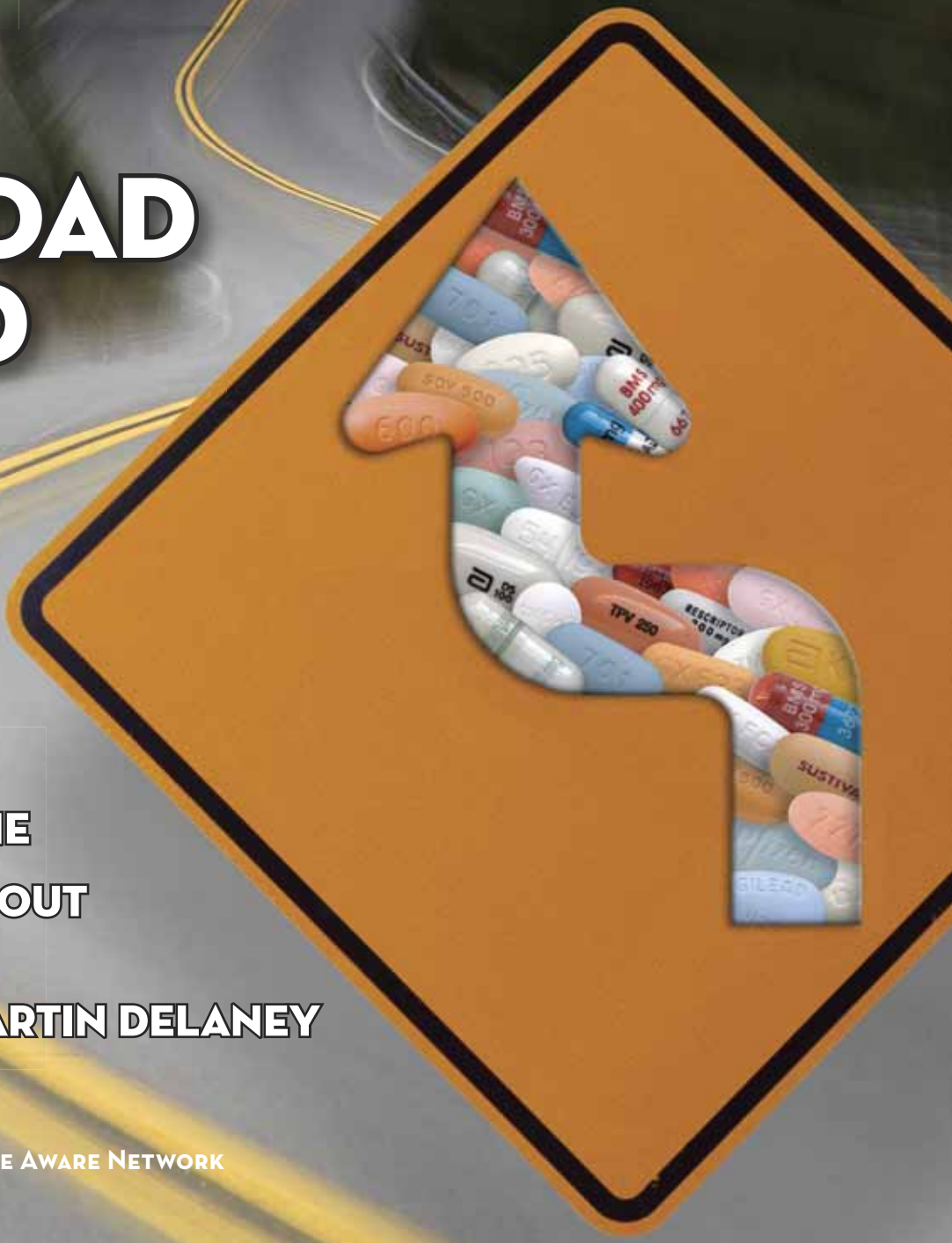
POSITIVELY AWARE
HIV Treatment and Health

THE 13TH ANNUAL HIV DRUG GUIDE

THE ROAD AHEAD



PLUS

HIV DRUGS IN THE PIPELINE

SPECIAL PULL-OUT DRUG CHART

TRIBUTE TO MARTIN DELANEY

March / April 2009
The Journal of Test Positive Aware Network

Please read Important Safety Information below, and talk to your healthcare professional to learn more about PREZISTA.

ABOUT PREZISTA

PREZISTA® (darunavir) is a prescription medicine. It is one treatment option in the class of HIV (human immunodeficiency virus) medicines known as protease inhibitors.

PREZISTA is always taken with and at the same time as ritonavir (Norvir®), in combination with other HIV medicines for the treatment of HIV infection in adults. PREZISTA should also be taken with food.

- The use of other medicines active against HIV in combination with PREZISTA/ritonavir (Norvir®) may increase the likelihood of your overall treatment response. Your healthcare professional will work with you to find the right combination of other HIV medicines
- The long-term effects of PREZISTA therapy are unknown at this time. It is important that you remain under the care of your healthcare professional

PREZISTA does not cure HIV infection or AIDS, and does not prevent passing HIV to others.

IMPORTANT SAFETY INFORMATION

- **PREZISTA, together with Norvir® (ritonavir), has rarely been observed to cause liver problems that may be life-threatening. It was not always clear if PREZISTA caused these liver problems because some patients had other illnesses or were taking other medicines. Your healthcare professional should do blood tests prior to initiating combination treatment including PREZISTA. If you have chronic hepatitis B or C infection, your healthcare professional should check your blood tests more often because you have an increased chance of developing liver problems**

  Talk to your healthcare professional about the signs and symptoms of liver problems. These may include yellowing of your skin or whites of your eyes, dark (tea-colored) urine, pale-colored stools (bowel movements), nausea, vomiting, loss of appetite, or pain, aching or sensitivity on your right side below your ribs
- **Skin rashes have been reported in patients taking PREZISTA. Rarely, PREZISTA has been reported to cause a severe or life-threatening rash. Contact your healthcare professional if you develop a rash**
- **Taking PREZISTA with certain medicines could cause serious and/or life-threatening side effects or may result in loss of its effectiveness. Do not take PREZISTA if you are taking the following medicines:** dihydroergotamine (D.H.E.45®, Migranal®), ergonovine, ergotamine (Wigraine®, Ergostat®, Cafergot®, Ergomar®), methylergonovine, cisapride (Propulsid®), pimozide (Orap®), oral midazolam, triazolam (Halcion®), rifampin (Rifadin®, Rifater®, Rifamate®), indinavir (Crixivan®), lopinavir/ritonavir (Kaletra®), saquinavir (Invirase®), lovastatin (Mevacor®), pravastatin (Pravachol®), simvastatin (Zocor®), or products containing St. John's wort
- Before taking PREZISTA, tell your healthcare professional if you are taking sildenafil (Viagra®), vardenafil (Levitra®), tadalafil (Cialis®), atorvastatin (Lipitor®), atorvastatin/amlodipine (Caduet®), or rosuvastatin (Crestor®). **This is not a complete**

Belief

in myself
in my doctor
in my care

PREZISTA now offers ONCE-DAILY dosing for adults taking HIV meds for the first time.

PREZISTA must be taken with and at the same time as ritonavir (Norvir®) and with food.

PREZISTA must be taken in combination with other HIV meds.

Talk to your doctor to see if PREZISTA is right for you.

PREZISTA®
(darunavir) tablets
NOW ONCE DAILY

Please visit **www.PREZISTA.com**

list of medicines. Be sure to tell your healthcare professional about all the medicines you are taking or plan to take, including prescription and nonprescription medicines, vitamins, and herbal supplements

- Tell your healthcare professional if you are taking estrogen-based contraceptives (birth control). PREZISTA might reduce the effectiveness of estrogen-based contraceptives. You must take additional precautions for birth control, such as condoms
- Before taking PREZISTA, tell your healthcare professional if you have any medical conditions, including allergy to sulfa medicines, diabetes, liver problems (including hepatitis B or C), or hemophilia
- Tell your healthcare professional if you are pregnant or planning to become pregnant, or are breastfeeding
  - The effects of PREZISTA on pregnant women or their unborn babies are not known. You and your healthcare professional will need to decide if taking PREZISTA is right for you
  - Do not breastfeed if you are taking PREZISTA. You should not breastfeed if you have HIV because of the chance of passing HIV to your baby
- High blood sugar, diabetes or worsening of diabetes, and increased bleeding in people with hemophilia have been reported in patients taking protease inhibitor medicines, including PREZISTA
- Changes in body fat have been seen in some patients taking HIV medicines, including PREZISTA. The cause and long-term health effects of these conditions are not known at this time
- As with other protease inhibitors, taking PREZISTA may strengthen the body's immune response, enabling it to begin to fight infections that have been hidden. Patients may experience signs and symptoms of inflammation that can include swelling, tenderness, or redness
- The most common side effects related to taking PREZISTA include diarrhea, nausea, headache, and abdominal pain. Uncommon but severe side effects such as inflammation of the pancreas and increased blood fat levels have also been rarely reported. This is not a complete list of all possible side effects. If you experience these or other symptoms, talk to your healthcare professional. Do not stop taking PREZISTA or any other medicines without first talking to your healthcare professional
- Please refer to the ritonavir (Norvir®) Product Information (PI and PPI) for additional information on precautionary measures

For adults taking HIV meds for the first time: PREZISTA 800 mg (two 400-mg tablets) must be taken at the same time with 100 mg Norvir® once daily *every day*. PREZISTA must be taken with food.

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

Please see Important Patient Information on the next page for more information, or visit www.PREZISTA.com.

If you or someone you know needs help paying for medicine, call 1-888-4PPA-NOW (1-888-477-2669) or go to www.pparx.org.

Distributed by: Tibotec Therapeutics/Division of Ortho Biotech Products, L.P.
Bridgewater, New Jersey 08807-0914

IMPORTANT PATIENT INFORMATION

FDA-Approved Patient Labeling

PREZISTA® (darunavir) Tablets

Patient Information about

PREZISTA (pre-ZIS-ta)

for HIV (Human Immunodeficiency Virus) Infection

Generic name: darunavir (da-ROO-nuh-veer)

ALERT: Find out about medicines that should NOT be taken with PREZISTA. Please also read the section "Who should not take PREZISTA?".

Please read this information before you start taking PREZISTA. Also, read the leaflet each time you renew your prescription, just in case anything has changed. Remember, this leaflet does not take the place of careful discussions with your doctor. You and your doctor should discuss your treatment with PREZISTA prior to the first time you take your medicine and at regular checkups. You should remain under a doctor's care when using PREZISTA and should not change or stop treatment without first talking with a doctor.

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT PREZISTA?

PREZISTA, together with NORVIR® (ritonavir), has rarely been observed to cause liver problems which may be life-threatening. It was not always clear if PREZISTA caused these liver problems because some patients had other illnesses or were taking other medicines. Your healthcare professional should do blood tests prior to initiating combination treatment including PREZISTA. If you have chronic hepatitis B or C infection, your healthcare professional should check your blood tests more often because you have an increased chance of developing liver problems. Please also read the section "What are the possible side effects of PREZISTA?".

Rarely, PREZISTA has been reported to cause a severe or life-threatening rash. Contact your healthcare provider if you develop a rash. Your healthcare provider will advise you whether your symptoms can be managed on therapy or whether PREZISTA should be stopped.

WHAT IS PREZISTA?

PREZISTA is an oral tablet used for the treatment of HIV (Human Immunodeficiency Virus) infection in adults. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome). PREZISTA is a type of anti-HIV medicine called a protease (PRO-tee-ase) inhibitor.

HOW DOES PREZISTA WORK?

PREZISTA blocks HIV protease, an enzyme which is needed for HIV to multiply. When used with other anti-HIV medicines, PREZISTA can help to reduce the amount of HIV in your blood (called "viral load") and increase your CD4 (T) cell count. HIV infection destroys CD4 (T) cells, which are important to the immune system. The immune system helps fight infection. Reducing the amount of HIV and increasing the CD4 (T) cell count may improve your immune system and, thus, reduce the risk of death or infections that can happen when your immune system is weak (opportunistic infections).

PREZISTA is always taken with and at the same time as ritonavir (NORVIR®), in combination with other anti-HIV medicines. PREZISTA should also be taken with food.

DOES PREZISTA CURE HIV OR AIDS?

PREZISTA does **not** cure HIV infection or AIDS. At present, there is no cure for HIV infection. People taking PREZISTA may still develop infections or other conditions associated with HIV infection. Because of this, it is very important for you to remain under the care of a doctor. Although PREZISTA is not a cure for HIV or AIDS, PREZISTA can help reduce your risks of getting illnesses associated with HIV infection (AIDS and opportunistic infection) and eventually dying from these conditions.

DOES PREZISTA REDUCE THE RISK OF PASSING HIV TO OTHERS?

PREZISTA does **not** reduce the risk of passing HIV to others 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 method to lower the chance of sexual contact with any body fluids such as semen, vaginal secretions, or blood. Never re-use or share needles.

Ask your doctor if you have any questions on how to prevent passing HIV to other people.

WHAT SHOULD I TELL MY DOCTOR BEFORE I TAKE PREZISTA?

Tell your doctor about all of your medical conditions, including if you:

- are allergic to sulfa medicines.
- have diabetes. In general, anti-HIV medicines, such as PREZISTA, might increase sugar levels in the blood.
- have liver problems, including hepatitis B and/or C.
- have hemophilia. Anti-HIV medicines, such as PREZISTA, might increase the risk of bleeding.
- are pregnant or planning to become pregnant. The effects of PREZISTA on pregnant women or their unborn babies are not known. You and your doctor will need to decide if taking PREZISTA is right for you. If you take PREZISTA while you are pregnant, talk to your doctor about how you can be included in the Antiretroviral Pregnancy Registry.
- are breastfeeding. Do not breastfeed if you are taking PREZISTA. You should not breastfeed if you have HIV because of the chance of passing HIV to your baby. Talk with your doctor about the best way to feed your baby.

WHO SHOULD NOT TAKE PREZISTA?**

Together with your doctor, you need to decide whether taking PREZISTA is right for you.

Do not take PREZISTA if you:

- are allergic to darunavir or any of the other ingredients in PREZISTA
- are allergic to ritonavir (NORVIR®)
- take any of the following types of medicines because you could experience serious side effects:

Type of Drug	Examples of Generic Names (Brand Names)
Ergot Derivatives (to treat migraine and headaches)	dihydroergotamine (D.H.E. 45®, Migranal®) ergonovine ergotamine (Cafergot®, Ergomar®) methylergonovine
Gastrointestinal Motility Agent (to treat some digestive conditions)	cisapride
Neuroleptic (to treat psychiatric conditions)	pimozide (Orap®)
Sedative/hypnotics (to treat trouble with sleeping and/or anxiety)	oral midazolam triazolam (Halcion®)
Herbal Product	St. John's wort (*Hypericum perforatum*)
HMG-CoA Reductase nhibitors (also known as statins) (to lower cholesterol levels)	lovastatin (Mevacor®, Altoprev®, Advicor®) simvastatin (Zocor®, Simcor®, Vytorin®)
Antimycobacterial (to treat tuberculosis or *Mycobacterium avium* complex)	rifampin (Rifadin®, Rifater®, Rifamate®, Rimactane®)

CAN PREZISTA BE TAKEN WITH OTHER MEDICATIONS?**

Tell your doctor about all the medicines you take including prescription and nonprescription medicines, vitamins, and herbal supplements. PREZISTA and many other medicines can interact. Sometimes serious side effects will happen if PREZISTA is taken with certain other medicines (see "Who should not take PREZISTA?").

Tell your doctor if you are taking estrogen-based contraceptives (birth control). PREZISTA might reduce the effectiveness of estrogen-based contraceptives. You must take additional precautions for birth control such as a condom.

Tell your doctor if you take other anti-HIV medicines. PREZISTA can be combined with some other anti-HIV medicines while other combinations are not recommended.

Tell your doctor if you are taking any of the following medicines:

Type of Drug	Examples of Generic Names (Brand Names)
Antiarrhythmics (to treat abnormal heart rhythms)	bepridil lidocaine (Lidoderm®) quinidine amiodarone (Cordarone®) digoxin (Lanoxin®) flecainide (Tambocor®) propafenone (Rythmol®)
Anticoagulants (to treat and prevent blood clots)	warfarin (Coumadin®)
Anticonvulsants (to treat epilepsy and prevent seizures)	carbamazepine (Tegretol®, Carbatrol®) phenobarbital phenytoin (Dilantin®, Phenytek®)
Antidepressants (to treat depression)	trazodone (Desyrel®) desipramine (Norpramin®)
Anti-infectives (to treat bacterial infections)	clarithromycin (Biaxin®)
Antifungals (to treat fungal infections)	ketoconazole (Nizoral®) itraconazole (Sporanox®) voriconazole (Vfend®)
Antimycobacterials (to treat tuberculosis or *Mycobacterium avium* complex)	rifabutin (Mycobutin®)
ß-Blockers (to treat high blood pressure, heart attack, or heart failure or to lower pressure in the eye)	metoprolol (Lopressor®, Toprol-XL®) timolol (Betimol®, Combigan®, Istalol®, Cosopt®, Timoptic®)
Benzodiazepines (to treat anxiety and/or trouble with sleeping)	midazolam administered by injection
Calcium Channel Blockers (to treat heart disease)	felodipine (Plendil®) nifedipine (Adalat®) nicardipine (Cardene®)
Corticosteroids (to treat inflammation or asthma)	dexamethasone fluticasone propionate (Advair Diskus®, Cutivate®, Flonase®, Flovent Diskus®)
HMG-CoA Reductase Inhibitors (also known as statins) (to lower cholesterol levels)	atorvastatin (Lipitor®) pravastatin (Pravachol®) rosuvastatin (Crestor®)

IMPORTANT PATIENT INFORMATION

Type of Drug	Examples of Generic Names (Brand Names) (cont.)
Immunosuppressants (to prevent organ transplant rejection)	cyclosporine (Sandimmune®, Neoral®) tacrolimus (Prograf®) sirolimus (Rapamune®)
Narcotic Analgesics (to treat narcotic withdrawal and dependence)	methadone
Neuroleptics (to treat schizophrenia or bipolar disorder)	risperidone (Risperdal®, Risperdal® Consta®, Risperdal® M-TAB®) thioridazine
PDE-5 Inhibitors (to treat erectile dysfunction)	sildenafil (Viagra®) vardenafil (Levitra®) tadalafil (Cialis®)
Selective Serotonin Reuptake Inhibitors (SSRIs) (to treat depression, anxiety, or panic disorder)	paroxetine (Paxil®) sertraline (Zoloft®)

Tell your doctor if you are taking any medicines that you obtained without a prescription.

This is **not** a complete list of medicines that you should tell your doctor that you are taking. Know and keep track of all the medicines you take and have a list of them with you. Show this list to all of your doctors and pharmacists any time you get a new medicine. Both your doctor and your pharmacist can tell you if you can take these other medicines with PREZISTA. Do not start any new medicines while you are taking PREZISTA without first talking with your doctor or pharmacist. You can ask your doctor or pharmacist for a list of medicines that can interact with PREZISTA.

HOW SHOULD I TAKE PREZISTA?

Take PREZISTA tablets every day exactly as prescribed by your doctor. You must take ritonavir (NORVIR®) at the same time as PREZISTA.

- For adults who have never taken anti-HIV medicines, the usual dose is 800 mg (two 400 mg tablets) of PREZISTA, together with 100 mg (one 100 mg capsule) of ritonavir (NORVIR®), once daily *every day*.
- For adults who have taken anti-HIV medicines in the past, the usual dose is 600 mg (one 600 mg tablet or two 300 mg tablets) of PREZISTA, together with 100 mg (one 100 mg capsule) of ritonavir (NORVIR®), twice daily *every day*. Do not take PREZISTA once daily if you have taken anti-HIV medicines in the past.

