve tablets in a small amount of water. Acidic food or juice (e.g. orange/apple juice or apple sauce) not recommended in combination with Viracept, 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 of at least 500 calories, with at least 20% to 50% of those calories coming from fat. Please see package insert for more complete potential side effects and interactions.

Doctor

Once upon a time, Viracept was the "kindler, gentler" PI, because it was easier to take (only five chalky tablets twice a day!) and was better tolerated (if you didn't mind lots of diarrhea) than its biggest competitor, Crixivan. Its other claim to fame was that cross-resistance wasn't as bad when you failed Viracept than when you failed other PIs. All that was true—it really *was* an improvement over what was out there at the time. But the standard of care has changed, leaving poor Viracept in the dust. Today, all PIs—with the lone exception of Viracept—are given with a low "boosting" dose of Norvir. This makes them more effective and means that rather than getting *better* mutations, you get *no* mutations at all. Most can be given once a day, and they all cause less diarrhea than Viracept. Just about every drug that's been compared with Viracept has come out on top. Until recently, the only remaining argument for the use of this drug was that it had a good safety record in pregnancy. But now that a carcinogen has been found in Viracept tablets, it's no longer recommended for pregnant women, either. I can't think of a good reason anymore to use this once very important drug.—Joel Gallant, M.D.

Activist

Viracept (nelfinavir) is one of the older protease inhibitors and is not widely used today. Viracept was relatively easy to use, not yet known to contribute to cholesterol problems, and relatively non-toxic. Its worst defect was that it caused diarrhea, which didn't sound all that bad. Over time though, daily diarrhea became intolerable to many people. There was also a nagging suspicion that Viracept just wasn't as potent as Crixivan. The drug sold well for a number of years, but only until something better came along. The solution, Kaletra, demonstrated fewer problems and greater potency and it quickly came to dominate the market, pushing Viracept on to the back shelf. An improved formulation of Viracept helped a bit with the diarrhea but by then it was too late to regain its position in the HIV marketplace. Though still available today, Viracept is seldom used. —Martin Delaney

CLASS: 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. No food restrictions (take with or without food). Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $2,333.93 / month for 90 mg kit

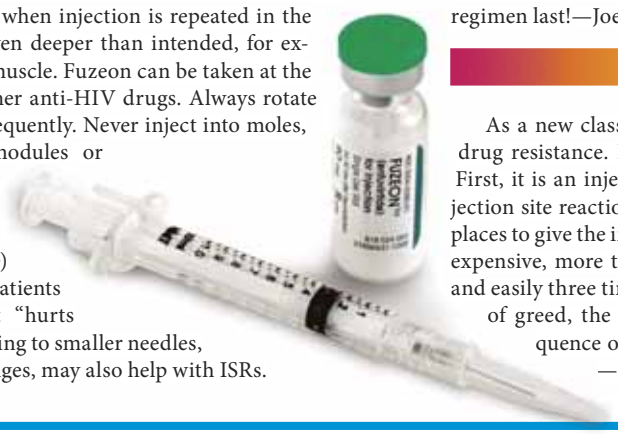
MANUFACTURER CONTACT: Roche Pharmaceuticals and Trimeris, www.rocheusa.com, www.trimeris.com, www.fuzeon.com, 1 (877) 4–FUZEON (438–9366)

AIDSINFO:
1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: The most common are Injection Site Reactions (ISRs), which occur in virtually all patients. The severity of reactions is variable, and for most is mild to moderate. Symptoms could include itching, swelling, redness, pain or tenderness, hardened skin or bumps; others include headache and fever. 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. Allergic 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 healthcare provider right away. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; report symptoms of illness, such as shingles and TB, to health care provider.

POTENTIAL DRUG INTERACTIONS: To date none found clinically significant.

TIPS: With other powerful new drugs on the market, the twice-daily injectable Fuzeon has truly become a medicine of last resort. In fact, some specialists are taking patients off Fuzeon and putting them on one of those newer drugs, Isentress. Fuzeon is intended for treatment of HIV in patients who are treatment-experienced. Preparing and injecting the Fuzeon can be complicated, so ask your healthcare provider how to do it. First, the drug needs to be dissolved with sterile water (provided in the kit), which may take 30 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 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. Fuzeon can be taken at the same time as other anti-HIV drugs. Always rotate injection sites frequently. Never inject into moles, scars, bruises, nodules or the navel. Study with a bioinjection (needleless injection device) was stopped; patients reported that it "hurts like hell." Switching to smaller needles, like insulin syringes, may also help with ISRs.



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 entered the pharmacy last year (see Selzentry). Because of injections, this drug will most likely be used in the heavily-treatment experienced and salvage therapy options. Two large Phase 3 studies showed good viral load decrease when added to an optimized antiviral combination in heavily treatment-experienced people, including those with protease inhibitor-resistant virus and those who've taken three drug classes. (Remember, though, there are now newer drugs on the market, including a newer drug class.) Participants used three to five antivirals in addition to Fuzeon, and both genotype and phenotype tests.

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 new active drugs, if possible, when changing therapy, to make it more effective. Please see package insert for more complete potential side effects and interactions.

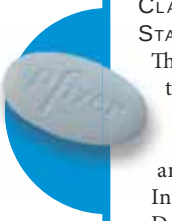
Doctor

Fuzeon, the only fusion inhibitor, stops HIV from entering the cell by preventing fusion of the envelope of the virus with the membrane of the cell. The TORO studies showed how effective it was—until TORO, we never expected people with extensive drug resistance to achieve undetectable viral loads. However, Fuzeon has generally been viewed as a temporary bridge to easier forms of "salvage therapy." It's given by twice-daily injection and leaves painful bumps under the skin that can last for days and can eventually leave people with thick, leathery skin at the injection sites. People who are currently taking Fuzeon and maintaining undetectable viral loads are switching to other drugs, especially Isentress, now that they're available. However, there will still be a need for Fuzeon in some patients with highly-resistant virus. For example, people who can't take Selzentry because they have the wrong tropism and who already have mutations that make them resistant to Prezista, Aptivus, and/or Intelence may need to take Fuzeon along with Isentress. For those of you not currently in need of Fuzeon, think of it as a strong incentive to make your current regimen last!—Joel Gallant, M.D.

As a new class of drug, Fuzeon is unaffected by previous drug resistance. It has very low toxicity. Just two problems. First, it is an injection. Nearly everyone develops painful injection site reactions (ISRs). Over time, people just run out of places to give the injections. Secondly, the drug is horrendously expensive, more than twice the price of any other HIV drug and easily three times the cost of most. Despite the appearance of greed, the high price really is unfortunately a consequence of the extreme difficulty of making the drug.
—Martin Delaney

BRAND NAME: **Fuzeon**

COMMON NAME: **enfuvirtide (ENF) or T-20**



BRAND NAME: **Selzentry**

COMMON NAME: **maraviroc (MVC, formerly UK-427,857)**

CLASS: CCR5 antagonist (a type of entry inhibitor)

STANDARD DOSE: Available in 150 mg and 300 mg tablets. The recommended dose varies depending on other medications the patient is taking: 150 mg twice daily if taken with a protease inhibitor (except for Aptivus) and Rescriptor; 300 mg twice daily if taken with Aptivus, Viramune, Fuzeon, and all of the nukes; 600 mg twice daily if taken with Sustiva, Intelence, rifampin, and some anti-seizure medications. Default to the CYP3A inhibitor dose (the PI group) when using medications from different groups (such as a PI with a non-nuke). 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: $1,044/month for 150 mg or 300 mg tablets

MANUFACTURER CONTACT: Pfizer Laboratories, www.Selzentry.com, 1-800-879-3477 (TRY-FIRST)

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

POTENTIAL SIDE EFFECTS AND TOXICITY: Most common include cough, fever, cold, rash, muscle and joint pain, stomach pain, and dizziness. Other potential side effects 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 include: low blood pressure when standing up that could lead to dizziness or fainting, diarrhea, edema (swelling), trouble sleeping, and urinary problems. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; report symptoms of illness, such as shingles and TB, to 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: Aptivus/Norvir, co-trimoxazole (Bactrim), and Viread have no interactions with Selzentry. Nizoral (ketoconazole), Kaletra, Norvir, Invirase, and Reyataz all increased Selzentry concentrations. Rifampin and Sustiva reduced Selzentry concentrations. Selzentry did not affect the concentrations of Versed (midazolam) and oral contraceptives.

TIPS: Maraviroc is the first oral entry inhibitor available on the market. It is indicated for the treatment-experieced 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 one of 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 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 available at the time of writing, Pfizer did not find that blocking R5 with maraviroc caused virus to shift to X4 or show any other negative effect in so-called "dual tropic" people (their virus can use either R5 or X4). Last year the company reported that a switch to X4 or dual tropic virus was transient and reversible when people went off maraviroc. In the MOTIVATE studies, 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. Selzentry has been studied in treatment-naïve patients (first time on therapy) with less than impressive results. It was unable to match Sustiva at viral loads less than 50 copies. For now, this drug seems to be limited to treatment-experienced patients with CCR5-tropic virus.

Doctor

Selzentry is the first available oral entry inhibitor. It works by preventing binding of the virus to the CCR5 coreceptor on the cell surface. Unfortunately, not all virus uses CCR5 to get into the cell—some gets in by binding to the other coreceptor, CXCR4. Only people with "R5-tropic virus" should take Selzentry. To find out your tropism, you need a tropism assay—the only one currently available is the pricey Trofile assay from Monogram Biosciences. If the test shows "X4-tropic virus" or "dual/mixed-tropic virus" (D/M), don't take Selzentry, because it won't suppress all your virus, and it won't protect your other drugs from resistance. The test is accurate most of the time, but very small amounts of D/M or X4 virus can sometimes be missed. When that happens, Selzentry is more likely to fail, because the drug will suppress only the R5 virus, leaving the D/M or X4 virus to replicate and become predominant. This may be a more common cause of Selzentry failure than drug resistance, at least early on. Selzentry was shown to be very effective and well tolerated in patients with highly resistant, R5 tropic virus in the MOTIVATE trials. However, because of the need for tropism testing, twice-daily dosing, and the lack of long-term safety data for this new class, it's not likely to be used for first-line therapy anytime soon. Also, since you need a viral load of at least 1,000 to get a tropism test, this is also not a drug that can be used to replace other drugs, such as Fuzeon, if your viral load is undetectable.—Joel Gallant, M.D.