PREZISTA and ritonavir (NORVIR®) should be taken together at the same time every day. If you have questions about when to take PREZISTA and ritonavir (NORVIR®), your doctor can help you decide which schedule works for you.

Take PREZISTA and ritonavir (NORVIR®) **with food**. Swallow the whole tablets with a drink such as water or milk. Do not chew the tablets.

Continue taking PREZISTA and ritonavir (NORVIR®) unless your doctor tells you to stop. Take the exact amount of PREZISTA and ritonavir (NORVIR®) that your doctor tells you to take, right from the very start. To help make sure you will benefit from PREZISTA and ritonavir (NORVIR®), you must not skip doses or interrupt therapy. If you don't take PREZISTA and ritonavir (NORVIR®) as prescribed, the beneficial effects of PREZISTA and ritonavir (NORVIR®) may be reduced or even lost.

Patients taking PREZISTA once daily

If you miss a dose of PREZISTA or ritonavir (NORVIR®) by more than 12 hours, wait and then take the next dose of PREZISTA and ritonavir (NORVIR®) at the regularly scheduled time. If you miss a dose of PREZISTA or ritonavir (NORVIR®) by less than 12 hours, take your missed dose of PREZISTA and ritonavir (NORVIR®) immediately. Then take your next dose of PREZISTA and ritonavir (NORVIR®) at the regularly scheduled time.

Patients taking PREZISTA twice daily

If you miss a dose of PREZISTA or ritonavir (NORVIR®) by more than 6 hours, wait and then take the next dose of PREZISTA and ritonavir (NORVIR®) at the regularly scheduled time. If you miss a dose of PREZISTA or ritonavir (NORVIR®) by less than 6 hours, take your missed dose of PREZISTA and ritonavir (NORVIR®) immediately. Then take your next dose of PREZISTA and ritonavir (NORVIR®) at the regularly scheduled time.

You should always take PREZISTA and ritonavir (NORVIR®) together with food.

If a dose of PREZISTA or ritonavir (NORVIR®) is skipped, do not double the next dose. Do not take more or less than your prescribed dose of PREZISTA or ritonavir (NORVIR®) at any one time.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF PREZISTA?

Like all prescription drugs, PREZISTA can cause side effects. The following is **not** a complete list of side effects reported with PREZISTA when taken either alone or with other anti-HIV medicines. Do not rely on this leaflet alone for information about side effects. Your doctor can discuss with you a more complete list of side effects.

PREZISTA, together with NORVIR® (ritonavir), has rarely been observed to cause liver problems which may be life-threatening. It was not always clear if PREZISTA caused these liver problems because some patients had other illnesses or were taking other medicines. Your healthcare professional should do blood tests prior to initiating combination treatment including PREZISTA. If you have chronic hepatitis B or C infection, your healthcare professional should check your blood tests more often because you have an increased chance of developing liver problems.

Talk to your healthcare professional about the signs and symptoms of liver problems. These may include yellowing of your skin or whites of your eyes, dark (tea colored) urine, pale colored stools (bowel movements), nausea, vomiting, loss of appetite, or pain, aching or sensitivity on your right side below your ribs.

Rash has been reported in 10.3% of subjects receiving PREZISTA. In some patients, PREZISTA has been reported to cause a severe or life-threatening rash. Contact your healthcare provider if you develop a rash. Your healthcare provider will advise you whether your symptoms can be managed on therapy or whether PREZISTA should be stopped.

Other relevant severe side effects reported at an uncommon or rare frequency were inflammation of the liver or pancreas, increased blood fat levels, diabetes, and changes in body fat.

Some side effects are typical for anti-HIV medicines in the same family as PREZISTA. These are:

- high blood sugar (hyperglycemia) and diabetes. This can happen in patients taking PREZISTA or other protease inhibitor medicines. Some patients have diabetes before starting treatment with PREZISTA which gets worse. Some patients get diabetes during treatment with PREZISTA. Some patients will need changes in their diabetes medicine. Some patients may need new diabetes medicine.
- increased bleeding in patients with hemophilia.
- changes in body fat. These changes can happen in patients taking anti-HIV medicines, including PREZISTA. The changes may include an increased amount of fat in the upper back and neck, breast, and around the back, chest, and stomach area. Loss of fat from the legs, arms, and face may also happen. The exact cause and long-term health effects of these conditions are not known.
- immune reconstitution syndrome. In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment, including PREZISTA, is started. It is believed that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms.

The most common side effects include diarrhea, nausea, headache, and abdominal pain.

Tell your doctor promptly about these or any other unusual symptoms. If the condition persists or worsens, seek medical attention.

WHAT DO PREZISTA TABLETS LOOK LIKE?

PREZISTA 300 mg tablets are orange, oval-shaped, film-coated tablets mentioning "300" on one side and "TMC114" on the other side.

PREZISTA 400 mg tablets are light orange, oval-shaped, film-coated tablets mentioning "400" on one side and "TMC" on the other side.

PREZISTA 600 mg tablets are orange, oval-shaped, film-coated tablets mentioning "600" on one side and "TMC" on the other side.

HOW SHOULD I STORE PREZISTA TABLETS?

Store PREZISTA tablets at room temperature (77°F (25°C)). Short-term exposure to higher or lower temperatures [from 59°F (15°C) to 86°F (30°C)] is acceptable. Ask your doctor or pharmacist if you have any questions about storing your tablets.

This medication is prescribed for your particular condition. Do not use it for any other condition or give it to anybody else. Keep PREZISTA and all of your medicines out of the reach of children. If you suspect that more than the prescribed dose of this medicine has been taken, contact your local poison control center or emergency room immediately.

This is a brief summary of information about PREZISTA. If you have any questions or concerns about either PREZISTA or HIV, talk to your doctor.

For additional information, you may also call Tibotec Therapeutics at 1-877-REACH-TT or 1-877-732-2488.

**The brands listed are the registered trademarks of their respective owners and are not trademarks of Tibotec Pharmaceuticals, Ltd.

tibotec THERAPEUTICS
DIVISION OF ORTHO BIOTECH PRODUCTS, L.P.

Manufactured for Tibotec, Inc. by: JOLLC, Gurabo, Puerto Rico

Distributed by:
Tibotec Therapeutics
Division of Ortho Biotech Products, L.P., Raritan NJ 08869

Patent Numbers: 5,843,946; 6,248,775; 6,335,460 and other US patents pending

Revised: December 2008 10101707P

TPAN PROGRAMS AND MEETINGS

- Support Groups
- Rapid HIV Testing
- Meditation, Reiki, Yoga, and Massage
- Needle Exchange Program
- Buddy Program
- Case Management
- 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
- 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

- Chicago Takes Off
  Saturday, March 7th, 2009
  Two shows!
  visit www.tpan.com
- Ride for AIDS
  June 6–7, 2009
  www.rideforaids.org

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

TEST POSITIVE AWARE NETWORK
Test Positive Aware Network
5537 North Broadway
Chicago, IL 60640

phone: (773) 989-9400
fax: (773) 989-9494
e-mail: tpan@tpan.com
www.tpan.com

Editor
Jeff Berry

Associate Editors
Keith R. Green
Enid Vázquez

Editorial Assistants
Sue Saltmarsh
Gregory Tate

Contributing Writers
Liz Highleyman, Laura Jones,
Jim Pickett, Sue Saltmarsh, Matt Sharp

Medical Advisory Board
Daniel S. Berger, M.D., Patrick G. Clay, Pharm.D.,
Rupali Jain, Pharm.D., and Ross M. Slotten, M.D.

Art Direction
Russell McGonagle

Advertising Inquiries
publications@tpan.com

Distribution
Joe Fierke
distribution@tpan.com

TABLE OF CONTENTS

March / April 2009 Volume 20 Number 2

Departments

Articles

Distribution of *Positively Aware* is supported in part through an unrestricted grant from GlaxoSmithKline

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

You can view these (and other stories from previous issues) online at www.tpan.com and www.positivelyaware.com

CONTRIBUTORS

Paul Djuricich, R.Ph., Pharm.D.

Paul Djuricich was born and raised in Evanston, Illinois. He attended Loyola University, Chicago and earned a bachelor's degree in biology. Immediately afterward, he proceeded on to Purdue University, where he earned his doctorate in pharmacy (Pharm.D.). Right after graduation, Paul went to work for Osco Pharmacy, where he was involved in the diabetes care program and immunizations. He also served as preceptor for Purdue University School of Pharmacy students who were in their last year of rotations. After a few years there, he was recruited for the position of Pharmacist in Charge at Bioscrip Pharmacy (formerly StatScript). Paul is thrilled to work in an environment that is vastly different than the traditional retail pharmacy setting. Throughout his time there, he has felt that he's been able to help several patients through tough times. Recently, Paul has become active with TPAN by providing presentations and talking to groups about their HIV treatment. In his spare time, Paul enjoys torturing himself with marathons and triathlons.

Frank M. Graziano, M.D., Ph.D.

Dr. Frank M. Graziano is Professor of Medicine at the University of Wisconsin Hospital and Clinics (UWHC), Madison, Wisconsin. He received his M.D. and Ph.D. (Microbiology and Immunology) from the University of Virginia, Charlottesville. He did his Internal Medicine residency at the UWHC and Fellowship in Allergy and Immunology and Rheumatology at Yale University School of Medicine. He is Board certified in Internal Medicine, Allergy and Immunology, Diagnostic Immunology and HIV Medicine. He has been a member of the Department of Medicine Sections of Rheumatology and Allergy and Immunology for the past 30 years. He is past Chair of the Section of Rheumatology and Current Director of the UWHC HIV Clinic. He has been treating HIV disease at the UWHC for the past 25 years.

Dr. Graziano has basic research interests in allergic inflammation of the airway and, most recently, the eye. He has been NIH funded for this research for the past 28 years. He is past Director of the University of Wisconsin Clinical Research K30 Award and the Clinical Research Scholar Award. His clinical research interests have centered on the treatment of HIV disease. For the past five years he has been collaborating with the Joint Clinical Research Centre of Uganda in their TREAT initiative. This initiative brings structure to the use of antiretroviral therapy in districts and villages where many are infected with HIV, but the choices for therapy are few.

Morris Jackson

Since 1986, Morris Jackson has found a home within the HIV/AIDS community whether in New York, South Carolina or California as an activist, advocate, case manager, clinical case manager, and/or treatment educator. Morris presently serves as a community member on the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents and is a member of the AIDS Treatment Activists Coalition (ATAC) Drug Development Committee and the ATAC Board of Directors. Morris is currently employed as a case manger with AIDS Project Los Angeles and will celebrate the 20th anniversary of his HIV diagnosis in April 2009.

Photos courtesy of contributors

EDITOR'S NOTE

The Road Ahead

This is the fifth *Positively Aware* HIV Drug Guide of which I have had the honor of serving as editor. More than any other issue, the Drug Guide continues to be our most popular issue throughout the year, serving as an invaluable reference tool for people living with HIV, as well as for those who care for them.

When reading through the drug guide, I myself learn something new every year, so I'd like to point out some of the things in this year's guide that you may find especially useful.

As in years past, each HIV drug that is currently available has a page devoted exclusively to it, which includes the drug's dose, food and liquid requirements, side effects, interactions, and tips on how to use the drug, as well as viewpoints from a doctor and an activist.

In the center of the issue, you'll find our ever-popular drug chart, which you can pull out and refer to quickly when you need to identify a certain drug or how to use it (always refer to the drug page or package insert for more information).

An article by this year's Drug Guide pharmacist, Paul Djuricich, R.Ph., Pharm.D., looks at some of the HIV drugs that are further along in the pipeline. Also included in this issue are handy reference charts that list some of the more common drug side effects and interactions.

The introduction to the Drug Guide gives a brief explanation of the different classes of HIV drugs and how they work, plus some quick tips on how to use the guide. With today's economy, we all know how important it is to find ways to stretch the dollar, so we've added a list of drug co-pay assistance programs that were available as of press time. All of these co-pay assistance programs have launched within the last year, and they pay all or part of your drug co-pay up to a certain amount, with some restrictions. Keep tuned to *PA* as hopefully more and more companies launch similar programs in the coming months and year.

These co-pay programs are a direct result of discussions and meetings with the Fair Pricing Coalition (FPC), which works on drug pricing issues, and was founded by Martin Delaney, who passed away on January 23. Martin Delaney was a true leader and advocate in the fight against HIV (see page 16 for a special tribute by Daniel Berger, M.D.).

Marty, as most of us knew him, worked with us on last year's drug guide, providing the activist viewpoint on the drugs. I also worked with Marty on the FPC and the AIDS Treatment Activists Coalition (ATAC). From the very beginning of the epidemic, he worked tirelessly to advocate on behalf of those with HIV, altering the course of HIV treatment forever, by ensuring quick access to lifesaving drugs and fighting to get them in the hands of those who needed them most.

And so, with that in mind, we'd like to dedicate the 13th Annual *Positively Aware* HIV Drug Guide to Martin Delaney. If any one individual exemplifies the progress we've made in the treatment of HIV, it's Marty.

To make it easier to interact with your peers and discuss what's on your mind, this year we invite you to join our online community forum at www.positivelyaware.com. The forum, which allows users to post and discuss topics of interest to them, has a newly-added drug guide section, where you can share your experience with various drugs, side effects, and drug interactions.

As always, the Drug Guide is an enormous undertaking, and would not be possible without the help of many talented individuals. I'd like to give special thanks to Enid Vázquez, Sue Saltmarsh, Russell McGonagle, Keith Green, Joe Fierke, Gregory Tate, Scott Grannan, Tom Setto, and Mark Larson.

If you'd like your organization to receive bulk shipments of *Positively Aware* magazine, please email us at distribution@tpan.com. To subscribe to the magazine, or to sign up for our *Positively Aware* E-mail Update newsletter, visit us at www.positivelyaware.com and click on "subscribe."

Remember, knowledge is power, and when you have power, you have control; control over your life, your health, and your destiny, giving you the ability to navigate the road ahead.

Take care of yourself, and each other.

Jeff Berry
Editor
publications@tpan.com

Photo © Russell McGonagle

USE OF TRUVADA:

TRUVADA is a type of medicine called an HIV-1 (human immunodeficiency virus) nucleoside analog reverse transcriptase inhibitor and combines EMTRIVA® (emtricitabine) and VIREAD® (tenofovir disoproxil fumarate [DF]) in one pill. TRUVADA is always used with other anti-HIV-1 medicines to treat adults with HIV-1 infection.

TRUVADA® does not cure HIV-1 infection or lower your chance of passing HIV-1 to others. TRUVADA should not be used with ATRIPLA® (efavirenz 600 mg/emtricitabine 200 mg/tenofovir DF 300 mg), VIREAD®, EMTRIVA®, Combivir® (lamivudine/zidovudine), Epivir® or Epivir-HBV® (lamivudine), Epzicom® (abacavir sulfate/lamivudine), or Trizivir® (abacavir sulfate/lamivudine/zidovudine) because these medicines contain the same or similar active ingredients. TRUVADA should not be used with HEPSERA® (adefovir dipivoxil).

IMPORTANT SAFETY INFORMATION:

Contact your healthcare provider right away if you experience any of the following side effects or conditions while taking TRUVADA:

- **Nausea, vomiting, unusual muscle pain, and/or weakness. These may be signs of a buildup of acid in the blood (lactic acidosis), which is a serious medical condition**
- **Light colored stools, dark colored urine, and/or if your skin or the whites of your eyes turn yellow. These may be signs of serious liver problems (hepatotoxicity), with liver enlargement (hepatomegaly), and fat in the liver (steatosis)**
- **If you have HIV-1 and hepatitis B virus (HBV) and stop taking TRUVADA, your liver disease may suddenly get worse. Your healthcare provider will monitor your condition for several months.**
- 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
- Lab tests show changes in the bones of patients treated with VIREAD, a medicine in TRUVADA. If you have had bone problems in the past, talk to your healthcare provider before taking TRUVADA. Also, bone pain and softening of the bone (which may contribute to fractures) may occur as a consequence of kidney problems.

Changes in body fat have been seen in some people taking TRUVADA and other anti-HIV-1 medicines.

If you notice any symptoms of infection soon after you start HIV treatment, talk to your doctor right away.

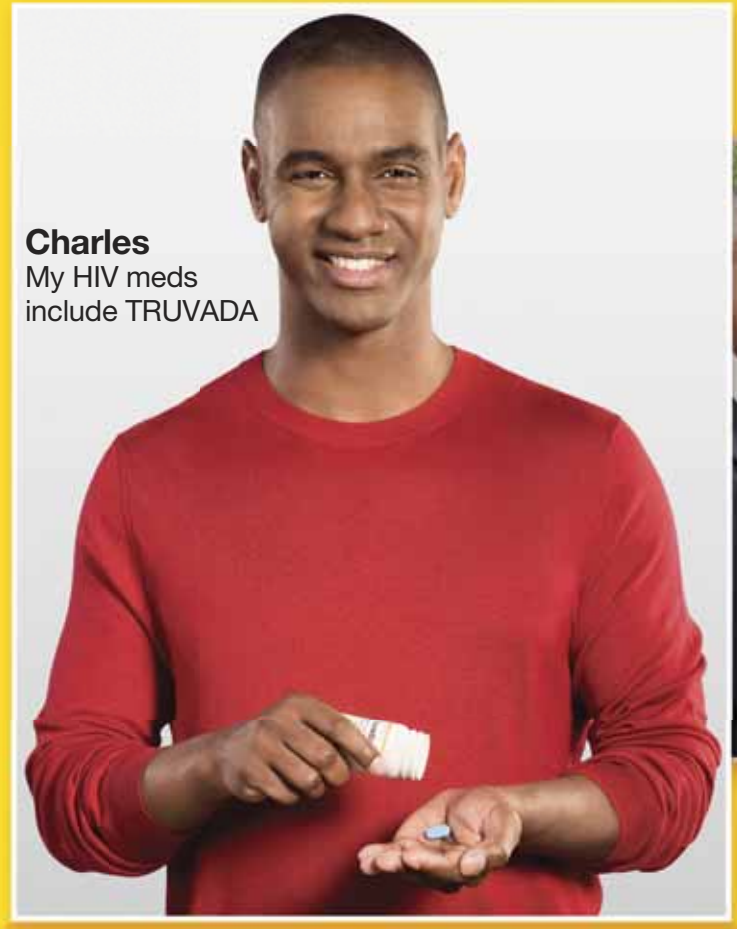
The most common side effects of the medicines in TRUVADA when taken with other anti-HIV-1 medicines are diarrhea, dizziness, nausea, headache, fatigue, abnormal dreams, sleeping problems, rash, depression, and vomiting. Additional side effects are kidney problems (including decline or failure of kidney function), inflammation of the pancreas, inflammation of the liver, allergic reaction, shortness of breath, pain, fatty liver, stomach pain, weakness, indigestion, and intestinal gas. High volume of urine and thirst, muscle pain and muscle weakness due to kidney problems have been reported. Skin discoloration (spots and freckles) may also happen with TRUVADA.

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® or Videx® EC (didanosine), Reyataz® (atazanavir sulfate), or Kaletra® (lopinavir/ritonavir) with TRUVADA.

Please see Full Prescribing Information, including **"What is the most important information I should know about TRUVADA?"** in the Patient Information section.

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.