Activist

Selzentry is another new entry inhibitor which blocks the ability of HIV to connect to what's called the CCR5 receptor, a key entry point for the virus. In studies Selzentry has proven itself very effective in people with advanced disease and high levels of drug resistance. To date it has had an excellent safety record, though there are some lingering doubts in this regard because it is the first drug of this type. Some scientists wonder whether there might be other consequences to blocking this CCR5 receptor, which is apparently used by the body in other ways that are not well known. Still, the data is the data, and to date it shows no evidence of any significant harm attributed to the drug. The drug's biggest drawback is the need to take an expensive test before using it. This drug is probably more useful than people give it credit for. It's highly potent, even in people with resistant virus, and shows little signs of toxicity. The biggest obstacle it faces is fear of the unknown.—Martin Delaney

CLASS: integrase inhibitor

STANDARD DOSE: One 400 mg film-coated tablet twice a day, with or without food. Take missed dose as soon as possible, but do not double up on your next dose.

AWP: $1,012.50 / month

MANUFACTURER CONTACT: Merck and Co., www.Isentress.com, 1 (800) 622–4477

AIDSINFO: 1 (800) HIV–0440 (448–0440), www.aidsinfo.nih.gov

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 lipodystrophy. Other observations with unclear relationship to Isentress include cancer (new and recurrent). Most patients had other risk factors for cancer, low white count (neutropenia), low platelets, and elevated liver tests. Elevated levels of a muscle enzyme (creatine kinase) on blood tests. Contact your healthcare provider if you experience unexplained muscle pain, tenderness, or weakness. 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; report symptoms of illness, such as shingles and TB, to health care provider.

POTENTIAL DRUG INTERACTIONS: Isentress is not expected to affect the drug concentrations of other PIs, non-nukes, methadone, cholesterol medications, antifungals, proton pump inhibitors (like Prilosec), oral contraceptives, and erectile-dysfunction drugs. It did have an effect on the concentrations of Epivir and Viread. Rifampin reduces the concentrations of Isentress; caution should be used when coadministering. 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. Caution advised in people taking medications that can cause muscle problems. Caution with rifampin, which reduces plasma concentrations of Isentress.

TIPS: According to treatment advocates, Isentress is a rising star. 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. Some HIV specialists are now switching patients off Fuzeon and on to Isentress. There are hopes of Isentress replacing a boosted PI. Isentress is exciting for several reasons. This is one of the truly new drugs that advanced patients are in so desperate need of. Isentress doesn't have to be boosted with the dreaded Norvir like so many other new HIV drugs, has had no major interactions with other HIV drugs, and can be taken with or without food. A big plus: cholesterol and triglyceride blood levels have not been a problem with Isentress, out to 48 weeks results. It's shown good potency in early (two weeks) results in both people on therapy for the first time and those who were heavily treatment-experienced, compared to the gold-standard Sustiva plus optimized background. The idea of such early and amazing potency—never seen with an HIV drug before—is exciting. An amazing number of people reached undetectable viral load in durable results: at 48 weeks, 64 to 71% of people on Isentress (depending on the dose used in study) had less than 400 viral load; 46 to 64% of them had less than 50. The majority of people with treatment failure, however, were those who had no other active drug to add along with Isentress. With so many new and newer HIV drugs on the market now (Prezista, Selzentry, Aptivus, Intelence, Fuzeon) that problem should be less common. The rate of side effects was similar to the study group taking placebo (both the placebo group and the Isentress group used an optimized background—the best drug combination they could take). In data presented to the FDA for approval, the people taking raltegravir had more than twice the decrease in viral load than seen in the placebo (dummy pill) group (-1.85 vs. -0.84 log). This drug did its best when used with Fuzeon. It was not, however, tested with other newer drugs now available in the pharmacy. In vitro (test tube) cross-resistance has been observed to other integrase inhibitors under development, which could limit this class in the future. More research is needed in this area. Please see package insert for more complete potential side effects and interactions.

Doctor

After the virus enters the cell, its RNA gets turned into DNA by reverse transcriptase. The viral DNA then enters the nucleus and gets inserted ("integrated") into human DNA. Integrase inhibitors block the step. The development of these drugs has been slow and painful, but they're finally here, and the first one out of the gate looks like a winner. Patients with extensive drug resistance in the BENCHMRK trials did extremely well if they took Isentress with at least one fully active drug. In fact, the results were at least as good as what we expect in patients starting therapy for the first time with no resistance. There's also a smaller trial comparing Isentress with Sustiva (in combination with Viread and Epivir) as first-line therapy, and both drugs looked great. Isentress drove the viral load down faster than Sustiva, though that may not make any difference in the long-term. Isentress is very well tolerated. Side effects in clinical trials have generally been "the same as placebo," and you can't do much better than that. Of course, with just one year's worth of data, it's too soon to declare it free of toxicity, but the early data are encouraging. We'll sort out the uses of Isentress with time, but if you've got resistant virus and need to put together a new regimen, using Isentress is a no-brainer. The more challenging question is what to combine it with to prevent resistance. Resistance to integrase inhibitors can occur rapidly if they're not combined with other active drugs. I'm hoping we'll use this drug wisely, so we don't see an epidemic of integrase inhibitor resistance a year from now.—Joel Gallant, M.D.