I feel positive



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

References: 1. Based on data from PHAST retail monthly data; September 2005-October 2008; Wolters Kluwer Health.

about my future.
TRUVADA helps make it possible.

#1 prescribed HIV med by doctors[1]

Individual results may vary.

With *once a day* TRUVADA for my HIV, I can plan for long-term success.

- Proven over the long term to reduce viral load to undetectable (<400 copies/mL) and increase CD4 cell count in 3 years of a clinical study
- Established long-term safety and tolerability

TRUVADA does not cure HIV-1 infection or prevent passing HIV-1 to others.

Ask your doctor about TRUVADA and go to www.TRUVADA.com.

Truvada®

200 mg emtricitabine-tenofovir disoproxil fumarate 300 mg

Think long term.* Starting now.

*Through 3 years of a clinical study.

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-1 (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-1 medicines to treat people with HIV-1 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-1 reverse transcriptase, a chemical in your body (enzyme) that is needed for HIV-1 to multiply. TRUVADA lowers the amount of HIV-1 in the blood (viral load). TRUVADA may also help to increase the number of T cells ($CD4^+$ cells). Lowering the amount of HIV-1 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-1 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-1 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-1 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® (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg), Combivir (lamivudine/zidovudine), EMTRIVA (emtricitabine), Epivir or Epivir-HBV (lamivudine), Epzicom (abacavir sulfate/lamivudine), Trizivir (abacavir sulfate/lamivudine/zidovudine), or VIREAD (tenofovir disoproxil fumarate) because these medicines contain the same or similar active ingredients.
- Do not take TRUVADA to treat your HIV infection if you are also taking HEPSERA® (adefovir dipivoxil) to treat your HBV infection.

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-1 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-1 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 (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg), Combivir (lamivudine/zidovudine), EMTRIVA (emtricitabine), Epivir or Epivir-HBV (lamivudine), Epzicom (abacavir sulfate/lamivudine), Trizivir (abacavir sulfate/lamivudine/zidovudine), or VIREAD (tenofovir disoproxil fumarate).

  TRUVADA should not be used with these medicines.
- TRUVADA should not be used with HEPSERA (adefovir dipivoxil).

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-1 and HBV infection. TRUVADA is not approved for the treatment of Hepatitis B Virus infection. If you have advanced liver disease and stop treatment with TRUVADA, the "flare-up" of hepatitis B may cause your liver function to decline.
- **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).** Laboratory tests show changes in the bones of patients treated with VIREAD, a component of TRUVADA. 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. Additionally, bone pain and softening of the bone (which may contribute to fractures) may occur as a consequence of kidney problems.

Other side effects with TRUVADA when used with other anti-HIV-1 medicines include:

- Changes in body fat have been seen in some patients taking TRUVADA and other anti-HIV-1 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.
- In some patients with advanced HIV infection (AIDS), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms. If you notice any symptoms of infection, please inform your doctor immediately.

The most common side effects of EMTRIVA (emtricitabine) or VIREAD (tenofovir disoproxil fumarate) when used with other anti-HIV-1 medicines are: diarrhea, dizziness, nausea, headache, fatigue, abnormal dreams, sleeping problems, rash, depression, and vomiting. Additional side effects are lactic acidosis, kidney problems (including decline or failure of kidney function), inflammation of the pancreas, inflammation of the liver, allergic reaction, shortness of breath, pain, fatty liver, stomach pain, weakness, indigestion, intestinal gas, and high volume of urine and thirst caused by kidney problems. Muscle pain and muscle weakness, bone pain, and softening of the bone (which may contribute to fractures) as a consequence of kidney problems have been reported. Skin discoloration (small spots or freckles) may also happen with TRUVADA.

These are not all the side effects of TRUVADA. 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.

Rx Only

November 2008

21-752-GS-022 041108

READERS FORUM

20th Anniversary Issue

Dear Jeff,

I read the latest edition of *PA*—the Special 20th Anniversary Issue—and sent off an e-mail to Steve Wakefield and to Enid [Vázquez] about the feelings that the issue brought up for me. I meant to send one to you first as editor, but I wanted to say a few things to both of them first as I have stayed in contact with them since I left Chicago. Having all of the editors write a piece, including words from ones who are not with us in body any more, was a spectacular and moving tribute to TPAN and all of us who have had connections to TPAN and *PA* for years. Seeing names of people who I had not thought of in so long was certainly touching and thought-provoking.

You were the first person that was involved with TPAN that I had contact with…in assembling *PA* in the side room there on Belmont. I hadn't thought about that huge undertaking in years. I remember taking yoga and other exercise classes there with you and Rick [Bejlovec]. It is sometimes hard to think about many of those years. I told Wakefield that I remember those days when I walked around with a cane and to church with a pillow since they had those hard wooden pews! Wakefield was the one who kicked my sorry ass to tell me to quit feeling sorry for myself and get down to TPA and volunteer. He always had a way of getting to the crux of the issue for me.

I can't tell you how often I brag about TPAN and *PA* to all who will listen. I was volunteer of the year once—don't know how that happened, but I still have that plaque on my wall. I feel like I was and am part of something that came from that meeting of some guys in 1987—five years after my diagnosis, via the MAC study blood samples drawn in '83. It's amazing how all that has changed since those dark days. I never thought that I would live past any of those times, let alone past the huge doses of AZT in the middle of the night. I never thought I would get rid of that cane (I didn't—still have them all) and never thought I would ride in the AIDS Ride in 2001, but I did. Like some of the guys who wrote in this issue, I don't know how I got through it and how I am still alive and well. I know it has to be a mystery to all of us long-term survivors. I do know, as I know you do, that for whatever reason, we are here and should give back, to help those suffering today and many less fortunate who do not have the resources and support to even hope. I know *PA* offers help there, as does TPAN. Now living in a totally different part of the country, I can see how far-advanced everything that TPAN and *PA* provides is. The HIV/AIDS services in the South are meager at best, with the exception of a few of the big cities (Asheville, NC). I am appalled at the total lack of any services or understanding in Knoxville, TN. I do help with the one-woman show here, the Hope Center, in teaching their workshop entitled "The Human Perspective of HIV/AIDS."

You put out such a magnificent magazine each issue, and I know that guys and women down here in the South look forward to finding one—often times it's mine that I drop off at the Hope Center. Your words in the "Editors Note" are so well-written that sometimes they bring me to tears—usually of joy, mind you! I love seeing Enid's News Briefs and can't wait to read what Jim Pickett has to say.

My best regards to you and everyone at TPAN on the 20th Anniversary of *PA*.

Greg Knepper, Maryville, TN

Jeff Berry responds:

Thank you for your wonderful letter. I was so moved that I forwarded it to the rest of the staff, as we sometimes need to be reminded of how many lives we touch by the work we all do.

As you well know, for many years when I first started working here, and when we were still a monthly publication, with the help of about 30 core volunteers we'd put together the mailing of PA at the TPAN office. One Saturday each month we'd spend about 5 or 6 hours stuffing, sealing, labeling, sorting, bundling and bagging the latest issue into about 30 huge canvas mailing bags to haul down to the main post office. We'd have donuts in the morning, and pizza for lunch. It was a lot of work, but it gave us all a sense of camaraderie and connectedness, and it was a way for the members to show their appreciation and an opportunity for them to give something back. Eventually the mailing became too large and complicated to do in-house and was farmed out to a mailing house, but it was truly a great experience. And it taught me the importance of who we serve, why we do the work we do, and the value of volunteerism. Plus it was a lot of fun! Many of those individuals are still here at TPAN, either on staff, working reception at the front desk, or attending the support groups.

Thank you for reminding me of those times, both the good and the not so good. I wouldn't trade it for anything.

Long-Term Couples Survey

We got a hit! [See "Long-Term Couples Survey" in January/February News Briefs.] A couple was referred to us by the Director of their non-profit who reads *Positively Aware*. Yea! Always a treat when we get participants who we haven't been begging and cajoling for months.

More importantly, it got me to check out *Positively Aware*. What a great maga-

Positively Aware will treat all communications (letters, faxes, e-mail, etc.) as letters to the editor unless otherwise instructed. We reserve the right to edit for length, style, or clarity. Please advise if we can use your name and city.

Write to: *Positively Aware*,
5537 North Broadway
Chicago, IL 60640

Fax: (773) 989-9494

E-mail: readersforum@tpan.com

zine. Very informative, intelligent, and easy to read. Congratulations on 20 years! That kind of longevity is a testament to perseverance, dedication and meaningfulness. The fact that all former editors were willing to contribute is impressive (we have more than our share of turf pissing and burned bridges in the Bay Area).

And btw, thanks for sharing Obama with the rest of us—what a great way to start the day—not only a new President, but a new kind of President.

Lanz Lowen and Blake Spears,
San Francisco, CA

Bravo Dr. Berger

I hope you remember me; my name is Kurt Weston and I was a patient of yours when I lived in Chicago. I ran a support group at TPAN called SWAN (Surviving with AIDS Network). You gave many lectures to my group during the early days of the epidemic. Reading your article took me back to those challenging early days. You provided so much hope for people, extended people's life spans and saved lives. I believe I would not have survived had I not been seeing you in Chicago before I moved to California. From your picture on the cover of *Positively Aware*, it appears you are doing well. I am, unfortunately, legally blind due to CMV retinitis, but I am still doing my photography. I recently received my Master of Fine Arts graduate degree from California State University, Fullerton. My photographs have been exhibited nationally. Having been diagnosed with full-blown AIDS at the age of 31, I never thought I would live to see 40, let alone live to the age of 51.

Your article made me feel so connected again. Very few people remember or know how it was in the early days of the epidemic, what a struggle it was, yet strangely unifying. You encapsulated the past 20 years authentically and accurately, thank you.

California has been a good place for me to live, but I often think about Chicago and the wonderful people there. I am so happy you are still on the front lines of the HIV/AIDS war, you are a brilliant clinician.

Check out my website at www.kurtweston.com. Keep up your amazing work, and thanks again for all that you have done, and are still doing.

Kurt Weston, via the Internet

Jeff Berry responds:
Hi Kurt,

I hope you are doing well. Dr. Berger forwarded me your great letter regarding his article, and I was wondering if we could get your permission to use it in our upcoming Readers Forum of Positively Aware *magazine. I don't know if you remember me, but I have worked at TPAN for almost 17 years now, and was there when SWAN was one of the support groups. I noticed on your website that it says SWAN stands for Surviving With AIDS Network, but for some reason I remember the last word as being "Naturally" when it was first formed—is that correct?*

Anyway, I enjoyed your photography on the website. Thanks, and I wish you continued success and good health.

Best,
Jeff

Dear Jeff,

Hello, thanks for your e-mail. Yes, of course you have my permission to publish my letter.

I do remember you, Jeff, and I want to thank you for all your years of commitment to TPAN and all the good work you do. SWAN did start out as "Surviving with AIDS Naturally," but I changed "naturally" to "network" when I started including lectures about pharmaceutical therapies. When SWAN first started there was only AZT monotherapy available and many PWA's who could not tolerate AZT were looking for herbal and other natural therapies that they could tolerate. Some of the participants were unhappy with the name change since, at that time, there was a lot of angst directed towards the pharmaceutical industry, but I didn't want to steer people in the wrong direction by using the word "naturally" since, by that time, I did believe that pharmaceuticals were necessary.

I recall how wonderful TPA was for me when I was diagnosed with full blown AIDS in 1991. I was scared and alone. With TPA I found a community of incredible people who were maintaining a great attitude and other non-positive volunteers who wanted to help and lend support. One of the most incredible people I met was Michael Thurnherr, who was the executive director until his passing. Michael was one of the first people I met; he had just recovered from a bout of PCP, which is what I had before coming to TPA. I remember him telling me at Ann Sather Restaurant—where we used to meet after meetings—that I would "be alright, that I was going to survive." I really took what he said to heart and I really believed that I could, that I would. People like Michael and so many others were my inspiration and hope. I don't know what the community at TPA is like now but at that time and in that space real magic happened.

I wish you all the best and thank you again for your very important work.

Sincerely,
Kurt Weston

Return to the closet

Thanks for the interesting read ["What's Goin' On?, January/February issue]. I think many of us have had similar experiences. Personally, I am finding my new career in health care satisfying at some level, but difficult nonetheless, because I am fearful of disclosing my orientation and status. It is a difficult transition, if, like me, you have led your life as more of an open book, working in more open, accepting environments. I live and work now in a more conservative area, and must say I am having difficulty dealing with the transition. Good luck in yours.

Anonymous, via the Internet

We Mourn Our Great Loss

1945–2009

Paying Homage to Martin Delaney

by Daniel S. Berger, M.D.

We mourn our loss. A great hero in the fight against HIV disease and a great friend to many, Martin Delaney died this morning, January 23, 2009.

Martin Delaney was well known to many people. He was a pioneer and leader, and a key figure within the AIDS movement from the beginning of the HIV epidemic to the present. The important role he played translated to the saving of many lives from HIV and AIDS. Besides his numerous and important accomplishments, he touched the hearts of almost any HIV-positive person he ever came in contact with.

It is exceedingly rare for someone who is not HIV-positive to completely and deeply understand what it is like to be infected. Marty was one of the few people who understood how HIV sufferers felt and what they had to deal with, without ever having the disease himself. It is also rare for someone who is HIV-negative to become an AIDS activist, let alone have the passion that Marty exhibited, combined with the tenacity and determination to accomplish as much as he did.

I first met Marty 22 years ago, and soon thereafter I had the good fortune of spending three to four days and evenings with him and Jim Corti in Ft. Lauderdale, talking non-stop about AIDS politics and treatment philosophy. Looking back, that time with Marty became one of the most important experiences of my life; its effect lasts to this day. Marty impressed me with his seemingly endless energy and efforts to get access to medications for people who needed them most, and his steadfast resolve to continue fighting, while considering different approaches.

Many times we talked about absolutely everything, including the important players in government and industry, which treatments were promising and not, how to lead the community and organize, and how to be objective while being activist-minded. Marty was the architect of various research agendas and was one of the key individuals responsible for helping create the "expanded access programs" for HIV drugs, which eventually became official policy. Marty was one of the greatest influences on my approach to building a research and treatment clinic. He gave me the courage to run contrary to the daily currents and bureaucracy, for which he himself was well-known. As a result, I have conducted every expanded access program ever available and more than 150 clinical trials. Marty's influence was clear. His picture has always been on the wall behind my desk.

During the early, dismal years when PWA's (People with AIDS, as they once were known) were so very sick, Marty was making runs across the Mexican border to bring ribavirin into the U.S. for his HIV-infected friends, and doing whatever was needed to help people survive. While Marty himself was not infected with HIV, he was constantly involved in trying to save the lives of those who were. Quickly becoming a public figure, he worked behind the scenes with officials and consistently urged that change be made with rapid speed; so that many infected individuals would not die needlessly. He was involved in smuggling medicines into the U.S., and worked with Dr. Larry Waites in bringing national attention to Compound Q, a Chinese antineoplastic drug that had anti-HIV activity. This story was featured on a nationally televised special

Photo courtesy of Drew Altizer

with Charlie Rose. He was often quoted in *The New York Times* and featured on many news and television interviews. He worked tirelessly with buyers clubs to obtain treatments that were not yet approved in the U.S. Later, he challenged drug companies on the pricing of HIV-related medications, and constantly worked to change government policy so that more people would have access to treatment.

Marty held regular educational meetings in San Francisco, and tirelessly spoke at educational seminars and meetings around the country, counseling countless people. In 1992, I arranged to hold a large community forum with Marty and myself, after attending a recent World AIDS conference. In a prior professional life Marty had taught public speaking, and I learned a great deal from his easygoing, simple, straightforward style. Our first forum together, held in the ballroom of the Belmont Hotel (located at Belmont and Sheridan) was a milestone for the Chicago HIV-positive community. It was attended by more than 400 people, and it was immediately apparent that all participants gained new hope and courage. A great deal of important information and education was provided on new antiviral research and how to deal with AIDS complications. That evening and later on he would encourage patients to learn what was available, and to take the initiative in discussing this openly with their doctor. Marty would say that if their physician was not amenable to being aggressive, then it was time to look for someone else for treatment. It was the first of 14 yearly updates that he and I conducted together in Chicago. These became extremely popular, and quite often a patient would inquire about when the "next one" would be scheduled.

Marty's yearly visit to Chicago was always a highlight for me because we'd spend some extra time together. Whenever we'd go out to eat, it was often to a restaurant in the community where we could "boy watch," while we discussed AIDS politics, treatment, research, and also gossip.

Marty was outspoken and not afraid to speak his mind, doing so without hesitation. To me, whenever Marty was outspoken and critical, which was not rare, he was never wrong. I marveled at his audacity. He often criticized the "system" and sometimes criticized pharmaceutical companies for their marketing approaches and pricing. I learned to maintain this sense of urgency from him, and when I was challenged for being outspoken or for a particular treatment approach, Marty would come to my aid. He was always insightful about evaluating results of HIV research, which oftentimes contradicted pharmaceutical company conclusions. I can still hear him say things like, "These pharmaceutical companies always say that." Although Marty did not hold a degree in medicine, he could converse with the most respected researchers on a very high level, and often interpreted results of technical research without difficulty.

On a Friday in 1996, Marty and I were both going to Washington, D.C. for different FDA Drug Advisory Committee meetings. Marty was present for the meetings discussing the approval of Norvir and Crixivan, and I was going to the FDA's Endocrinologic and Metabolic Drugs Advisory Committee to testify in support of Serono's human growth hormone for AIDS wasting. We met up to talk after both meetings concluded. While Marty recounted the unanimous vote for the approval of the two protease inhibitors, my committee voted 7-6 against approval of growth hormone treatment, which we felt was saving countless lives of people affected with wasting. During those early days, AIDS activism was made Marty Delaney-style. He immediately knew how to mount pressure on the FDA. Behind the scenes, there became a focused drive that compelled the FDA into granting accelerated approval despite the committee's vote against it; little did many know about the efforts of Marty as well as other activists including Bill Thorne and Jeff Getty of ACT UP Golden Gate (now known as Survive AIDS), Treatment Action Group (TAG), and AIDS Project Los Angeles.

Despite our geographical distance, we made a point of talking by phone on a regular basis. I had visited him many times in San Francisco, and we always made a point of doing dinner during many of the major conferences. During one conference in Amsterdam, we both coincidently bumped into each other at the same boy strip bar, and we laughed so hard that night.

Marty was one of the few AIDS activists that rubbed shoulders with the likes of Robert Gallo, the co-discoverer of HIV, and Tony Fauci, Director of the National Institute of Allergy and Infectious Diseases (NIAID), on a regular basis. He understood government politics and knew how to maneuver among policy makers. He knew everyone in industry and was well respected throughout. As founding director of Project Inform (1985), he was instrumental in leading national HIV treatment, policy, and advocacy until 2008, but continued being involved and working on other AIDS-related projects until his death. He founded the Fair Pricing Coalition, which works on drug pricing issues with pharmaceutical companies in the field of HIV/AIDS and hepatitis, and was a member of the AIDS Treatment Activists Coalition (ATAC). He was also a member of NIAID's National Advisory Council from 1995-98, as well as numerous other committees and boards, and was recently honored with the NIAID Director's Special Recognition Award for his many contributions in the fight against HIV/AIDS. Without Marty, many individuals would have died long ago.

Over the years, it always impressed me how Marty had a knack for making any HIV-positive individual feel hopeful. During many community meetings, individuals would come up to him for advice on all sorts of HIV-related problems, sometimes dismal, but they'd come away feeling better and more optimistic. He always made time for everyone. I do not exaggerate when I describe Martin Delaney as being something of an angel on earth. He had the biggest of hearts. If there ever was a true saint, Marty is one. He was a true hero and I am blessed to have known him and for him to have been my friend. I, and countless others, will miss him dearly. ✠

Daniel Berger is Clinical Associate Professor of Medicine at the University of Illinois at Chicago, and founder and medical director of Northstar Medical Center. He serves on the Medical Issues Committee for the Illinois AIDS Drug Assistance Program, and is a member of the board of directors of AIDS Foundation of Chicago. Dr. Berger has been honored by Test Positive Aware Network with the Charles E. Clifton Leadership Award. E-mail Dr. Berger at DSBergerMD@aol.com.

ATRIPLA

AD

PAGE

HERE

ATRIPLA

AD

PAGE

HERE

ATRIPLA

P.I.

PAGE HERE

ATRIPLA

P.I.

PAGE HERE

HIV drugs in the pipeline

Over the last two years the release of three new HIV medications has been providing new treatment options and hope for treatment-experienced patients. It is reassuring to know that there are several medications further along in the pipeline that provide an expansion of existing classes, as well as the addition of new classes.

Amdoxovir is an experimental nucleoside reverse transcriptase inhibitor (NRTI), currently in Phase 2, that is being developed by RFS Pharma. The medication is being studied either at doses of 300 mg or 500 mg twice daily and has been shown to be active against HIV strains that are resistant to Retrovir (zidovudine) and Epivir. Apricitabine is another NRTI, currently in Phase 2b, which is currently under development by Avexa. It is similar in chemical structure to Epivir and Emtriva, and is being shown active against strains resistant to Retrovir and Epivir. Side effects noted so far have been congestion, nausea, diarrhea, and modest increases in triglycerides.

Elvitegravir is an integrase inhibitor, currently in the planning stages of Phase 3, being developed by Gilead. The medication is dosed at 150 mg twice daily, boosted with 100 mg Norvir. So far few side effects have been noted. Gilead is planning to begin study of the first "quad fixed dose combination," a four-in-one-drug combining elvitegravir, Truvada and a new boosting compound being developed by Gilead. Watch for another potential blockbuster combination pill (one pill, once daily) which would be especially useful for those who can't take Atripla.

RDEA806 is a new non-nucleoside reverse transcriptase inhibitor (NNRTI), now in Phase 2, that is being developed by Ardea. The medication has been shown to be effective against strains resistant to Sustiva and has an added beneficial effect of reducing uric acid levels. IDX899, another NNRTI by Idenix, currently in Phase 2, has been shown to be potent, and is less susceptible to resistance compared to Sustiva and Viramune. [*Editor's note: GSK acquired the rights to IDX899 as* PA *went to press.*] Tibotec's NNRTI rilpivirine (TMC-278), currently in Phase 3, has been shown to cause minimal changes in lipids and glucose levels during the course of a 48-week treatment.

Vicriviroc, the newest CCR5 antagonist being developed by Schering-Plough, is currently in Phase 3. The medication is boosted significantly by Norvir, and has been shown to be active against strains that are resistant to other medications, including Fuzeon.

Bevirimat (PA-457), a derivative of the Chinese herb *Syzigium claviflorum,* is part of a new class called maturation inhibitors that is being developed by Panacos. Currently in Phase 2 trials, it could be useful for treatment in new and experienced patients. So far, the medication is only available in liquid form due to issues with tablet formulation. Panacos was recently acquired by Myriad Pharmaceuticals, which has another maturation inhibitor in early development, vivecon (MPC-9055).

PRO 140 is an entry inhibitor, currently in Phase 2, being developed by Progenics, that is administered intravenously. The medication contains engineered antibodies called monoclonal antibodies that bind to the CCR5 receptors on CD4 cells to prevent entry by HIV. TNX-355 is the entry inhibitor that was being developed by Tanox, which was bought out by Genentech. It is also administered intravenously, every 2 weeks. Since the mechanism of action is different for this class, it can be used when resistance to other treatments is present.

Although there are a number of new medications that are under development, it will be a few years before they would be available. In the meantime, it is important to be compliant to your current regimen.

A concise summary of drugs further along in development

by Paul Djuricich, R.Ph. Pharm.D.

Drugs in the pipeline* †

Agent	Class	Sponsor	Status
AMD11070	CXCR4 blocker	Anormed	Suspended/ Phase 2
amdoxovir	NRTI	RFS Pharma	Phase 2
apricitabine	NRTI	Avexa Limited	Phase 2/3
bevirimat (PA-457)	Maturation inhibitor	Panacos / Myriad	Phase 2
elvitegravir	Integrase inhibitor	Gilead Sciences	Phase 2
IDX899	NNRTI	Idenix Pharmaceuticals	Phase 2
KP-1461	Viral decay accelerator	Koronis Pharmaceuticals	Suspended /Phase 2
PRO 140	Entry inhibitor / monoclonal antibody	Progenics Pharmaceuticals	Phase 2
RDEA806	NNRTI	Ardea Biosciences	Phase 2
rilpivirine (TMC-278)	NNRTI	Tibotec Pharmaceuticals	Phase 3
TNX-355	CD4 blocker/ monoclonal antibody	Genentech	Phase 2
vicriviroc	CCR5 antagonist	Schering-Plough	Phase 3

*Taken in part from the *2008 Pipeline Report* by Treatment Action Group (TAG).
Visit www.treatmentactiongroup.org for the complete report.

†Many other compounds are in pre-clinical and early development that are not included in this article or table.

INTRODUCTION

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 (if you count CCR5 antagonists and fusion inhibitors, both types of entry inhibitors, as separate classes). 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 taken with a low dose of ritonavir (Norvir), which boosts drug levels and simplifies dosing (see "Norvir"). New PIs and new formulations of old PIs have also expanded options and have made PIs a lot easier to take than they used to be. Still, it's important to be aware of PI toxicity. To varying degrees, the PIs can raise lipids (cholesterol and triglycerides), can cause insulin resistance (which can lead to diabetes), and 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). In 2007, 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.

Drug Class	
Drug	page
Nucleoside Reverse Transcriptase Inhibitors (also called nucleoside analogs, NRTIs, or nukes)	
Combivir (Epivir/Retrovir)	28
Emtriva (emtricitabine, or FTC)	29
Epivir (lamivudine, or 3TC)	30
Epzicom (Epivir/Ziagen)	31
Retrovir (zidovudine, or AZT)	32
Trizivir (Epivir/Retrovir/Ziagen)	33
Truvada (Emtriva/Viread)	34
Videx & Videx EC (didanosine, or ddI)	35
Viread (tenofovir)	36
Zerit (stavudine, or d4T)	37
Ziagen (abacavir)	38
Non-Nucleoside Reverse Transcriptase Inhibitors (also called non-nucleoside analogs, NNRTIs, or non-nukes)	
Intelence (etravirine, or TMC-125)	39
Rescriptor (delavirdine)	40
Sustiva (efavirenz)	41
Viramune (nevirapine)	42
Dual-Class Fixed Dose Combination	
Atripla (Sustiva/Truvada [Emtriva plus Viread])	43
Protease Inhibitors (PIs)	
Aptivus (tipranavir)	44
Crixivan (indinavir)	45
Invirase (saquinavir)	46
Kaletra (lopinavir/ritonavir)	47
Lexiva (fos-amprenavir)	48
Norvir (ritonavir)	49
Prezista (darunavir)	50
Reyataz (atazanavir)	51
Viracept (nelfinavir)	52
Entry Inhibitor	
Fuzeon (enfuvirtide, or T-20)	53
Selzentry (maraviroc)	54
Integrase Inhibitor	
Isentress (raltegravir)	55

ASSISTANCE

Patient assistance and drug co-pay programs

Most, if not all, HIV pharmaceutical companies provide some level of patient assistance to individuals who are unable to afford their HIV medications; ask your health care provider or contact the manufacturer directly (see manufacturer contact on individual drug page) for details on a specific drug.

Several companies have also recently instituted co-pay assistance programs, which may cover all or part of the drug co-pay for many privately-insured patients, up to a specified amount, and for a pre-determined period of time (for example, up to one year). Certain restrictions and eligibility requirements apply (for example, Medicare, and Medicaid not accepted); eligibility requirements may vary from program to program. Once eligible, most companies will then provide you with a co-pay card which you can bring to your pharmacist or provide to your mail-order pharmacy when filling your prescription.

The following companies currently have HIV drug co-pay assistance programs.

Abbott: Positive Partnership PLUS Card—In 2009, Abbott is launching a pilot program which will expand to the Positive Partnership PLUS Card. Includes 12 months of co-pay savings to cover Kaletra plus other ARVs, no income or co-pay eligibility criteria. Patients can save up to $50 toward their Kaletra co-pay, plus up to $100 of the cost of other HIV medications (up to $50 for each additional ARV with a limit of $100 total—must be part of a Kaletra regimen.) Visit www.kaletra.com for more information.

GSK: MySupportCard—Card is valid for the amount of your actual out-of-pocket cost up to a maximum of $100 for each prescription. All HIV drugs (Combivir, Epivir, Epzicom, Lexiva, Retrovir, Trizivir, and Ziagen) are covered. Go to www.mysupportcard.com for more information and to print out the card.

Gilead: Truvada Co-pay Assistance Program—Covers Truvada, Emtriva, and Viread. For high co-pays only—kicks in above $50 and up to $200/month. If health care provider does not have the card, you can call toll-free 1-888-358-0398 and it will be mailed to you. Atripla is currently *not* part of this program.

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

Tips for using this guide

by Jeff Berry

- Drugs are color-coded by class and are listed alphabetically within each class by brand name.
- A fixed dose combination (FDC) is a formulation that combines two or more drugs, and is 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.
- The side effects and drug interactions charts make it easier to quickly find some of the more common side effects and interactions associated with each drug. Always refer to the individual drug pages, the manufacturer's package insert, and your physician or pharmacist for more information.
- Our special pull-out chart allows you to easily pinpoint dosing information and food and liquid requirements for each drug. 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. Visit www.aidsinfo.nih.gov/guidelines

SAVE UP TO $100
OFF OUT-OF-POCKET COSTS*

YOU might be eligible for treatment savings.

- Up to $100 off each monthly out-of-pocket expense
- Off each GlaxoSmithKline HIV medication*
- Up to 2 years

*Subject to eligibility. Restrictions apply as described on www.PatientSavingsSite.com.

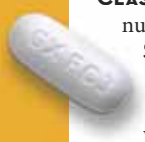
Visit **www.PatientSavingsSite.com**
to start saving today, or talk with your healthcare professional.

gsk GlaxoSmithKline

COMBIVIR

COMBO DRUG

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR



Common Name: zidovudine (AZT) and lamivudine (3TC)
Brand Name: Combivir
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: $921.44 / 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: See drug pages for Epivir (lamivudine, 3TC) and Retrovir (zidovudine, AZT) for more details. May be taken with food to decrease potential nausea associated with AZT.

Potential drug interactions: See the drugs contained in Combivir—Epivir (lamivudine, 3TC), and Retrovir (zidovudine, AZT). 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. Rare but potentially fatal toxicity with all NRTIs: hepatomegaly with steatosis (enlarged, fatty liver) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance).

Tips: 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. Combivir has been shown in multiple clinical trials to be a potent regimen with either a protease inhibitor or an NNRTI. The AZT in Combivir can cause fatigue and anemia—it isn't pretty in those at risk for developing anemias (see Retrovir). One head-to-head study against Truvada found greater toxicity with Combivir, due to anemia. See Retrovir. 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 health care 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 their implication in lipoatrophy (thinning of the arms, legs, and face). The wasting of "AZT butt" could be irreversible or take a long time to rebuild. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Combivir (combination AZT/3TC) was the first fixed dose combination antiretroviral therapy approved (1997) for HIV infection. It simplified and revolutionized treatment and quickly became the "gold standard" for HIV therapy. It made a significant impact on the lives of those infected with HIV at the time. Unlike other fixed dose combinations, Combivir was never approved for once-daily usage. The short half life of AZT in the cell necessitated twice-daily dosing (for efficacy). Among the advantages of this drug are the reduced number of pills and the potential positive effect of the 3TC mutation (M184V) on the efficacy of AZT. The disadvantages rest primarily with the major toxicities of AZT (see Retrovir). With the approval of other, better tolerated, once-daily fixed dose combinations, our use of this drug has decreased significantly. Approximately 5% of our clinic population is currently taking Combivir. The area of greatest usage is pregnancy. Most of the data for the reduction of mother-to-child transmission was done with AZT. From a global standpoint, and specifically in Uganda, Combivir is the most frequently used first-line agent (used more than AZT and/or 3TC separately) in HAART regimens. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Seemingly just when AZT's patent was about to expire, Burroughs-Wellcome (now GlaxoSmithKline) came along with the maverick of fixed dose combination therapy. Combivir reduced pill burden, the number of pills taken every day, simplifying HIV therapy and other dual fixed dose combinations would follow (Epzicom, Truvada); and eventually, triple fixed dose combinations (Trizivir, Atripla). What we learned from Combivir: Know what you're taking! Combivir still had the same side effects of its components, AZT and 3TC, but the new drug came along before HAART and many got caught in the "new and improved" trap. Many who swore they would never take AZT did so unwittingly. Though Combivir is safe, tolerable, and durable, it is a DHHS Guidelines Panel "alternative" dual-NRTI. Epivir/3TC has a mutation that has been linked to increased resistance to Retrovir/AZT; thus, the sum is not greater than its parts. —Morris Jackson

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

EMTRIVA

Common Name: emtricitabine or FTC
Brand Name: Emtriva
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: $430.13 / month; $99.13 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. Side effects (rarely seen) may include headache, diarrhea, nausea, and rash. Skin discoloration (darkening of the skin on the palms and the soles of the feet) can occur. More hyperpigmentation seen in pediatric studies than adult studies. Rare but potentially fatal toxicity with all NRTIs: 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 NRTIs for a long time; it is 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, difficulty breathing or shortness of breath, and enlarged, fatty liver.

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

Flare-up of HBV in people co-infected with HIV/HBV has occurred when Emtriva was discontinued. This makes sense, since competitor Epivir is known to be effective against hepatitis B and has a hep B formulation; stopping the medicine could thus take the suppression off the hep B virus. 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. Truvada is now the only NRTI combination on the preferred list of U.S. HIV treatment guidelines for the NRTI component of an HIV regimen. In 2006, Emtriva was combined with Sustiva (efavirenz) and Viread in one pill, which is known as Atripla. Atripla is probably the most commonly prescribed medication for people taking HIV medicine for the first time. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Emtriva (emtricitabine, also known as FTC) was approved as a stand-alone antiretroviral for once-daily treatment of HIV infection in 2003, and in the fixed dose combinations Truvada (tenofovir/emtricitabine) in 2004, and Atripla (tenofovir/emtricitabine/efavirenz) in 2006. This antiretroviral is closely related to 3TC and should not be combined with this drug or the other fixed dose combinations (described above) in HAART therapy. In our clinic FTC is used primarily in the fixed dose combination formulations. While FTC has activity against hepatitis B, it is not currently approved for this viral infection. FTC is well tolerated, but a side effect observed in a number of individuals in our clinic is discoloration of the skin and nails. Like 3TC, FTC should be dose adjusted in those with decreased kidney function. If Truvada or Atripla is being used, separate the FTC from the other components of the fixed dose combination for correct dosing. Is there any difference between 3TC and FTC? Yes, FTC stays in the cell longer than 3TC and may be a reason why Truvada performs a little better than 3TC fixed dose combinations. FTC and 3TC share the M184V mutation and individuals resistant to 3TC will also be resistant to FTC. On the positive side, FTC (as with 3TC) may boost the activity of AZT and tenofovir when this mutation is present. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

It's probably no small coincidence that Emtriva is also called FTC: it is very similar to 3TC (Epivir). So much so that Emtriva and Epivir should not be taken together; nor should Emtriva be taken with any fixed dosed combination containing it or its cousin Epivir (Truvada, Atripla, Combivir, Epzicom, or Trizivir). And like Epivir, Emtriva is effective in combating the hepatitis B virus (but has not been FDA approved to treat HBV). Emtriva has a longer half-life than Epivir, meaning that it stays in the bloodstream longer. This is why you can take a lower dose of Emtriva just once a day (200 mg) than Epivir (300 mg), and perhaps over time, Emtriva may be less toxic to the liver. Emtriva combined with Viread gives us Truvada, and is a component of Atripla (Truvada and Sustiva), further reducing pill burden. Potential for and actual incidence of side effects can vary, as always, from person to person, but also across races with Emtriva: hyperpigmentation (skin darkening of the palms of hands and soles of feet) can occur more often in Blacks/African Americans. —Morris Jackson

EPIVIR

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: lamivudine or 3TC
Brand Name: Epivir
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: $424.98 / month for 300 mg, $113.34 / month for 240 ml bottle
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. Side effects (rarely seen) may include headache, nausea, vomiting, diarrhea, fever, fatigue, hair loss, insomnia, malaise (general ill feeling), nasal symptoms, cough, peripheral neuropathy, low white blood cells, and anemia.

Rare but potentially fatal toxicity with all NRTIs: 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 NRTIs for a long time; it is 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, 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 bleeding. Children should be watched for signs of pancreatitis.

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

Tips: Exciting benefit: drug resistance that the virus develops against Epivir—the M184V mutation—makes the virus less fit to replicate and has even been shown to keep T-cells from dropping during a treatment interruption as much as they would have otherwise. It is also approved for treatment of hepatitis B virus (HBV), under the brand name Epivir-HBV. 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 monitored by their physician. Epivir is also available combined with Retrovir (zidovudine, AZT), called Combivir (one tablet twice a day), in a once daily formula with Ziagen (Epzicom, one tablet daily), and in a triple combination with both Retrovir and Ziagen (Trizivir, one tablet twice a day). Please see package insert for more complete potential side effects and interactions.

DOCTOR

Epivir (lamivudine, known to most as 3TC) was first synthesized in 1989 by a Canadian biochemical firm that licensed the drug to GSK (Glaxo at the time) for a share of sales. 3TC was approved by the FDA in 1995 for twice-daily dosing and again in 2002 for once-daily dosing. Epivir is also approved for hepatitis B infection and is a component of the fixed dose combinations Combivir, Trizivir, and Epzicom. This antiretroviral agent, or its close "relative" emtricitabine [Emtriva], forms the nucleoside backbone for virtually all HAART regimens used in our clinic. We have found 3TC to be the best tolerated of all the antiretroviral agents. This does not mean there are no adverse events associated with 3TC use. On occasion we have seen bone marrow toxicity (anemia and low white cells), and have also diagnosed pancreatitis (reported with use of 3TC) in one of our patients on the drug. In Ugandan children, pancreatitis is seen with a little more frequency. Because of the tolerability of Epivir, I have found it easy to forget that it must be dose adjusted in individuals who have reduced kidney function. Failure to dose adjust 3TC may lead to increased levels of the drug in the blood and an increase in adverse events. Resistance to 3TC can occur rapidly (that's the bad part). The 3TC signature M184V mutation, however, may improve the antivretroviral activity of AZT and tenofovir and the mutated virus is less able to produce more copies of itself (that's the good part). Tolerability of 3TC and the resistance benefits makes it a key component of any HAART regimen. It's the best damn drug in town! —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Almost the Energizer Bunny of ARVs, Epivir just keeps going and going. It is contained in Combivir, Trizivir, and Epzicom; can be taken as a single nuke with a PI (usually boosted with ritonavir [Norvir]) or NNRTI-containing regimen; and, is FDA-approved to treat hepatitis B. HIV tends to develop resistance to Epivir quickly (the M184V gene mutation), but even that turns out to be a good thing. This specific gene mutation weakens HIV "viral fitness," rendering HIV less able to make copies of itself. Thus Epivir remains effective in a back-handed sort of way, which accounts for why it is still so widely used. —Morris Jackson

EPZICOM

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: abacavir sulfate and lamivudine
Brand Name: Epzicom
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: $996.03 / 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. There have been studies showing that medications containing abacavir increase the risk of cardiovascular events, including heart attacks and strokes. This applies to people with greater risk factors, (such as smoking, diabetes, and high blood pressure), and is reversible upon discontinuation.