Activist

In very advanced patients, Isentress, like Selzentry, showed little or no evidence of any added toxicity. Unlike Selzentry, people don't seem to have many lingering doubts about Isentress. Its availability has been met with a level of enthusiasm not seen for any drug in many years. This is backed up by initial sales in the marketplace, which have taken off like a rocket and have even carried some other new drugs, such as Prezista, along with it.—Martin Delaney

BRAND NAME: **Isentress**

COMMON NAME: **raltegravir (RAL, formerly MK-0518)**

CURRENT DHHS TREATMENT GUIDELINES

Clinicians are recommended to construct an initial regimen (for first time therapy) by choosing one component from Column A plus one component from Column B*

	Column A		Column B
	NNRTI	PI	2-NRTI
Preferred (alphabetical order)	Efavirenz [1]	Atazanavir + ritonavir Fosamprenavir + ritonavir (twice daily) Lopinavir/ritonavir (twice daily)	Tenofovir/emtricitabine [3] Zidovudine/lamivudine [3]
Alternative (alphabetical order)	Nevirapine [2]	Atazanavir [4] (unboosted) Fosamprenavir (unboosted) Fosamprenavir + ritonavir once daily Lopinavir/ritonavir once daily	Abacavir/lamivudine [3] Didanosine + lamivudine [3]

[1] Except during first trimester of pregnancy or in women with high pregnancy potential

[2] 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] Emtricitabine and lamivudine are interchangeable

[4] Atazanavir must be boosted with ritonavir if used in combination with tenofovir.

Editor's note: Above drug names are generic. Please refer to the individual drug pages for brand names, or visit www.tpan.com.

** Panel on Antiretroviral Guidelines for Adult and Adolescents. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Department of Health and Human Services. December 1, 2006; 1–136. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed November 16, 2007; page 59, Table 6a.*

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DRUG INTERACTIONS CHART

An abbreviated, at-a-glance guide to HIV drug interactions

Updated by Mariela Diaz-Linares and Enid Vázquez

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 healthcare 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)	
Potential drug class interactions	None.
Combivir	See Epivir and zidovudine (Retrovir). Do not take with zidovudine, Epivir, Epzicom, Trizivir, Emtriva, Truvada, or Atripla while taking Combivir, since all or part of these medications are already in Combivir or have equivalent medications.
Emtriva (emtricitabine, FTC)	No significant drug interactions. Do not take Truvada, Atripla, Epivir, Epzicom, Combivir, or Trizivir while taking Emtriva, since they contain Emtriva or medication equivalent to it.
Epivir (lamivudine, 3TC)	No significant drug interactions. Do not take Epzicom, Combivir, Trizivir, Truvada, or Atripla while taking Epivir, since they contain Epivir or medication equivalent to it.
Epzicom	See Epivir and Ziagen. Do not take with Combivir, Epivir, Trizivir, Emtriva, Truvada, or Atripla while taking Epzicom, since all or part of these medications are already in Epzicom or have equivalent medications.
Retrovir (zidovudine or ZDV, AZT)	Do not take with Combivir or Trizivir, since zidovudine is already in these medications. Amphotericin B, Benemid, Biaxin, Cytovene, dapsone, Depakote, Dilantin, doxorubicin, flucytosine, ganciclovir, hydroxyurea, interferon-alpha, Mycobutin, pentamidine, Rebetol, ribavirin, rifampin, sulfadiazine, Valcyte, Vitrasert, and Zerit.
Trizivir	See Epivir, Retrovir, and Ziagen. Do not take with zidovudine (Retrovir), Epivir, Ziagen, Emtriva, Truvada, or Atripla while taking Trizivir, since all or part of these medications are already in Trizivir or have equivalent medications.
Truvada	See Emtriva and Viread. Do not take with Emtriva, Viread, Atripla, Epivir, Combivir, Epzicom, or Trizivir, since all or part of these medications are already in Truvada or have equivalent medications.
Videx & Videx EC (didanosine, ddI)	Alcohol, Cytovene, dapsone, HIV protease inhibitors, hydroxyurea, methadone, NebuPent, Nizoral, pentamidine, Rescriptor, Retrovir, ribavirin, Sporanox, Tagamet, Viread, and Zerit.
Viread (tenofovir)	Do not take Truvada or Atripla, since Viread is in these medications. Kaletra, Norvir, Reyataz, Videx and Videx-EC.
Zerit (stavudine, d4T)	Cytovene, dapsone, Foscavir, Fungizone, pentamidine, Valcyte, Videx and Videx-EC, Vitrasert, and zidovudine (AZT, Retrovir).
Ziagen (abacavir sulfate, ABC)	Do not take with Epzicom or Trizivir, since Ziagen is already in these medications. Alcohol.

Non-Nucleoside Reverse Transcriptase Inhibitors (also called non-nucleoside analogs, NNRTIs, or non-nukes)	
Potential drug class interactions	HIV protease inhibitors; methadone.
Intelence (etravirine, TMC-125)	Aptivus/Norvir, Kaletra, Lexiva/Norvir, Norvir, Reyataz/Norvir, Selzentry, Sustiva, and unboosted PIs.
Rescriptor (delavirdine)	Adalat, Agenerase, certain amphetamines and antiarrhythmic drugs, Biaxin, birth control pills, Cafergot, carbamazepine (Tegretol and others), Cialis, Coumadin, Crixivan, dapsone, Dilantin, fluticasone (Advair, Flonase, Flovent), immunosuppressants, Invirase, Kaletra, Levitra, Lexiva, methadone, Methergine, lovastatin, midazolam, Mycobutin, Norvasc, Norvir, Orap, phenobarbital, pimozide, Plendil, Procardia, Propulsid, quinidine, rifampin, Reyataz, simvastatin, St. John's wort, triazolam, trazodone, Viagra, Viracept, Vytorin, Wigraine, and Xanax.
Sustiva (efavirenz)	Do not take with Atripla, since Sustiva is already in Atripla. Biaxin, bepridil, birth control pills, Cafergot, carbamazepine (Tegretol and others), Coumadin, Crixivan, Dilantin, Invirase, Kaletra, Lexiva, Lipitor, methadone, Methergine, midazolam, Mycobutin, Norvir, pravastatin, Reyataz, rifabutin, rifampin, phenobarbital, simvastatin, Sporanox, St. John's wort, triazolam, Vfend, and Wigraine.
Viramune (nevirapine)	Biaxin, birth control pills, calcium channel blockers, Coumadin, Diflucon (flucanozole), HIV protease inhibitors, methadone, midazolam, Mycobutin (rifabutin), Nizoral (ketoconazole), prednisone, rifampin, St. John's wort, and triazolam. See drug page for more.
Dual-class Fixed Dose Combination	
Atripla (Sustiva/Truvada)	See Sustiva and Truvada (Emtriva/Viread). Do not take Sustiva, Emtriva, Truvada, Viread, Epivir, 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, migraine medications, erectile dysfunction drugs, sedatives, tuberculosis drugs.
Aptivus (tipranavir) (must be taken with Norvir; see Norvir)	Aptivus/Norvir interacts with many other drugs, so it is important to tell your healthcare professonial all the medications you are taking. See the manufacturer package insert for the most complete list. Antabuse, birth control pills, Cafergot, carbamazepine (Tegretol and others), Cialis, Cordarone, Coumadin, Crestor, D.H.E. 45, Diflucan, Dilantin, Flagyl, fluticasone (Advair, Flonase, and Flovent), other HIV protease inhibitors, immunosuppressants, ketoconazole, Lescol, Levitra, Lipitor, lovastatin, methadone, Methergine, midazolam, Mycobutin, Norvasc, Orap, Paxil, phenobarbital, pravastatin, Procardia, quinidine, rifampin, Rythmol, simvastatin, St. John's wort, Sporanox, Tambocor, trazodone, triazolam, Viagra, Vfend, Videx, Vytorin, Wigraine, Ziagen, zidovudine, and Zoloft.
Crixivan (indinavir sulfate)	Birth control pills, Cafergot, Cialis, Crestor, D.H.E. 45, fluticasone (Advair, Flonase, Flovent), garlic supplements, Lescol, Levitra, Lipitor, lovastatin, methadone, Methergine, midazolam, Mycobutin, Nizoral, Orap, pravastatin, Rescriptor, Reyataz, rifampin, Rythmol, simvastatin, Sporanax, St. John's wort, Sustiva, Tambocor, triazolam, Viagra, Viramune, Vytorin, and Wigraine. See drug page for more.
Invirase (saquinavir) (must be taken with Norvir; see Norvir)	Aptivus, Biaxin, birth control pills, Cafergot, Cialis, Cordarone, Crestol, Crixivan, D.H.E. 45, fluticasone (Advair, Flonase, Flovent), garlic supplements, Kaletra, Lanoxin, Lescol, Levitra, Lipitor, lovastatin, methadone, Methergine, midazolam, Mycobutin, Nizoral, Norvir, Orap, pravastatin, quindine, rifampin, Rescriptor, Reyataz, Rythmol, simvastatin, St. John's wort, Sporanox, Sustiva, Tambocor, trazodone, triazolam, Viracept, Viagra, Viramune, Vytorin, and Wigraine.