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 of Ziagen in the blood over 24 hours (bioequivalency) as Ziagen twice a day. As of last year, U.S. HIV treatment guidelines recommend Truvada as the only preferred medication for the NRTI component of a treatment regimen. Epzicom was briefly on the preferred list when a simple and inexpensive test helped to greatly decrease the potential for HSR. But Epzicom was on a roller coaster, and it came back down when studies found that Ziagen was associated with increased cardiovascular disease in people already at high risk for it. Last year, the guidelines added the statement, "Pending additional data, [Epzicom] should be used with caution in individuals who have plasma HIV RNA [viral load] greater than 100,000 copies/mL, as well as in persons at higher risk for cardiovascular disease." Truvada, however, is associated with kidney toxicity, although that hasn't been a big problem to date. 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 the potential for this reaction. If HSR is suspected or cannot be ruled out, abacavir products should be discontinued. New drug label change last year states that persons who had a previous suspected HSR may try abacavir again but only if they test negative on the HLA test. The test should never be used to diagnose HSR. The incidence of HSR was the same between Epzicom and Ziagen twice daily (8% vs. 9%), but the incidence of severe reactions was higher with Epzicom (5% vs. 2%). Remember that the HSR cited may have been suspected, not definitely diagnosed. 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 (fixed dose 3TC/abacavir) was approved for once-daily dosing in the treatment of HIV in 2004. This fixed dose combination is well tolerated, has no food restrictions, and plays a significant role in HAART simplification. One must remember that Epzicom contains abacavir and this combination should not be given to an individual who has had an abacavir hypersensitivity reaction (HSR—see Ziagen). An HLA-B*5701 gene test should be done prior to use of Epzicom in an individual who has never had the drug. If an individual has significant kidney and/or liver problems, fixed dose Epzicom is contraindicated. The reason—3TC must be dose adjusted for kidney failure (abacavir is not) and abacavir must be dose adjusted for significant liver failure (3TC is not). To continue therapy with the components of Epzicom in this situation, the drugs should be given separately and dose adjusted as appropriate. You should be aware that there is data that demonstrates Epzicom performed poorly when compared to Truvada (ACTG 5202 study) in individuals with viral loads of greater than 100,000 copies/ml. At the 2008 ICAAC conference, Epzicom was found to perform better than Truvada in those with viral loads less than 100,000 copies/ml (HEAT study). Personally, I find the data confusing and will continue to use Epzicom in my patients until more substantial information is obtained. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Because of the inherent risks associated with its Ziagen component (see Ziagen/abacavir), Epzicom was downgraded from a "preferred" to an "alternative" dual-NRTI in the November 2008 update of the DHHS Guidelines. There really isn't much else to say except talk with your medical provider to see if this is a good drug for you, especially if you develop a rash or think you may be at increased risk for a heart attack (again, see Ziagen/abacavir). —Morris Jackson

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: zidovudine (ZDV) or AZT
Brand Name: Retrovir
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 is available.
AWP: $496.56 (generic $356.04) / month, $64.61 (generic $48.13) for 240 ml syrup
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: May include headaches, fever, chills, muscle soreness, fatigue, nausea, and fingernail discoloration. Zidovudine (AZT) has been associated with alteration of various cells in the blood through bone marrow suppression resulting in anemia (low red blood cell counts) and/or neutropenia (low white blood cell counts), particularly during the first three months in people with advanced HIV. Potential exists for severe anemia requiring blood transfusion, erythropoietin injections, or hospitalization when used on its own or in combination with hydroxyurea. Rare but potentially fatal toxicity with all NRTIs: 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 NRTIs for a long time; it is 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, 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 bleeding. 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 didanosine (Videx).

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 suppression should be monitored with use of Cytovene (ganciclovir), Valcyte, amphotericin B, pentamidine, dapsone, flucytosine, sulfadiazine, interferon-alpha, ribavirin (Rebetol), and with cancer treatments such as hydroxyurea and doxorubicin. Ribavirin and zidovudine may cancel each other out, so this combination should be monitored closely. New Procrit or Epogen warning: if hemoglobin target is above manufacturer's recommendation (12 g/dL), the risk for serious and life-threatening cardiovascular complications significantly increases. For zidovudine patients, measure hemoglobin once a week after starting the anemia drugs until hemoglobin has stabilized. Notify health care provider if experiencing pain and/or swelling in the legs, worsening in shortness of breath, increases in blood pressure, dizziness or loss of consciousness, extreme tiredness, or blood clots in hemodialysis vascular access ports. Do not take with Combivir or Trizivir, since zidovudine is already in these medications.

Tips: The not-so-good news for people adding zidovudine: the fatigue and the potential anemia. You can start taking erythropoietin (Procrit or Epogen) for some anemias, but that's adding an expensive weekly injectable. Some doctors would prefer switching out the zidovudine for another drug. Also, some clinicians avoid the "T" drugs, or thymidine analogs (zidovudine and Zerit) because of their implication in lipoatrophy (fat loss, seen in the arms, legs, and face). 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 (zidovudine, known to most as AZT, generic form available in the U.S.) was the first antiretroviral developed and has had a significant impact on the course of HIV infection. Historically, AZT development has served as an example of a highly successful government and industry partnership to combat a lethal disease. In reality, conflict and controversy surrounded its development and can make some interesting reading if one so desires to explore this issue. The conflict and controversy surrounding this drug, however, led many patients to refuse AZT therapy. In our clinic, AZT is primarily used in the fixed dose combinations Combivir or Trizivir. Since the approval of other more powerful and convenient antiretrovirals, the use of AZT as a stand-alone drug (or in combination) in HAART therapy has decreased significantly. In developing countries, where the number of individuals infected with HIV is large but the antiretroviral choices small, AZT (alone or in fixed dose combination) is first-line therapy. My most vivid memory of AZT is its use as monotherapy in the first patients we treated many years ago in our clinic. We watched the CD4 count increase (marginally) for a few months (we didn't have HIV RNA at that time) and then drop to levels lower than when they started therapy. This was the first hint that a single drug would not be enough to treat HIV. While I would never advocate use of AZT as monotherapy, I have to be honest, I do have one patient who uses AZT as monotherapy (all of us have "that one patient"). This was his first therapy and his immune system is good, virus undetectable, and no adverse effects. I did convince him once to go off AZT ("he obviously didn't need it"). To prove that every individual is unique, when off the drug, his immune system decreased and virus appeared. There went my credibility as far as AZT monotherapy with this patient. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

In the beginning, there was AZT. This failed oral chemotherapy was pulled out of the archives and received FDA approval as the first anti-HIV drug in March 1987. Originally prescribed at what we now know to be overdosed levels (400 mg every four hours), AZT was toxic. It was eventually reformulated to one 300 mg tablet taken twice a day and the lower dosage decreased toxicity and the side effects (anemia, bone marrow suppression, and neuropathy) became manageable, if not completely tolerable. Despite being the oldest (and most widely studied) drug in the arsenal of antiretrovirals, AZT remains efficacious, particularly since it is one of the few ARVs capable of penetrating the blood-brain barrier. AZT is a component of Combivir and Trizivir. —Morris Jackson

Common Name: abacavir sulfate, zidovudine, and lamivudine
Brand Name: Trizivir
Class: fixed dose combination—nucleoside analogs (also called nucleoside reverse transcriptase inhibitors, NRTIs or nukes)
Standard dose: One tablet (300 mg 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: $1,492.49 / 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, Retrovir (zidovudine, AZT), and Ziagen. See those pages for more information. Side effects associated with Trizivir may include headache, nausea, upset stomach, and fatigue. May be taken with food to decrease potential nausea associated with Retrovir. 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 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 Ziagen. New drug label change last year states that persons who had a previous suspected HSR may try abacavir again but only if they test negative on the HLA test. Check with your doctor if you have any side effects after taking this medicine—don't just stop! There have been studies showing that medications containing abacavir increase the risk of cardiovascular events, including heart attacks and strokes. This applies to people with greater risk factors, (such as smoking, diabetes, and high blood pressure), and is reversible upon discontinuation.

Potential drug interactions: See also the drugs contained in Trizivir—Epivir, Retrovir (zidovudine, AZT), and Ziagen, for more information. Do not take Retrovir (zidovudine, AZT), Epivir, Epivir-HBV, 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 (pyrimethamine), flucytosine, Fungizone (amphotericin B), doxorubicin, and hydroxyurea.

Tips: See the drugs contained in Trizivir: Epivir, Retrovir (zidovudine, AZT), 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 about certain toxicities or drug interactions. 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 Retrovir, which is one of the drugs in Trizivir, measure hemoglobin once a week after starting the anemia drugs until hemoglobin has stabilized. Notify health care provider if experiencing pain and/or swelling in the legs, worsening in shortness of breath, increases in blood pressure, dizziness or loss of consciousness, extreme tiredness, or blood clots in hemodialysis vascular access ports. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Trizivir (AZT/3TC/abacavir) was approved for twice-daily dosing in the treatment of HIV infection in 2000. This was the first fixed dose triple combination antiretroviral to be produced. Initially, Trizivir (alone) was a popular choice because it greatly simplified therapy for HIV. It soon became apparent that another drug had to be added to this combination to improve efficacy. In our clinic, Trizivir as stand-alone therapy continues in the few patients who have taken it for a long period of time, have a healthy immune system, controlled viral load, and refuse to change the regimen. It is important to remember which antiretroviral components make up Trizivir. In kidney or liver failure, the components may have to be dose adjusted. This will necessitate giving each antiretroviral component separately in the appropriate dose. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

The maverick of triple-combination therapy, Trizivir was the first drug to combine three drugs (AZT, 3TC, and abacavir) into a single, once-a-day pill. All three components target the reverse transcription stage of the HIV lifecycle, and studies have shown that if used alone, drug resistance can develop rather quickly in some people. And because the whole is only as good as the sum of its parts, due consideration must be given to AZT toxicities and potential Ziagen adverse events. Frankly, Trizivir just isn't as long-lasting, as strong, or as effective as Atripla. Trizivir by itself "is generally not recommended and should only be used when a preferred or an alternative NNRTI-based or PI-based regimen is less desirable because of concerns about toxicities, drug interactions, or regimen complexity." (DHHS Guidelines, November 3, 2008). It bears repeating the lesson learned from Combivir: Know what you're taking! —Morris Jackson

TRUVADA

COMBO DRUG

NUCLEOSIDE / NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: emtricitabine and tenofovir DF
Brand Name: Truvada
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: $1,099.70 / 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 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, Epivir-HBV, 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 (didanosine, ddI) are increased by 44–60% when taken at the same time as Viread, which is in Truvada. Therefore, a dose reduction to 250 mg for Videx is recommended for people who weigh more than 60 kg (132 pounds). Higher ddI concentrations could increase the risk of ddI-associated adverse events, including neuropathy. See tips. Viread decreases the concentration levels of Reyataz. In addition, Reyataz (and Kaletra) 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 taken 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 the only preferred medication 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. Kidney function 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 (fixed dose tenofovir/emtricitabine) was approved for once-daily dosing in the treatment of HIV infection in 2004. This fixed dose combination is at the top of the list in sales of antiretroviral agents. Truvada is the most common NRTI backbone that our clinic uses in HAART regimens. Because of Truvada's excellent tolerability profile, Combivir usage has substantially decreased. Please see tenofovir and emtricitabine for more specific comments about the component drugs in this fixed dose combination. Important issues to re-emphasize here include: 1. Using this drug in an individual with reduced kidney and/or liver function requires dose adjustment. This will necessitate stopping Truvada and taking the component drugs separately in the appropriate dose. 2. Remember there are drug interactions between tenofovir and Videx. 3. When used with Reyataz, Norvir must be added to the HAART regimen. 4. Because of the bone health issues (see tenofovir), I would be cautious with general use in young children with active growth plates. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Like its fixed dosed combination predecessors Combivir and Epzicom, Truvada is a single pill combining two drugs that simplifies treatment, but appears to be less toxic. "Appears" is the operative word though—future studies could show possible impaired kidney function and reduced bone mineral density related to the Viread component of Truvada. But, Truvada is a highly favored treatment option, both widely prescribed by docs and well tolerated by patients. Truvada is the DHHS Guidelines "preferred" dual-nuke for treatment naïve patents. Overall, it is safe, it works, and is generally well tolerated. Truvada, like its Viread component, may cause gas. —Morris Jackson

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

VIDEX EC

Common Name: didanosine or ddI
Brand Name: Videx & Videx EC
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 capsules.) 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. Approved for children weighing at least 44 pounds. Take missed dose as soon as possible, but do not double up on your next dose. Generic Videx EC is available.
AWP: $426.10 for Videx EC (generic enteric-coated $368.72) / 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 possible 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: 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 NRTIs for a long time; it is 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, 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 bleeding. Risks for pancreatitis include higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Stop all HIV medications and see a health care provider right away. Body fat redistribution/accumulation has also been reported with ddI.

Potential drug interactions: The levels of ddI are increased by 44–60% when taken 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). The combined use of ddI and Retrovir (zidovudine, AZT) 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. 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, or lactic acidosis. Swallow the capsules whole. The capsules eliminate the bad taste and texture of the tablets and the enteric coating reduces diarrhea. If you have reduced kidney function, you may require a lower dose. Notify your doctor right away if peripheral neuropathy is suspected. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Videx (didanosine, known to most as ddI) was approved for use in HIV infection in 1991. This was the second antiretroviral drug produced and those who failed AZT were started on Videx. This trend of sequential monotherapy continued for several years before we understood that combination therapy (HAART) was more potent and durable. The unfortunate fallout from this was the emergence of multi-resistant virus in those who survived, and death for many who had untreatable resistant virus. Videx is poorly absorbed in the gut and was first formulated in a chewable tablet containing antacid to increase absorption. I can vividly remember the chewable tablets—most patients hated chewing up to 4 tablets two times daily. I made all health care workers who rotated through our clinic chew a placebo Videx tablet (including me, ugh!). This forever imprinted in their memory what patients had to do twice daily and on an empty stomach. In 2000, BMS formulated and patented a Videx EC capsule. This dosing formulation replaced the chewable tablets. Dosing is now one capsule daily (dose dependent on weight and kidney function), but the dietary restriction remains. A generic form of Videx capsules was also approved for sale in the U.S. in 2004. Videx is a very difficult drug to use. In addition to the dietary restrictions, neuropathy, hepatitis, pancreatitis, and lipodystrophy changes accompany the use of this drug. Combining it with stavudine [Zerit] enhances the occurrence of all of the above. Early on, when tenofovir [Viread] first came out, we learned the hard way (severe patient morbidity) that the dose of Videx had to be reduced when used with tenofovir. An increased risk of myocardial infarction (heart attack) was found with current use of Videx (as seen with abacavir) in the D.A.D. observational study. Videx use in our clinic is currently minimal. Some stalwart patients continue it to this day. They fear failure with other antiretrovirals. Occasionally, we will use Videx (if we can show it has activity) in those needing a second, third, or fourth drug in salvage therapy. In developing countries, ddI continues to be an important component of HAART therapy (especially in Africa). All the adverse effects of the drug are observed and often the chewable tablets are the only dosage form available. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Videx was once a major player with the anti-HIV drugs, but now it's pretty much just a benchwarmer, only being called into play when nothing else seems to be working. The early version was just plain nasty—both in terms of taste and side effects. The new, improved "enteric-coated" version only eliminated the antacid buffer, improving the taste aspect and making it easier to take, but the major side effects of peripheral neuropathy and pancreatitis remain. The neuropathy can be painfully debilitating and the pancreatitis, acute and deadly. And like its early counterpart AZT, Videx is associated with mitochondrial toxicity and can cause lactic acidosis, a buildup of lactic acid in the blood resulting from abnormal production of energy within a cell. Videx also has significant drug-drug interactions, particularly with Viread, and should be taken in a smaller dose than the usual 400 mg enteric-coated capsule when used with Viread. —Morris Jackson

VIREAD

NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: tenofovir disoproxil fumarate (TDF)
Brand Name: Viread
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: $690.31 / 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 is also approved for the treatment of hepatitis B in adults, and some individuals 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 Retrovir (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 taken at the same time as Viread. Therefore, a dose reduction to 250 mg of Videx is recommended for people who weigh more than 60 kg (132 pounds). Data are not available to recommend a dose adjustment of didanosine for patients weighing less than 60 kg. 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. You should not take Viread with Hepsera, a hepatitis B treatment.

Tips: Viread along with Emtriva (also available as Truvada and in Atripla) are considered the preferred NRTI combination by U.S. HIV treatment guidelines. The body clears 70–80% of Viread through the kidneys 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.

Viread in combination with Videx did not perform well in a small study of treatment-naïve individuals. T-cells were barely raised in people who were undetectable, and those who started with less than 200 T-cells and more than 100,000 viral load failed to reach undetectable levels.

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. The K65R mutation is selected by Viread (as well as Ziagen and Videx). This mutation can reduce susceptibility to other NRTIs. The activity of Viread can be reduced in patients who have acquired resistance to other NRTIs. The complex interaction of NRTI resistance and Viread susceptibility is an area in which further research needs to be done. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Viread (tenofovir, also known as TDF) was approved (once-daily dosing) by the FDA in 2001 for the treatment of HIV and in 2008 for the treatment of chronic hepatitis B. Also available are once-daily fixed dose combinations of emtricitabine and tenofovir (Truvada) and tenofovir, emtricitabine, and efavirenz (Atripla). I can still remember my delight several years ago when my patient with HIV and hepatitis B (HBV) co-infection had an undetectable HIV viral load, normalized liver function, and an undetectable HBV viral load on HAART containing TDF. I knew what happened, but had not actually seen the additional benefit of TDF activity against hepatitis B. It is important to remember that stopping tenofovir in someone co-infected with HBV may lead to worsening of the HBV infection. In our patients taking tenofovir we do not commonly observe general side effects such as nausea, diarrhea, and weakness. More serious adverse events including lactic acidosis, pancreatitis, and lipoatrophy (fat wasting) are also uncommon. Abnormalities of kidney function may occur with use of TDF in those with normal kidneys. So far, this has not been a common occurrence and it has not deterred use of the drug. If a patient has abnormal kidney function to start with, caution using the drug is advised and dose adjustment is important. I do have concern for bone health with use of tenofovir. There are some studies that suggest an effect of TDF on bones. There is no definitive answer to this potential problem and, for now, I try to be very attentive to low-impact bone fractures (in both women and men). —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Viread is actually a nucleo*tide* reverse transcriptase inhibitor but is generally classed with NRTIs. Like the nukes, Viread works to prevent HIV from changing its genetic makeup inside a healthy CD4+ T-cell, but it requires one less step in doing so because it enters the body already phosphorylated (chemically ready to do its job). Viread has shown efficacy in those who have developed resistance to AZT, Zerit, Videx/Videx-EC, Ziagen, and even Epivir. And like Epivir, Viread has some activity against the hepatitis B virus, but has not been FDA-approved to treat hepatitis B. Viread is also being studied as a PrEP (pre-exposure prophylaxis) drug—a prevention theory to treat high-risk individuals before HIV infection. About the worst thing that can be said for this drug is that it may have a potential to cause kidney problems, but that hasn't yet been definitively ascertained. Viread is in Truvada and Atripla. Be forewarned: Viread can make one a little "gassy," if you know what I mean (and I think you do). —Morris Jackson

Common Name: stavudine or d4T
Brand Name: Zerit
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. Generic now available. Take missed dose as soon as possible, but do not double up on your next dose.
AWP: $456.89 (generic $410.70) / 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 can occur 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 may include headache, chills/fever, malaise (general ill feeling), insomnia, anxiety, depression, rash, upset stomach (nausea and vomiting), diarrhea and abdominal pain. Rare but potentially fatal toxicity with all NRTIs: 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 NRTIs for a long time; it is 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, 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 experiencing symptoms of pancreatitis and seek medical attention right away. 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 Retrovir (zidovudine, AZT) 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. Retrovir (zidovudine, AZT) and Zerit should not be used together due to evidence that one limits the other's effectiveness. Because of additive neurotoxicity, if possible, Zerit should not be combined with Videx.