Protease inhibitors (PIs) Continuedd	
Kaletra (lopinavir/ritonavir)	Antabuse, Biaxin, birth control pills, Cafergot, carbamazepine (Tegretol and others), certain calcium channel blockers, Cialis, Cordarone, Coumadin, D.H.E. 45, digoxin, Flagyl, fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, Lescol, Levitra, Lexiva, Lipitor, lovastatin, Mepron, methadone, Methergine, midazolam, Mycobutin, Orap, phenobarbital, phenytoin (Dilantin and others), pravastatin, Procardia, rifabutin, rifampin, Retrovir, Rythmol, simvastatin, St. John's wort, Sporanox, steroids (especially Decadron), Sustiva, trazodone, triazolam, Uroxatral, Viagra, Videx, Viramune, Vytorin, Wigraine, and Ziagen.
Lexiva (fos-amprenavir calcium)	Antabuse, birth control pills, Cafergot, certain calcium channel blockers, Cialis, Crestor, D.H.E. 45, Flagyl, fluticasone (Advair, Flonase, Flovent), Kaletra, Lipitor, Lescol, Levitra, lovastatin, Orap, pravastatin, Rescriptor, Rythmol, methadone, Methergine, midazolam, Mycobutin, rifampin, simvastatin, St. John's wort, steroids, Sustiva, Tambocor, trazodone, triazolam, Viagra, warfarin, and Wigraine.
Norvir (ritonavir)	See the manufacturer package insert for the most complete list. Alcohol, Antabuse, Biaxin, birth control pills, Cafergot, Cialis, Cordarone, D.H.E. 45, Ecstasy, Flagyl, fluticasone (Advair, Flonase, Flovent), garlic supplements, GHB, Lescol, Levitra, Lipitor, lovastatin, Methergine, midazolam, Orap, pravastatin, rifampin, Rythmol, simvastatin, St. John's wort, Tambocor, tobacco, trazodone, triazolam, Uroxatral, Viagra, and Wigraine.
Prezista (darunavir)	Biaxin, birth control pills, Cafergot, calcium channel blockers (Norvasc, Procardia, and others), Cialis, Coumadin, Crestor, D.H.E. 45, Decadron, fluticasone (Advair, Flonase, and Flovent), immunosuppressants, Invirase, itraconazole, Kaletra, ketoconazole, Lanoxin, Levitra, Lidoderm, Lipitor, lovastatin, methadone, Methergine, methadone, midazolam, Norvasc, Paxil, pravastatin, Procardia, rifabutin, simvastatin, St. John's wort, Sporanox, trazodone, triazolam, Vascor, Vfend, Viagra, Vytorin, Wigraine, and Zoloft.
Reyataz (atazanavir sulfate)	Aciphex (or any proton-pump inhibitor), birth control pills, Cialis, Cafergot, D.H.E. 45, fluticasone (Advair, Flonase, Flovent), garlic supplements, Lescol, Levitra, Lipitor, lovastatin, Methergine, midazolam, Mylanta, Nexium, Orap, pravastatin, Prevacid, Prilosec-OTC, rifabutin, rifampin, Rythmol, simvastatin, St. John's wort, Sustiva, Tambocor, triazolam, trazodone, Viagra, Videx and Videx-EC, Viread, and Wigraine. See drug page for more.
Viracept (nelfinavir)	Birth control pills, Cafergot, carbamazepine (Tegretol and others), Cialis, Cordarone, Crixivan, D.H.E. 45, fluticasone (Advair, Flonase, Flovent), garlic supplements, Invirase, Lescol, Levitra, Lipitor, lovastatin, methadone, Methergine, midazolam, Mycobutin, phenobarbital, phenytoin, pravastatin, Prilosec-OTC, rifampin, simvastatin, St. John's wort, triazolam, trazodone, Viagra, and Wigraine.
Entry Inhibitors	
Fuzeon (enfuvirtide, T-20)	None found to be clinically significant.
Selzentry (maraviroc)	Invirase, Kaletra, ketoconazole, Norvir, Reyataz, rifampin, and Sustiva.
Integrase Inhibitor	
Isentress (raltegravir, formerly MK-0518)	Aptivus/Norvir, Epivir, medications that can cause muscle problems, Reyataz, Reyataz/Norvir, rifampin, and Viread.

SIDE EFFECTS CHART

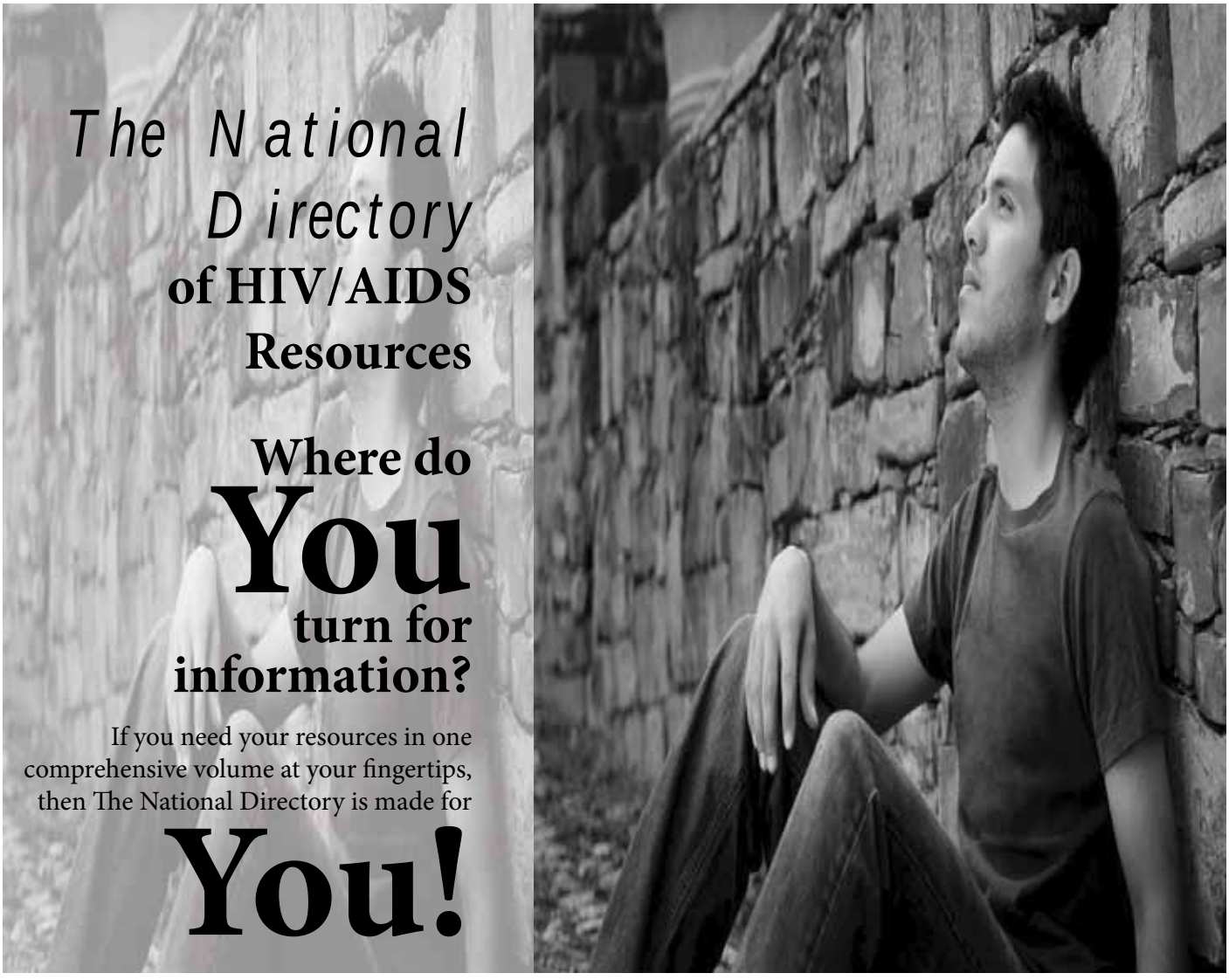
An abbreviated, at-a-glance guide to potential HIV drug side effects

Updated by Mariela Diaz-Linares, Pharm.D. and Enid Vázquez

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 healthcare providers, including your pharmacist, since small reactions may become serious. There may also be management techniques for the side effect. Visit www.acria.org/treatment/treatment_edu_side_effects.html.

Nucleoside Reverse Transcriptase Inhibitors (also called nucleoside analogs, NRTIs, or nukes)	
Potential class side effects	Pancreatitis (inflammation of the pancreas), enlarged, fatty liver, and lactic acidosis.
Combivir (Retrovir and Epivir)	See Epivir and Retrovir.
Emtriva (emtricitabine, FTC)	A very tolerable drug, but potential side effects include headache, diarrhea, nausea and rash. Darkening of the skin on the palms and the soles of the feet.
Epivir (lamivudine, 3TC)	A very tolerable drug, but potential side effects include headache, nausea, diarrhea, fatigue, hair loss, insomnia, malaise (general ill feeling), nasal symptoms, cough, peripheral neuropathy, low white blood cells and anemia. Children note pancreatitis (inflammation of the pancreas).
Epzicom (Epivir and Ziagen)	See Epivir and Ziagen.
Retrovir (zidovudine or ZDV, AZT)	Headaches, fever, chills, muscle soreness, fatigue, nausea, fingernail discoloration, anemia, and neutropenia.
Trizivir (Epivir, Retrovir, and Ziagen)	Headache, nausea, upset stomach, and fatigue. See Epivir, Retrovir, and Ziagen. Note the hypersensitivity warning on Ziagen.
Truvada (Viread and Emtriva)	See Viread and Emtriva.
Videx & Videx EC (didanosine, ddI)	Peripheral neuropathy, upset stomach, diarrhea, headache, pancreatitis (inflammation of the pancreas), eye changes and optic neuritis, increased uric acid levels, and insomnia.
Viread (tenofovir disoproxil fumarate, TDF)	Overall fairly well tolerated; however, individuals may experience the following: nausea, headache, rash, diarrhea, vomiting, asthenia (fatigue, weakness), flatulence (gas), abdominal distension/pain, loss of appetite, kidney toxicities, bone changes, pancreatitis (inflammation of the pancreas), and low blood phosphate.
Zerit (stavudine, d4T)	Peripheral neuropathy, facial wasting, mitochondrial toxicities, headache, chills/fever, malaise, insomnia, anxiety, depression, rash, upset stomach, diarrhea, abdominal pain, and blood lipid increases. Children note peripheral neuropathy.
Ziagen (abacavir sulfate, ABC)	Hypersensitivity reaction, nausea, vomiting, diarrhea, fatigue, headache, fever, rash, and loss of appetite.