Tips: Zerit is now not commonly used in the U.S., due to its toxicity and the availability of newer medications. Contact your health care provider right away if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your health care provider. Studies show that Zerit crosses the blood-brain barrier to a useful degree, which may be beneficial for patients at risk for neurological damage (such as dementia) from HIV. Zerit is associated with facial wasting 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

Zerit (stavudine, known to most as d4T) was the fourth antiretroviral developed and was approved for use in HIV infection in 1994. This drug has had a very long run in the treatment of those infected with HIV. It was and still is a very effective antiretroviral, but after years of use, the adverse events associated with the drug (outlined above) virtually stopped the prescription of d4T as part of HAART therapy. There are still some patients in our clinic (doing well and with no adverse events) who refuse to stop d4T. There are some studies that show low-dose d4T is still effective with fewer adverse events. This data has not persuaded many health care providers treating HIV to use the drug. Zerit has always been a twice-a-day drug. In 2002, the FDA approved an extended-release formulation of Zerit for once-daily dosing. Zerit XR was used in several important clinical trials, but BMS never brought the drug to market. This company "silence" speaks volumes. In developing countries, d4T is a very important antiretroviral. It is used as first-line therapy in the fixed dose combination called Triomune (lamivudine, stavudine, nevirapine) dosed twice daily. This drug has made a huge impact on the HIV epidemic in Africa, but the many adverse effects associated with long-term use of d4T are now becoming apparent. Often this is the only antiretroviral that is available to those infected with HIV and having AIDS in Africa. Interestingly, in Uganda, the major clinic treating HIV/AIDS (The Joint Clinical Research Centre) and the Ministry of Health are attempting to reduce the use of d4T as part of HAART regimens. The alternative is the fixed dose combination Combivir (see Combivir). —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Zerit is proof positive that hindsight is indeed 20/20. Once thought to be less toxic than its close rival AZT, Zerit was the great hope for replacing AZT. But over the years data began to show that Zerit was the culprit for the lion's share of nucleoside-associated lipoatrophy (loss of body fat particularly in the face, limbs, and ass) and peripheral neuropathy. Zerit has also been associated with hyperlipidemia (increased levels of LDL, the "bad" cholesterol). Consequently, Zerit has fallen out of grace and favor—in the U.S. Unfortunately, because it is now available as a cheaper, generic drug, it is being widely used in developing countries highly impacted by HIV/AIDS. I, for one, think that's reprehensible. Believe me, having survived highly dosed AZT monotherapy, I *understand* that desperation for taking whatever drug may be available, but we know better now, and to pass Zerit along without any improvement in its side effect profile is unconscionable. —Morris Jackson

ZIAGEN

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: abacavir sulfate (ABC)
Brand Name: Ziagen
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); new scored tablets available for children. A strawberry/banana flavored liquid is available. Take missed dose as soon as possible, but do not double up on your next dose.
AWP: $571.05 / month, $150.13 for liquid
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). 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, you 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, and 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. 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. New label change states that persons who had a previous suspected HSR may try abacavir again, but only if they test negative on the HLA test. More common side effects may include nausea, vomiting, diarrhea, fatigue, headache, fever, rash, and anorexia (loss of appetite). Studies show that abacavir increases the risk of cardiovascular events, including heart attacks and strokes. This applies to people with greater risk factors (such as smoking), and is reversible upon discontinuation.

Rare but potentially fatal toxicity with all NRTIs: 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 severe in women, people who are obese, and people who have been taking NRTIs for a long time; it is 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, 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. Stop all HIV medications and see a health care provider right away.

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: The U.S. HIV treatment guidelines now state, "Pending additional data, [Epzicom] should be used with caution in individuals who have plasma HIV RNA [viral load] greater than 100,000 copies/mL, as well as in persons at higher risk for cardiovascular disease." The manufacturer also recommends that people with symptoms of acute respiratory disease consider HSR even if another 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

Ziagen (abacavir), first developed as a twice-daily drug, was later approved as a once-daily agent (2004) and in the fixed dose combinations Trizivir (3TC/AZT/abacavir in 2000) and Epzicom (3TC/abacavir in 2004). Abacavir rapidly became an easy to take and popular component of HAART therapy. At first the hypersensitivity reaction (HSR—potentially fatal), seen in a relatively small number of individuals (~8%), gave pause to those of us prescribing the drug. I can remember the HSR conversation with patients and the wide-eyed look when I said it could be "potentially fatal." The finding that those who have a specific gene (HLA-B*5701) are most susceptible to having the HSR made use of the drug safer. This meant all patients needed a gene test before prescribing abacavir which added cost and time to the antiretroviral decision. My experience with the HSR and HLA-B*5701 gene has been colored somewhat by a patient treated with Ziagen in our clinic. This individual was re-challenged with abacavir after a question of an abacavir HSR but negative HLA-B*5701 gene test. The patient had a severe HSR within an hour of the first re-challenge dose. Subsequent abacavir skin patch testing was found to be negative. While I strongly believe that the gene test has significantly reduced the incidence of HSR with abacavir, I suggest a small number of individuals are still at risk for HSR through a mechanism not associated with the HLA-B*5701 gene. I would advise continued vigilance during the first weeks of abacavir dosing and never restart abacavir after an HSR. A major issue clouding abacavir use is the reported increased risk of myocardial infarction (MI, or heart attack) with current exposure to the drug. This finding was a total surprise to us. Until we get more definitive clinical trial data, I primarily avoid use of the drug in those with documented increased MI risk factors. Personally, I continue to find abacavir alone or in fixed dose combination a valuable part of HAART therapy. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

As always, really talk with your doctor to be sure you understand any possible side effects before starting a medication. This is especially true with drugs containing abacavir (Ziagen, Epzicom, and Trizivir). If considering starting an abacavir-containing drug, have a HLA-B*5701 test done to screen for abacavir hypersensitivity reaction (HSR). HSR is an allergic reaction to abacavir that usually occurs within the first six weeks of therapy and typically only affects less than 10% of people taking it, but it can be severe and sometimes fatal. Those who test positive for HLA-B*5701 should not take this drug. Another cautionary note: studies also show increased risk for a cardiac event (heart attack) in people taking an abacavir-containing drug, particularly for those with five or more cardiovascular risk factors (smoking, male, obese, high cholesterol, Black/Latino, etc.). Recently FDA-approved for child dosing according to body weight. (Interestingly, the U.S. patent for abacavir expires in December 2009.) —Morris Jackson

INTELENCE

Common Name: etravirine
Brand Name: Intelence
Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)
Standard dose: Two 100 mg tablets twice a day, with food. Take missed dose as soon as possible, but do not double up on your next dose.
AWP: $817.50
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 (19%), diarrhea (18%), nausea (15%), and headache (11%). 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 and, in rare cases, Rescriptor) 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. Should not be taken with Reyataz/Norvir, Lexiva/Norvir, or Aptivus/Norvir. Since Kaletra increases Intelence blood levels, use together with caution. Intelence may be taken without dose adjustment with Isentress and the experimental integrase inhibitor elvitegravir, but Selzentry does require dose adjustment to 600 mg twice a day with Intelence when used without a boosted PI. In people with failed therapy with other NNRTIs, Intelence should not be taken only with NRTIs (including Viread). No interaction was found with the acid suppressants ranitidine (Zantac and others) or Prilosec (omeprazole) when taken with Intelence. There was also no interaction with methadone and Intelence.

Tips: Intelence is a badly needed drug in the NNRTI class. The older NNRTIs can develop resistance quickly, and with only one mutation in the virus. 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 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 taken 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. Published Phase 3 DUET studies demonstrated good activity when combined with Prezista in treatment-experienced people with NNRTI resistance. At 48 weeks, a significantly greater number (61%) treated with Intelence than placebo (40%) 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 drug. Tibotec is also developing another NNRTI, rilpivarine (TMC-278), for treatment-naïve people (first time on HIV therapy), which may have pharmacologic advantages over Intelence, including the ability to dose once a day. Those unable to swallow the tablets can stir them in water until there's a milky appearance and drink the solution. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Intelence (etravirine) was approved in 2008 for use in combination with other antiretroviral drugs for therapy-experienced individuals (two tablets twice daily following a meal). It is not approved for those individuals who are naïve to HIV therapy. There is extensive cross-resistance among the drugs in the NNRTI class. Failure with one NNRTI may lead to all others in the class being ineffective. Etravirine is a second generation NNRTI and, unlike the currently available agents in the class, resistance to other NNRTIs does not necessarily confer resistance to etravirine. Resistance testing should be performed for appropriate use of this drug. Etravirine has been fairly well tolerated in our patient population. The general side effects of nausea, rash, and diarrhea have not been a major issue. I believe that drug interactions with etravirine, however, are an issue. When this drug is prescribed as part of HAART therapy, all drugs being taken (including over the counter) should be evaluated for a potential interaction with etravirine. For example, St. John's wort will reduce the level of etravirine in the bloodstream and levels of erectile dysfunction drugs may be reduced if used with etravirine. This antiretroviral should not be used in combination with others in the NNRTI class (remember, this includes Atripla). Etravirine has been a welcome addition to our antiretroviral armamentarium, but its use must be implemented with care in order to ensure a successful outcome of therapy. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Approved by the FDA in January 2008, Intelence is a "second generation" non-nuke—the first approved since Sustiva in 1998. Ten years is a long time in the world of ARVs, but Intelence seems to have been worth the wait. Before Intelence, if you developed resistance to any one of the non-nukes (Viramune, Sustiva, and Rescriptor), you developed cross-resistance to the entire class. That isn't the case with Intelence: it is an active drug against NNRTI resistant strains of HIV. Basically, it restores the ability to interfere with the specific reverse transcription process in the HIV lifecycle where NNRTIs are designed to work. Intelence is a twice-daily drug, but so what? For the time being, it has a good side effect profile. Not yet indicated, approved, or recommended for initial therapy. —Morris Jackson

RESCRIPTOR

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: delavirdine (DLV)
Brand Name: Rescriptor
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: $344.83 / 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, and itchy skin or rash. A serious side effect of the NNRTI class is rash, which can be life-threatening. Most rashes occur within the first 1–3 weeks after starting Rescriptor. If you experience blistering, mouth lesions, conjunctivitis (redness or inflammation of 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 medication, so seek medical attention right away. Body fat accumulation or redistribution may occur.

Potential drug interactions: You cannot take Rescriptor with oral Versed (midazolam), Halcion (triazolam), 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 health care provider if you have a history of heart or blood pressure problems. Potential toxicity when taken with Biaxin (clarithromycin), dapsone, Mycobutin (rifabutin), Procardia or Adalat (nifedipine), Norvasc (amlodipine), Plendil (felodipine), Coumadin (warfarin), and quinidine. Use caution with Tegretol (carbamazepine, an anti-seizure medication, also 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 or 2.5 mg Levitra per 72 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 to increase stomach acidity. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Rescriptor (delavirdine) was approved for the treatment of HIV infection in 1997. The dosing regimen of this antiretroviral is a good example of the large number of pills that had to be taken multiple times per day in the past. The original dosing schedule was 4 tablets three times daily (thankfully no dietary restrictions). When the pill size changed, it came down to 2 pills three times per day. In general, this antiretroviral is not used to any great extent in current HAART therapy. Our clinic participated in the first clinical trials with this drug. The most common problems we observed with delavirdine were skin rash and liver function abnormalities. Data is available suggesting delavirdine can be used (like Norvir) to boost levels of other protease inhibitors (mostly indinavir, nelfinavir, saquinavir ,and amprenavir), but the drug has to be taken in full dose to be effective. That would be a painful reminder of yesteryear! —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Rescriptor, the first non-nuke, was quickly overshadowed and superseded by Viramune and Sustiva. It has a myriad of drug-drug interactions from Flonase to Viagra and everything in-between; and comparatively speaking, has a high pill burden (two 200 mg tablets, three times a day). Rescriptor has all but vanished into obscurity. —Morris Jackson

Common Name: efavirenz (EFV)
Brand Name: Sustiva
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: $627.06 / 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 may include rash, nausea, vomiting, diarrhea, fever, and increased liver enzymes. These symptoms occur early and generally resolve within two to four weeks. A serious side effect of the NNRTI class is rash, which can be life-threatening. Rash is more common, and more severe, in children, as is diarrhea, fever, and low levels of some blood cells. May raise levels of triglycerides and the good cholesterol (HDL). May lead to false positive tests for use of marijuana. Women taking Sustiva should not become pregnant or breast-feed because of the risk of birth defects. Increases in liver enzymes in people with hepatitis B and/or C can occur and should be monitored.

Potential drug interactions: Do not take with Atripla, since Sustiva is already in Atripla. You cannot take the following medications with Sustiva: midazolam, triazolam, 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.

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. Be careful when stopping Sustiva, so that you avoid the rapid development of HIV resistance to it—check with your doctor or pharmacist first. It is usually recommended that you continue your other HIV medications for several days after stopping Sustiva. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Sustiva (efavirenz) dosed once daily was approved for HIV infection in 2002. This antiretroviral in combination with Truvada and in the fixed dose combination Atripla (tenofovir/emtricitibine/efavirenz) is preferred by patients and the health care workers who treat HIV infection. CNS side effects (dizziness, headache, vivid dreams, concentration difficulty, worsening depression, etc.) are a prominent issue with its use. We see them in about 30% of our patients. I always tell my patients that means 70% have no or minimal side effects. We do not give this drug to someone who has or has had significant depression. We learned the hard way that suicidal ideation can be part of the depression. Rarely, I have seen seizures increase (in patients with a seizure disorder) with use of efavirenz. In general, the most prominent side effects (dizziness, vivid dreams) do truly decrease within 3-4 weeks. Difficulty concentrating is the major reason for discontinuation of the drug in my patients. Since taking the drug with food increases its concentration in the bloodstream (possibly leading to more CNS side effects), efavirenz is generally dosed at night (you are asleep and don't perceive the problems) and on an empty stomach. This does not mean it cannot be taken with food. I do have patients who take it with food and have no adverse effects. Efavirenz is a category D medication in pregnancy. Its potential effects on the fetus are well documented, and it shouldn't be given to women who are planning pregnancy. Women of child-bearing potential should consider contraception if they are taking efavirenz (remember Atripla contains efavirenz). —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Sustiva is the "preferred" DHHS Guidelines NNRTI. It is conveniently dosed once a day in both the 600 mg tablet and as the non-nuke component in Atripla. Sustiva has a long half-life, it stays in the body longer (more so in African-Americans and Hispanics); it is potent and it works. But Sustiva can cause birth defects and should not be used by pregnant women, particularly during the first trimester, and should be avoided by women wanting to have children. Because side effects can affect the central nervous system, Sustiva is probably not the drug of choice for those with a history of depression or other mental health conditions. Heed the warning "Do not drive or operate heavy machinery when taking this drug." Sustiva should be taken at bedtime as it can cause "wooziness." The enhanced dream states that you've all heard about don't last forever, usually going away within time—a blessing or disappointment. Personally, I thoroughly enjoyed mine. —Morris Jackson

VIRAMUNE

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR

Common Name: nevirapine (NVP)
Brand Name: Viramune
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: $535.21 / 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 health care 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 right away. Do not increase dose if rash develops during dose escalation or if you develop any rash accompanied by the above listed conditions. Label change last year states that dose escalation should not last longer than 28 days. An increase in liver enzyme levels has been observed and in rare instances, the development of hepatitis. May need to stop taking Viramune until liver function returns to normal. Permanently discontinue it if abnormalities return. Rarely, severe and life-threatening hepatotoxicity (liver damage), including 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. Be careful when stopping Viramune, so that you avoid the rapid development of HIV resistance to it—check with your doctor or pharmacist first. It is usually recommended that you continue your other HIV medications for several days after stopping Viramune. Viramune has also been shown to have a positive impact on triglycerides and cholesterol levels. When given around the time of labor, Viramune has demonstrated effectiveness in preventing the transmission of HIV from mother to child, but there was an increase in HIV drug resistance when given alone. The use of at least one other HIV drug helped to cut down the incidence of resistance, and women have been shown to experience effectiveness with the drug six months after giving birth. Viramune was updated from Pregnancy Class C to Class B in 2007, meaning that it was found to be even safer. Single- or two-dose Viramune may be used for babies born to HIV-positive mothers. Mothers should not breastfeed their infants while taking Viramune. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Viramune (nevirapine) was approved for twice-daily dosing in 1996. It was the first drug approved in the NNRTI class. All of the issues with use of nevirapine are outlined in my comments on the other NNRTIs. To avoid rash, the drug should be taken as one pill per day for two weeks before going to the full dose of one pill twice daily. Interestingly, with all the potential problems with nevirapine, it is still an effective and relatively safe drug. While we do not start as many individuals on nevirapine now as previously, a good 5% of my patients still take it as part of HAART therapy and are doing well. I believe this speaks well of the efficacy and durability of this drug. In Africa, nevirapine is used only as a component of the fixed dose combination Triomune (3TC/d4T/nevirapine). —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Viramune was the first of the non-nukes and continues to hold its own against Sustiva. It is particularly effective with pregnant women in preventing HIV mother-to-child transmission, and does not affect the central nervous system. But Viramune can seriously mess with the liver in both male and female treatment-naïve patients. Studies have shown increased serious hepatic (liver) events in those with higher pre-treatment CD4 counts: greater than 250 in women and 400 in men. Why? Who knows? —Morris Jackson

Common Name: efavirenz, emtricitabine, and tenofovir DF
Brand Name: Atripla
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 (Sustiva [600 mg] and Truvada [200 mg Emtriva and 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: $1,727.76 / 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: See the drugs contained in Atripla—Sustiva, Emtriva, and Viread. Nausea, diarrhea, and rash. 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, Epivir-HBV, 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. Atripla is probably the most commonly prescribed medication for people taking HIV medicine for the first time. 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

Atripla (tenofovir/emtricitabine/efavirenz) was approved for once-daily dosing for HIV infection in 2006. This was the first dual-class complete HAART regimen in one pill formulation and dosed once daily. When this fixed dose combination became available, the "old timers" (those of us who have been treating HIV from the beginning) shouted, "It's finally here!" While our treatment of HIV has progressed greatly, we can all remember the early years when often 40 pills per day was the norm. The early drugs made a profound impact on HIV infection, but it was a full-time job for the patient to take them (especially when you consider that antiretrovirals were only part of their total treatment regimen). Many of those individuals who braved all the sickness, excessive number of pills, and side effects are now gone. They are true heroes.

Interestingly, some patients in our clinic will stay on Truvada/Sustiva rather than switching to Atripla due to fear of change. It is important that you and your health care provider remember that Atripla cannot be stopped abruptly. Because efavirenz (Sustiva) remains in the bloodstream a long time after stopping the drug (and the other components of Atripla don't), you could be receiving monotherapy with Sustiva. This can lead to Sustiva resistance. If Atripla is to be stopped, you should be given Truvada alone for at least a week to protect Sustiva. One must also remember that the pregnancy warning with Sustiva applies also to this fixed dose combination. In developing countries (especially Africa), Atripla has marginal use at best. On the other hand, the dual class fixed dose combination Triomune (3TC/d4T/nevirapine), dosed twice daily, has been around for some time and is the primary drug used in HAART therapy. Knowing the number of patients infected in developing countries, there is little doubt that Triomune, in a global perspective, is used more than any other antiretroviral. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

In case you haven't heard: Atripla is a complete, effective HIV regimen in a one-pill, once-a-day treatment option, combining three drugs from two ARV classes. It contains the DHHS on Antiretroviral Guidelines "preferred" drugs from both classes: the NRTI Truvada (Emtriva/Viread) and the NNRTI Sustiva. Atripla is the only dual-class fixed dose combination drug on the market; and of historic note, it is the first single product of two competing pharmaceutical companies. (See what can happen when we all play nice?) The lesson learned from Combivir, HIV's first co-formulated drug, bears repeating here: Know what you're taking—the whole is only as good as the sum of its parts. And again, because of its Viread component, it may cause gas. —Morris Jackson

APTIVUS

PROTEASE INHIBITOR

Common Name: tipranavir (TPV)
Brand Name: Aptivus
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. Oral solution available; both formulas available for children and adults. Must be taken with food. Take missed dose as soon as possible but do not double up on your next dose.
AWP: $1,172.26 / month for Aptivus only
Manufacturer contact: Boehringer-Ingelheim, www.aptivus.com, 1 (800) 542–6257
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, has occurred with Aptivus. Rash was more common in children. Also, women taking birth control pills may be at higher risk for rash. If a severe rash occurs, Aptivus should be discontinued. See Viramune. Stop using Aptivus if rash appears with joint pain or stiffness, throat tightness, generalized itching, muscle aches, fever, redness, blisters, or peeling of the skin, and call your health care provider right away. Other side effects may include headache, fever, fatigue, dry mouth, and dizziness. Caution should be used in people with mild liver impairment, since Aptivus concentrations may be increased. Should not be taken by people with moderate to severe 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, anticoagulants, or supplemental high doses of vitamin E. 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 (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and 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 health care professional of the medications you are taking. See the package insert. Aptivus lowers Intelence levels, and the two should not be combined. Do not take with Tambocor, Rythmol, quinidine, oral Versed (midazolam), Halcion, rifampin, pimozide, ergot alkaloids (such as Cafergot, Wigraine, Methergine, and D.H.E. 45), or the herb St. John's wort. Do not use simvastatin 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 Retrovir (zidovudine, AZT). The clinical significance of this interaction is not known. No significant changes were seen when combining Aptivus with Sustiva or Viramune. Should not be taken with other protease inhibitors because it greatly lowers their blood levels. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Methadone doses may need to be increased. Trazodone concentrations may increase; a lower dose of trazodone is recommended. 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 should be used with valproic acid, which may be less effective due to decreased concentrations when used with Aptivus. Caution must be exercised when using itraconazole or fluconazole. Rifabutin requires a reduced dose. Norvir and Aptivus capsules contain alcohol (but should not be enough to trigger relapse), so be cautious with Antabuse or Flagyl. Oral solution contains vitamin E; do not take with additional vitamin E beyond that found in a standard multivitamin.

Tips: Due to its resistance profile and its drug interactions, Aptivus is less popular than the other newer PI, Prezista. Take with food to minimize stomach problems. Do not take at the same time as antacids. Aptivus is expected to do less well for people with combinations of certain protease-related mutations. See package insert 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. Aptivus must be used within 60 days after the bottle is opened, and then can be stored at temperatures between 59 to 85°F. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Aptivus (two capsules of tipranavir plus two capsules of ritonavir) was approved in 2005 for combination antiretroviral treatment only in those individuals with HIV infection who have evidence of viral replication, are highly treatment-experienced, and/or have HIV strains resistant to multiple protease inhibitors. This antiretroviral was approved for use in the pediatric population in 2008. While Aptivus gives us an active drug choice in those who have failed multiple PIs, the data suggesting a drug effect on clotting cells and brain hemorrhage with its use made it difficult to see the sunlight on Aptivus from underneath this shadow. Personally, I have not seen either of these problems with use of the drug. Problematic for us has been liver function and lipid abnormalities (not helped by the ritonavir dosing). With newer drugs in the PI and other antiretroviral classes now available, we have not used much of this drug. However, when an active PI is needed for salvage therapy, tipranavir may be a viable choice, though genetic testing should be done to confirm that. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Aptivus is considered a "salvage" drug—not for first-timers or those just starting antiretroviral therapy. Aptivus seems to have efficacy when taken with Fuzeon, but should never be taken with another PI (other than Norvir), as it decreases other PI levels. Aptivus has to be taken twice a day and may also increase lipid levels and cause more liver toxicity than other PIs on the market. Required refrigeration may also be problematic, particularly in developing countries. —Morris Jackson

CRIXIVAN

Common Name: indinavir sulfate (IDV)
Brand Name: Crixivan
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 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: $570.95 / 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 health care 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 (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and 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, itraconazole (200 mg twice a day), or ketoconazole (200 mg once a day). The dose of Mycobutin should be reduced by 50% and Crixivan dose increased to 1,000 mg every eight hours when taken together.

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

Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception. Additional monitoring may be required when taking Coumadin (warfarin), immunosuppressants, or calcium channel blockers (such as Norvasc, Procardia, and others). Carbamazepine (Tegretol and others), Dilantin (phenytoin), or phenobarbital may decrease Crixivan, so alternate seizure medications should be used. Crixivan may decrease levels of methadone but withdrawal rarely occurs. 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

Crixivan (indinavir, known to many as Crix) was approved for use with other antiretroviral drugs in HIV infection in 1996. While we were trying to figure out what to do with Invirase, Crixivan became a major choice for our patients. Dietary restriction with use of this drug was an issue for some. Two capsules had to be ingested every eight hours on an empty stomach. I can remember vividly patients having great difficulty taking the regimen (Crixivan without food, other drugs with food), but how could they stop? They were better. Crixivan helped many of our patients and the number dying in our practice dropped significantly. The dosing is now easier (two capsules twice daily with one ritonavir twice daily—no food restrictions), but we rarely use the drug. General gastrointestinal side effects occurred in 10-15 % of our patients. Other complications, not as common, but significant, were kidney stones and kidney failure. We asked our patients to drink lots of water (almost to the point of wanting to "pee" all the time) to avoid kidney stones. "Crix belly" (increased abdominal girth) was the rage for a while. Of course we later learned this was lipodystrophy and not specific to Crixivan. I still have a few patients on Crixivan and they refuse to go off the drug ("I'm doing okay—why?"). Crixivan served our patients well during a very difficult time. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Back in the day (1996), Crixivan was part of "the cocktail" that rescued us from the brink of death, thus ushering in the era of HAART (Highly Active Antiretroviral Therapy). And because it was saving us, we didn't care that we had to schedule our lives around Crixivan. It had to be taken every eight hours and came with food restrictions and liquid intake requirements: take on an empty stomach, an hour before or two hours after eating a high-fat meal, and drink 64 ounces of water a day or you could very well get kidney stones, one of its highly possible side effects. Crixivan came to be associated with fat redistribution, thus the old monikers "Crix belly" and "buffalo hump" that we now call lipodystrophy. Crixivan is the granddaddy of the PIs and lives in retirement and in the memories of those of us who reaped its benefits. —Morris Jackson

INVIRASE

PROTEASE INHIBITOR

Common Name: saquinavir (SQV)
Brand Name: Invirase
Class: HIV protease inhibitor (PI)

Standard dose: Two 500 mg film-coated tablets with 100 mg Norvir two times a day with food, or within two hours after a meal. Must be taken with Norvir. Take 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: $952.26 / month for 500 mg and $931.83 / 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 (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and 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: 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. Rescriptor, Crixivan, Norvir, Viracept and Kaletra all significantly increase Invirase's concentrations. No dosage change when taken with Kaletra.

Do not take with Tambocor (flecainide), Rythmol (propafenone), Biaxin (clarithromycin), dexamethasone, Cordarone (amiodarone), oral Versed (midazolam), Halcion (triazolam), Rifadin (rifampin), Orap (pimozide), Lanoxin (digoxin), ergot derivatives (such as Cafergot, D.H.E. 45, Methergine, and Wigraine), 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. Trazodone concentrations may increase; a lower dose of trazodone is recommended. Use calcium channel blockers with caution.

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

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

Tips: 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

Invirase (saquinavir) was the first protease inhibitor approved (in 1995) for combination therapy in the treatment of HIV infection. It is difficult to convey the anticipation and excitement this new class of antiretrovirals brought for our patients sick with AIDS or untreatable because of HIV resistance to their current antiretrovirals. Unfortunately, for some with resistance mutations, Invirase was monotherapy. We had no other active drugs to combine with it. The history of Invirase in the treatment of HIV infection, however, appears to me to be a lesson in "pressure to get a drug to market." Dosing of this drug was three hard-gel capsules taken three times daily in combination with two other antiretrovirals. Invirase was relatively well tolerated but very poorly absorbed in the gut. To improve absorption a full and/or high-fat meal was required each time it was taken. I remember this being difficult for many patients to do. Those who did, gained weight (not a bad thing for those who were very thin) and often a lot of weight (for some a problem). Because of the difficulty obtaining adequate blood levels of Invirase, failure of HAART therapy with this drug was observed. In 1997, a soft gel saquinavir capsule (Fortovase) was approved. With Fortovase, better blood levels were obtained, but gastrointestinal side effects meant tolerability was decreased. The number of pills, dietary needs (still needed the full meal), and tolerability issues led to poor adherence for some and, eventually, failure to control the virus. Things came full circle in 2005 when Fortovase was taken off the market and Invirase (now 500 mg capsules dosed two capsules twice daily with a meal) boosted with low-dose ritonavir (one 100 mg capsule, twice daily) showed efficacy. Now, blood levels are consistent and tolerability is not as much an issue. However, with the newer protease inhibitors now available, use of Invirase has not measurably increased. Invirase is a drug to consider (with testing for genotype and phenotype) for those new to HAART therapy. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Invirase is the newer version of Fortovase which went bye-bye three years ago. Invirase was the first FDA-approved PI compound marketed back in 1995, but because it wasn't absorbed well, it was basically useless. Its low bioavailability also allowed for drug resistance to develop quickly, wiping out the entire PI class for many before most of them were even developed. Invirase, reformulated as a 500 mg tablet about a year ago, is the third attempt to make it a more useful drug, and boosted with Norvir twice a day, it seems to be doing a better job. —Morris Jackson

KALETRA

Common Name: lopinavir/ritonavir (LPV/r)
Brand Name: Kaletra
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 people or those taking it with Sustiva or Viramune. Half-strength film-coated tablet available: 100 mg lopinavir 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: $876.98 / 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, and increased cholesterol, triglycerides (fats in the blood), and elevated liver enzymes, a sign of liver damage—this may be more common in people with hepatitis B or C. As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and 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, oral Versed (midazolam), 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 (such as Norvasc, Procardia, and others).

Dosage of methadone may need to be increased when taken with Kaletra. Increase Kaletra dose to three tablets twice a day with food 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 Retrovir (zidovudine, AZT) and Ziagen. Videx should be taken 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 (itraconazole) or Nizoral (ketoconazole) doses greater than 200 mg per day with Kaletra. Decreases Vfend (voriconazole) levels. People with kidney impairment may require lower Biaxin doses with Kaletra. Immunosuppressants 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 or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Tips: Kaletra once or twice daily is one of four protease inhibitors recommended by U.S. HIV treatment guidelines for first-time therapy, but the other three are easier to take. Also, Prezista and Reyataz were found to be more effective for people with more than 100,000 viral load in large studies last year. Still, HIV has a high barrier against developing resistance to Kaletra, a real plus. Kaletra has even been shown to work well all by itself (monotherapy), but this is still an experimental dose. Great viral load results out to 7 years in people on their first HIV regimen. Good results also seen in heavily treatment-experienced adults, even those with protease inhibitor resistance. Use Kaletra with caution in people with mild to moderate liver impairment. Four tablets once daily can increase side effects, especially diarrhea. However, avoid extreme heat and bright light. Carefully follow instructions on pediatric dosing. New change last year: should not be taken only once a day by children under 18. Avoid the oral solution during pregnancy. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Kaletra (lopinavir/ritonavir) was approved as a capsule (dosed as three capsules twice daily) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2000. In 2005, Kaletra tablets were approved for dosing at two tablets twice daily. Studies in individuals who are new to HAART have demonstrated that Kaletra can be given in a once-daily dosing schedule (four tablets daily). Kaletra monotherapy has been studied, but I don't believe this dosing is durable. A liquid preparation of Kaletra is available and the tablet form does not have to be refrigerated. Kaletra is the only co-formulated (one pill) protease inhibitor that takes advantage of the ritonavir boosting effect. I have generally believed that those patients with low CD4 cells and high viral loads (greater than 100,000 copies per ml) get better immunologic reconstitution with a boosted PI regimen. In general, studies have not proved this, but as an immunologist, I believe there may be a particle of truth to it. The major clinical adverse effect with Kaletra is diarrhea and, from a laboratory standpoint, elevated liver test results. Lipids take a hit with this drug. High triglycerides and cholesterol occur a little more commonly with Kaletra. This becomes important because we don't want our patients dying from a heart attack when they have pushed back the "fatal tag" to HIV infection. With the ability to boost other protease inhibitors which have better side effect profiles and are more tolerable, Kaletra has found competition. Since the problems with Viracept in pregnancy, Kaletra has become our choice for treatment of pregnant women with HIV infection. In Africa (specifically Uganda), Kaletra (Alluvia) is virtually the only protease inhibitor used (second-line therapy). —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

More bang for the buck, literally. Kaletra is the first and only co-formulated ritonavir-boosted PI—Kaletra doesn't have to be boosted because it comes with Norvir/ritonavir already in it. This allows for fewer prescription co-pays. Kaletra is indicated for both treatment-naïve and treatment-experienced patients and its once-daily dosing gets it on the DHHS Guidelines Panel's "preferred" list of PIs. Kaletra works well to reduce high viral loads and increase low CD4 counts, and also replaces Viracept as the only recommended PI for pregnant women. It now comes in a more heat-stable form (Meltrex formulation), an important consideration for HIV treatment in the developing world. —Morris Jackson

LEXIVA

PROTEASE INHIBITOR

Common Name: fos-amprenavir calcium (FPV)
Brand name: Lexiva
Class: HIV protease inhibitor (PI)
Standard dose: Once a day—two 700 mg tablets with either one 100 or two 100 mg Norvir. Twice daily: 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: $806.79 / month for tablets and $120.65 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" component, it should be used with caution in patients with allergies to sulfa drugs. The most common moderate to severe side effects may include nausea, rash, diarrhea, headache, vomiting, fatigue, and abdominal pain. Rash occurred in about 19% of patients, but severe rashes were uncommon. If you experience a rash, notify your doctor. For mild or moderate rashes, your doctor may choose to continue Lexiva, with close 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 (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and 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 insufficient 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, oral 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) and 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 (such as Norvasc, Procardia, and others). 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. Trazodone concentrations may increase; a lower dose of trazodone is recommended. 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 or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours.

Tips: Lexiva is one of the four protease inhibitors recommended by the U.S. HIV treatment guidelines for people on antiviral therapy for the first time, but is probably the least popular of the bunch. It can be taken once daily in treatment-naïve patients. The lower dose of Norvir may cause 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 it with your doctor. The FDA points out that the study comparing Lexiva/Norvir against Kaletra in protease inhibitor-experienced patients was not large enough to show that the combination was clinically equivalent to Kaletra. A liquid formula of Lexiva is available. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Lexiva (fos-amprenavir) was approved (two tablets twice daily) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2003. Fos-amprenavir becomes amprenavir once in the body. Amprenavir (Agenerase) was approved by the FDA in 1997. I took an amprenavir *once* and I had difficulty getting it down. How were my patients going to take a lot of these daily? The answer—amprenavir was discontinued when Lexiva came to market. In 2007, fos-amprenavir was approved for once-daily dosing (two tablets) with low dose ritonavir. The DHHS Guidelines Panel has listed ritonavir-boosted Lexiva as one of the four preferred PI options. If you have a "sulfa allergy" (can't take Bactrim for instance) you should let your health care provider know. We have observed significant rash in such individuals using Lexiva. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Lexiva is the new and improved Agenerase (now defunct), which after it is absorbed turns into amprenavir. Lexiva is better formulated than its earlier version, requiring fewer pills, has better absorption, and does not require Norvir boosting, if it is one's first PI. But when boosted for the PI-experienced, it can have activity against some PI-resistant virus and as such, is a "preferred" PI-based regimen of the DHHS guidelines. Lexiva is generally well tolerated but, because it contains sulfur, it can cause a rash if you are allergic to sulfa-based drugs such as Bactrim/Septra. And, resistance to Lexiva can develop quickly, putting one at risk for developing cross-resistance across the entire PI class if strict adherence is not maintained. —Morris Jackson

Common Name: ritonavir (RTV)
Brand Name: Norvir
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 daily, 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 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. (*As PA went to press, Abbott filed with the FDA to register a new tablet formulation of Norvir that will not require refrigeration.*)
AWP: $321.46 / 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 NRTIs), and alcohol intolerance.

As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, 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 an increase in liver enzymes (AST, ALT, and GGT), hepatitis, or jaundice (yellowing of skin), and increased muscle enzyme (CPK) and uric acid. People with hepatitis B or C may be at increased risk.

Potential drug interactions: Norvir interacts with many other drugs. See the manufacturer package insert for the most complete list. Do not take with Tambocor, Rythmol, Cordarone, oral 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). Trazodone concentrations may increase; a lower dose of trazodone is recommended. Norvir and Aptivus may decrease levels of methadone, but withdrawal rarely occurs. Methadone doses may need to be increased.