Non-Nucleoside Reverse Transcriptase Inhibitors (also called non-nucleoside analogs, NNRTIs, or non-nukes)	
Potential class side effects	Rash.
Intelence (etravirine, TMC-125)	Rash, diarrhea, nausea, and headache.
Rescriptor (delavirdine, DLV)	Headache, nausea, vomiting, diarrhea, fatigue, elevated liver enzymes, itchy skin or rash.
Sustiva (efavirenz, EFV)	Central nervous system (CNS) and psychiatric symptoms. Rash, nausea, vomiting, diarrhea, fever, insomnia and increased triglycercides, good cholesterol (HDL) and liver enzymes. False positive tests for use of marijuana. Birth defects.
Viramune (nevirapine, NVP)	Headache, nausea, vomiting, fever, rash, Stevens-Johnson syndrome, and drug-induced hepatitis.
Dual-class Fixed Dose Combination	
Atripla (Sustiva/Truvada)	See Sustiva and Truvada (Emtriva and Viread). Atripla dose cannot be adjusted for people with kidney problems. Nausea, diarrhea, rash, Immune Reconstitution Inflammatory Syndrome (IRIS).
Protease inhibitors (PIs)	
Potential class side effects	Increased levels of cholesterol and triglycerides (except possibly unboosted Reyataz), lipodystrophy, onset of new cases or worsening of diabetes, Immune Reconstitution Inflammatory Syndrome (IRIS), and increased bleeding in hemophiliacs.
Aptivus (tipranavir)	Gastrointestinal-related—mild diarrhea, nausea, vomiting, abdominal pain, and fatigue. Headaches, dry mouth, rash (including sensitivity to sun), dizziness, hepatotoxicity, 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.
Crixivan (indinavir sulfate)	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, and liver toxicity. Itchy/dry skin, ingrown toenails and hair loss. Kidney stones. Increased bilirubin.
Invirase (saquinavir)	Stomach related—diarrhea, abdominal discomfort, and nausea. Also see Norvir.
Kaletra (lopinavir/ritonavir)	Rash, diarrhea, nausea, vomiting, stomach pain, headache, muscle weakness, increased cholesterol and triglycerides, and elevated liver function test. Also see Norvir.
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, and alcohol intolerance. Liver problems, increased muscle enzymes, and uric acid.
Prezista (darunavir)	Rash, diarrhea, nausea, headache, and common cold. Prezista contains a "sulfa" part to it and should be used cautiously in patients with "sulfa" allergies. See also Norvir.
Reyataz (atazanavir sulfate)	Dizziness, lightheadedness, rash, kidney stones, and elevated liver function tests. Elevated levels of unconjugated bilirubin.
Viracept (nelfinavir)	Diarrhea, stomach discomfort, nausea, gas, weakness, and rash.
Entry Inhibitors	
Fuzeon (enfuvirtide, T-20)	Injection site reactions (ISRs), Immune Reconstitution Inflammatory Syndrome (IRIS), and pneumonia. Allergic reactions are possible.
Selzentry (maraviroc)	Cough, fever, cold, rash, muscle and joint pain, stomach pain, dizziness, liver toxicity, allergic reaction, low blood pressure, diarrhea, edema (swelling), trouble sleeping, urinary problems. Possible increased risk of infections and cancer.
Integrase Inhibitor	
Isentress (raltegravir, formerly MK-0518)	Diarrhea, nausea, vomiting, headache, fever, abdominal pain, fatigue, weakness, dizziness, and lipodystrophy.



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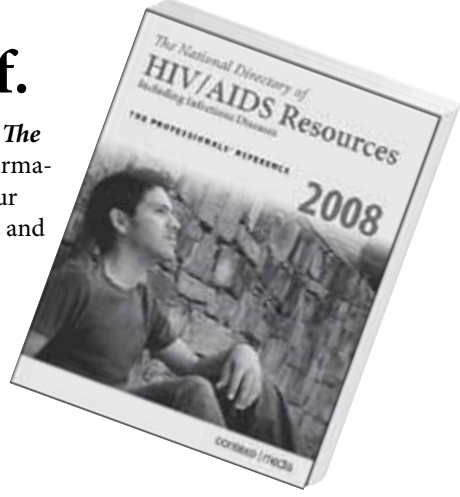

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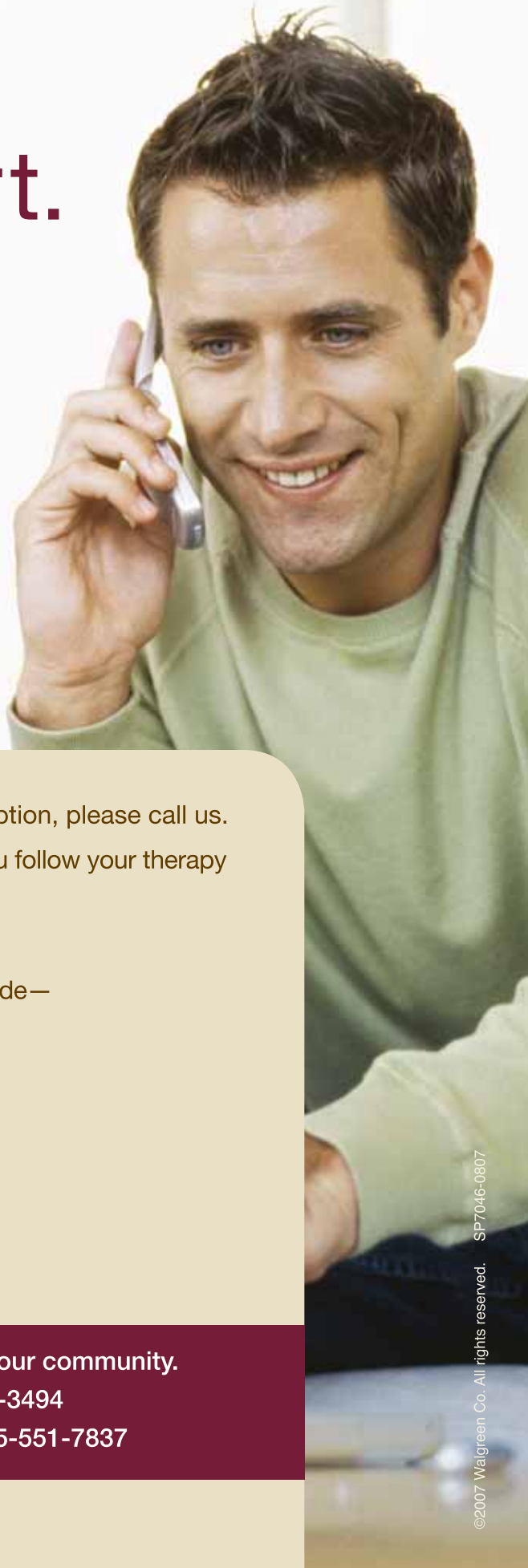

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