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

The effectiveness of birth control pills may be decreased when taking Norvir; 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%. Rifampin decreases Norvir levels by 35%. 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 taste. Blood concentration increases in people with hepatic (liver) impairment. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Norvir (ritonavir) was originally approved for use in combination with other antiretroviral drugs in the treatment of HIV infection in 1996. In 1999, a soft-gel capsule formulation of the drug was approved and the original formulation was discontinued. This antiretroviral was difficult to take and few could tolerate it. Before the soft gel capsule, there was a time when only ritonavir liquid was available. This stuff was not palatable. "I'd rather eat re-fried cow pies than take that liquid," said one of my patients. I tried it and totally agreed. Even with the new formulation of the drug (no refrigeration needed), acceptance of this drug was poor. It was dead in the water. Drug interactions with other PIs saved this drug. Now ritonavir is used not so much for its antiretroviral activity, but more for its ability to inhibit the enzyme that breaks down other protease inhibitors (leading to higher blood levels of the PIs). This allows health care providers to lower the dose and frequency of the PI administration, while improving efficacy. Most all protease inhibitor drugs are now boosted with low-dose ritonavir. While the search is ongoing for another protease booster drug, low-dose Norvir has made a significant impact on the efficacy and durability of HAART therapy. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Norvir was initially used as a stand-alone PI when it came onto the market in 1997. Twelve pills a day, a bad side effect profile and a myriad of drug interactions made it of little use. But that didn't stop Norvir's manufacturer, Abbott Laboratories, from jacking up its price by 400% (I would be remiss if I didn't mention this egregious fact). Today, Norvir is primarily prescribed as a 100 mg booster of other PIs (except with Aptivus), thus lowering their dosing requirements and raising their blood levels. But in doing so, it stifles a natural liver function, keeping the liver from doing what it was designed to do: filter out and protect the body from harmful substances. Norvir can still cause gastrointestinal side effects, but taking it with foods high in fat, like peanut butter (provided the January 2009 salmonella scare abates) or avocado, can help reduce stomach issues. I won't even discuss the liquid version except to say that it exists. —Morris Jackson

PREZISTA

PROTEASE INHIBITOR

Common Name: darunavir (DRV, formerly TMC-114)
Brand Name: Prezista
Class: HIV protease inhibitor (PI)
Standard dose: 800 mg (two 400 mg tablets) once daily for first-time therapy or 600 mg (one 600 mg tablet) twice a day for treatment-experienced patients. All doses must be taken with 100 mg Norvir and food. 75 mg tablet available for children over six (five to eight tablets twice a day based on weight). Take missed dose as soon as possible, but if more than 12 hours late on the once-daily (or six hours late on the twice-daily dose), do not double up on your next dose; take the next dose on schedule.
AWP: $1,027.65 / 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 may include diarrhea, nausea, headache, and abdominal pain. New warning last year: measure liver function before starting Prezista/Norvir. Also, increased monitoring should be considered for people with underlying chronic hepatitis, cirrhosis, or elevated levels of AST/ALT (lab measures of liver function), especially during the first several months of therapy. The rare risk of liver toxicity seems to be greater in people who: have advanced HIV disease and are taking many other medications; have hepatitis B or C; and/or develop IRIS (see below). No dose adjustment is necessary for those with mild to moderate liver disease, but Prezista/Norvir is not recommended for people with severe liver impairment. Severe rash, while very rare, can be life-threatening. 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), seek medical attention immediately. You may need to stop all medications. Prezista contains a "sulfa" component 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 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 oral midazolam, triazolam (Halcion), ergot derivatives (D.H.E. 45, Migranal, Cafergot, Ergomar, ergonovine, methylergonovine), or the herb St. John's wort, Cisapride, pimozide (Orap), and rifampin. Prezista may cause decrease in the levels of phenytoin (Dilantin) and phenobarbital (seizure medications); blood levels of these anticonvulsants should be monitored. A similar recommendation applies to the anticonvulsant carbamazepine (Tegretol). A reduced dose of rifabutin is recommended. Do not use Zocor, Simcor, Vytorin, Mevacor, Altoprev, Advicor, or Pravachol; lipid-lowering alternatives such as Lipitor or Crestor can be used with caution. The antifungal drugs such as itraconazole and ketoconazole may increase levels of Prezista, and Prezista may increase theirs, so caution must be exercised when used together (maximum dose is 200 mg a day for the antifungals). Blood levels of voriconazole (Vfend) may decrease. Voriconazole should not be administered unless benefit/risk justifies its use.

Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Prezista may increase levels of blood pressure medications called calcium channel blockers, such as Norvasc and others, and clinical monitoring of patients is recommended. A lower dose of trazodone and desimpramine 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, Flonase, and Flovent) can occur and therefore alternatives should be considered, particularly for long-term use. Effectiveness of birth control pills may decrease. Alternative methods of non-hormonal contraception are recommended.

Tips: Once-daily Prezista was approved last year for people taking HIV therapy for the first time (called "treatment naïve"), in addition to its approval for those who are treatment experienced. The new approval is based on 48-week results of the ARTEMIS study. Prezista is one of the four recommended PIs for initial therapy in treatment-naïve people in the U.S. DHHS and IAS-USA HIV guidelines. Tibotec received community kudos for not pricing Prezista higher than other new PIs. In one study it demonstrated superior viral load responses when compared to Kaletra. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Prezista (darunavir, known to some as TMC 114) co-administered with ritonavir was approved in 2006 for treatment of HIV infection in antiretroviral treatment-experienced adults having resistance strains to more than one PI. In 2008, Prezista was approved for once-daily dosing in those individuals infected with HIV and naïve to therapy. Prezista now has the best of both worlds. Multiple studies have shown the drug to be effective in PI-experienced individuals with fewer short-term adverse events and fewer lipid abnormalities with long-term use. The 2008 DHHS Guidelines Panel elevated ritonavir-boosted darunavir to one of the four preferred PI combinations for treatment of HIV infection. Tolerability, ease of administration, reduced adverse events, and favorable resistance patterns have made Prezista a popular PI choice with patients and health care workers. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Prezista, the most recent protease inhibitor, recently received FDA approval for 800 mg with 100 mg Norvir/ritonavir-boosted once daily dosing in newcomers to HIV therapy and can now be dosed for children based on body weight. For us old-timers of HIV treatment, Prezista's prescribed dosing is still 600 mg (300 mg, twice a day) with 100 mg Norvir/ritonavir-boosting. Prezista is a good option for those resistant to other protease inhibitors: it is very good at quickly reducing viral load and it is an easy drug, in terms of both dosing and side effects compared to other PIs. Prezista makes the DHHS guidelines "preferred" listing of PI-based regimens. And as an aside, Tibotec, the maker of Prezista, included it in a first of its kind study, the GRACE (Gender, Race, and Clinical Experience) study, which investigated gender differences in HIV drugs. To their credit, Tibotec took great pains to recruit and enroll more women than men in this study, even going so far as to limit men's enrollment to one man for every three women. —Morris Jackson

REYATAZ

Common Name: atazanavir sulfate (ATV)
Brand Name: Reyataz
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 4-9% of individuals taking Reyataz. However, no evidence of liver problems was reported. Nevertheless, report jaundice to your health care provider right away. Other side effects may include rash, kidney stones, and elevated liver function enzymes, a sign of liver damage; this may be more common in people with hepatitis B or C.

As seen with other protease inhibitors (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. 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 twice a day if treatment-experienced or 40 mg twice 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 the 400 mg Reyataz/100 mg Norvir dose for treatment-experienced people. When taking Reyataz *without* Norvir, dose can be taken at least two hours before and at least 10 hours after Pepcid, Zantac, or Axid. Reyataz should be taken two hours before or one hour after antacids (Rolaids, Tums, and Mylanta). Do not take with rifampin, Camptosar (irinotecan), oral Versed (midazolam), 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). Treatment-naïve people should 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 taking Reyataz and Viread should be monitored for Viread-associated adverse events. The heart medications bepridil, 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. Oral contraception should contain no more than 30 mcg of ethinyl estradiol if taking Reyataz without Norvir and and at least 30 mcg if taken with Norvir. 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 or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Calcium channel blockers should be monitored. A lower dose of trazodone is recommended.

Tips: Unboosted Reyataz is now one of the four protease inhibitors recommended by the U.S. HIV treatment guidelines for people on antiviral therapy for the first time, and probably the most popular of the four. Boosted Reyataz was already on the list. And look, Ma! A PI that doesn't have to be taken with Norvir in treatment-experienced people! Needs an acidic environment, so take it with food. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Reyataz (atazanavir) was approved (two 200 mg capsules once daily) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2003. Atazanavir was the first protease inhibitor to be approved for once-daily dosing. This was a "wow" moment—a protease inhibitor taken once daily. All those pioneer patients who suffered (some lost their lives) through endless pill numbers and multiple dosing schedules smiled. Atazanavir is generally boosted with low dose ritonavir, although I do use unboosted atazanavir with Epzicom in a few of my patients. The HAART regimen of atazanavir/Truvada/ritonavir (three pills once daily) is frequently used in our clinic. Atazanavir is a well tolerated antiretroviral medication, but there are two issues of concern—yellow discoloration of the skin and eyes and the potential for elevated bilirubin levels in blood. Both are benign problems. Those individuals who do get the skin changes, however, don't appreciate the yellow hue (the most common reason for stopping atazanavir). I am usually not that concerned about an elevated bilirubin in the blood, but it can cause confusion for health care workers if gallbladder disease is an issue or the patient has hepatitis C. We have seen one patient in our clinic with an atazanavir kidney stone. Elevated lipid levels (as seen with other PIs) are not a common issue with atazanavir usage, and most prefer this drug if lipids are a problem. Atazanavir has been a huge step forward in HAART therapy and many patients have taken advantage of it. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Reyataz, when boosted with Norvir, is the only once-a-day "preferred" DHHS guidelines PI-based treatment option. Unlike most other PIs, Reyataz doesn't seem to raise cholesterol and triglyceride levels, and a study has shown that it may even increase "good" cholesterol (HDL), thus offering protection against heart disease. On the down side, it can cause hyperbilirubinemia, a fancy word for jaundice, or yellowing of the skin or eyes. Jaundice is benign, it just ain't pretty; fortunately, it only affects a relatively small percentage of people and goes away when the drug is no longer taken. —Morris Jackson

VIRACEPT

PROTEASE INHIBITOR

Common Name: nelfinavir (NFV)
Brand Name: Viracept
Class: HIV protease inhibitor (PI)
Standard dose: 1,250 mg taken as either two 625 mg tablets or five 250 mg tablets twice daily 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: $640.92 / month for 625 mg
Manufacturer contact: Agouron Pharmaceuticals, 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 (except unboosted Reyataz), there can be increased levels of cholesterol and triglycerides which may be associated with an increased risk of heart disease. Other possible side effects seen with protease inhibitors are lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and 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. Invirase levels increase three-to-five-fold and Crixivan increases 50% (see Crixivan for potential drug interactions), so dose adjustments may be needed. Do not take with oral Versed (midazolam), Cordarone (amiodarone), Halcion (triazolam), Rifadin (rifampin), Prilosec-OTC (omeprazole), ergot derivatives (such as Cafergot, D.H.E. 45, Methergine, Wigraine), garlic supplements, or the herb St. John's wort (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. Use calcium channel blockers with caution.

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

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

Increased levels of the inhaled and nasal sprays with fluticasone, a steroid for asthma or allergies (found in Advair, Flonase, and Flovent), can occur and therefore should be used with caution. The effectiveness of birth control pills may be decreased; 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

Viracept (nelfinavir) was approved (three tablets three times daily) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 1997. In 2003, the dosage formulation of nelfinavir was changed to two tablets twice daily. The level of drug in the bloodstream is increased when taken with food. We used a lot of nelfinavir when it came to market. Diarrhea was its most prominent problem (20% of our patients) and we tried all sorts of tactics to plug the "hole in back"—calcium ingestion, more food, scheduled anti-diarrhea drugs, etc. Nelfinavir had a good antiviral effect and most patients just endured the problem. Interestingly, nelfinavir is one protease inhibitor that is not boosted by low-dose ritonavir. HAART therapy containing nelfinavir was the combination of choice for pregnant women until recently. The concern that nelfinavir may have been contaminated with cancer-producing chemicals was a major blow to use of this drug in pregnancy. With newer protease inhibitors available with better tolerability and fewer pills to ingest, nelfinavir use has significantly decreased. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

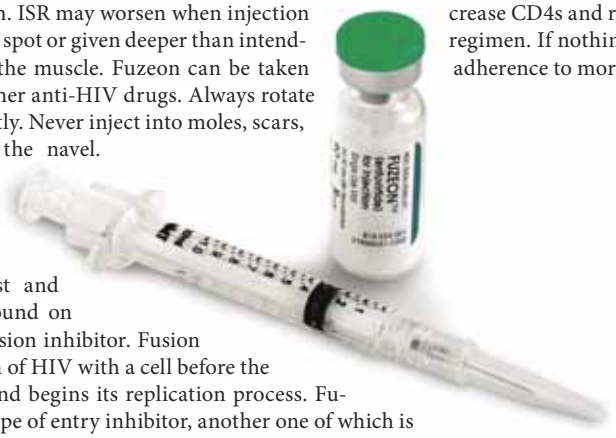
Viracept can cause inconvenient and intermittent explosive diarrhea! But that's just the bias of my personal experience. To be fair, the gastrointestinal distress is supposedly less extreme with the new formulation—and thankfully, fewer pills; but its significant number of drug-drug interactions remains a concern. Viracept is the only PI that does not require boosting and it seems to work well in preventing mother-to-child transmission in pregnant patients and those with bad livers. *But*, I'd at least think twice before opting for this drug: it is no longer recommended by the DHHS Guidelines Panel for initial therapy. —Morris Jackson

Common Name: enfuvirtide (ENF) or T-20
Brand Name: Fuzeon
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: $2,841.20 / 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. Bumps termed "nodules" seem to occur more frequently and severely in areas of high muscle mass (most notably the center of the stomach—the abs—and the legs). They will hurt with movement. Other side effects may include headache and fever. 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 health care provider immediately. 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 have been taking patients off Fuzeon and putting them on one of those newer drugs, Isentress. Several studies have shown good results with this strategy. Fuzeon is intended for treatment of HIV in patients who are treatment experienced. Preparing and injecting the Fuzeon can be complicated, so ask your health care provider how to do it. First, the drug needs to be dissolved with sterile water (provided in the kit), which may take 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. 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 is in the pharmacy (Selzentry, taken orally). 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. (Since those studies, however, there are now more drugs on the market, including another 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 active drugs, if possible, when changing therapy, to make it more effective. Please see package insert for more complete potential side effects and interactions.

DOCTOR

Fuzeon (enfuvirtide, known to most as T-20) was approved (injection twice daily) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2003. Fuzeon is the first drug approved in the class of antiretrovirals called "entry inhibitors." Since this class of drug stops the virus from entering the CD4 cell, they are potentially a significant step forward for HIV therapy. The drawbacks to this drug are its high cost, need for injection, and injection site reactions. Injection site reactions (especially since injections are done twice daily) are a major issue with Fuzeon. If you have ever seen or are an individual who has injected T-20—you know. The "lumps" can be horrible and the skin leathery. In general, viral control with this drug has been good and at times even when viral control wasn't the best, the patient clinically felt well. Approval of other newer, more tolerable antiretrovirals has made Fuzeon an antiretroviral saved for deep salvage when an active drug is required. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Not for the faint of heart or those squeamish over needles, and definitely no fun. Fuzeon is a twice-daily injectable drug that must go through a fairly complicated "mixing" process (reconstitution) just to get it in the needle. Then, one has to contend with rather painful injection site reactions—and it's woefully expensive. Fuzeon has the dubious reputation of being a measure of last resort, a salvage drug for the heavily treatment-experienced, but seems to increase CD4s and reduce viral loads when added to a multiple-drug regimen. If nothing else, Fuzeon can be an excellent motivator for adherence to more user-friendly treatment. —Morris Jackson

SELZENTRY

ENTRY INHIBITOR

Common Name: maraviroc (MVC, formerly UK-427,857)
Brand Name: Selzentry
Class: CCR5 antagonist (a type of entry inhibitor)
Standard dose: Available in 150 mg and 300 mg tablets. No food restrictions (take with or without food). 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 NRTIs; 600 mg twice daily if taken with Sustiva, Intelence, rifampin, and some anti-convulsant medications such as phenobarbital, phenytoin, and carbamazepine. Default to the CYP3A inhibitor dose (the PI group) when using medications from different groups (such as a PI with a NNRTI). Concurrent use of Selzentry and other medications that can either inhibit or induce liver metabolism will affect the dose of Selzentry. Your doctor or pharmacist can determine which medications will affect Selzentry.
AWP: $1,147.31/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 may include liver toxicity; an allergic reaction may happen before the liver problems. It is recommended Selzentry be stopped and your doctor contacted right away if you develop a rash, yellowing of your eyes or skin, and/or dark urine, vomiting, and upper stomach pain. Other rare side effects may include low blood pressure when standing up that could lead to dizziness or fainting, 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: Nizoral (ketoconazole), Kaletra, Norvir, Invirase, and Reyataz all increase Selzentry concentrations. Rifampin and Sustiva reduce Selzentry concentrations. Selzentry did not affect the concentrations of oral Versed (midazolam) and oral contraceptives.

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

Viral tropism refers to 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, 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). In 2007 the company reported that a switch to X4- or dual-tropic virus was transient and reversible when people went off maraviroc. In studies, a large number of patients were excluded because they did not have exclusive CCR5-tropic virus, limiting the number of patients who could truly benefit from this drug. A sub-analysis reported last year that Selzentry seems to have minimal impact on lipid levels. 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 (maraviroc) was approved (one tablet twice daily—no food restriction) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2007. This antiretroviral is the first *oral* entry inhibitor produced and is approved only for those who have failed other antiretroviral regimens. In general, this drug has been tolerated, but liver toxicity is a potential problem and liver function should be followed. Maraviroc interacts with a number of PIs and it must be dose adjusted when used with these antiretrovirals. To understand this important drug, you should have knowledge of how it works. For HIV to get into a cell (infect it) it needs to bind to two targets on the cell. Both of these targets are what we call receptors (R). One is the CD4 receptor and the other is called the chemokine receptor. While the virus must use both receptors to get into the cell, for this discussion we will only discuss the chemokine receptor. In general, virus in early infection uses the R5 chemokine receptor (and is called R5 virus) to enter the cell. The virus present in late infection uses the X4 receptor (called X4 virus). Virus in mid-disease can use either the R5 or X4 receptor (DM or dual mixed virus) for cell entry. Maraviroc blocks only the R5 receptor and entry of the R5 virus into a cell. If other virus (X4 or DM) is present, it won't be effective or it works only marginally. Hence an issue with maraviroc, you must know which virus you are dealing with (R5, X4, DM) before using the drug. The Trofile assay can give you this answer. The first version of the assay did not pick up lower levels of X4 virus, but the newer version is said to be more sensitive. Personally, I haven't found many patients (in a salvage situation) with R5 virus and use of the drug in our clinic is relatively small. Oh yeah, it is tempting to substitute maraviroc for T-20, but if the patient has an undetectable viral load, you can't determine if his/her virus is R5 (I hate that!). While this goes against current thought, I believe maraviroc will best serve our patients if used early in infection (seems obvious). Unless we have long-term tolerability data for this drug and other issues are settled, this won't happen. —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Selzentry, FDA-approved in 2007, is an oral Entry Inhibitor. Although classified as an Entry Inhibitor, this drug is technically a CCR5 antagonist, a "pre-entry inhibitor," if you will. Selzentry works to prevent HIV from binding onto the CCR5 molecule receptor outside of, and thus entering, a healthy CD4 cell. Selzentry requires an expensive test, a tropism assay, to determine if it can be prescribed. Selzentry should only be taken if one has "R5-tropic" virus, not "X4-tropic" or "dual/mixed-tropic" (CXCR4 is the other CD4+ T-cell molecule receptor). And if you have an undetectable viral load or it is less than 1,000, you don't have enough virus for a tropism assay. —Morris Jackson

ISENTRESS

Common Name: raltegravir (RAL, formerly MK-0518)
Brand Name: Isentress
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: $1,072.34 / 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 enzymes. May cause elevated levels of a muscle enzyme (creatine kinase) on blood tests. Contact your health care provider if you experience unexplained muscle pain, tenderness, or weakness. May cause hypersensitivity (allergic reaction), anemia, neutropenia, and gastritis. Increases in ALT, AST, and total bilirubin, all signs of liver toxicity, seen in around 8% of people taking Isentress. Increases were more likely in people also infected with hepatitis B or C. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; report symptoms of illness, such as shingles and TB, to health care provider.

Potential drug interactions: Isentress had 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 is advised in people taking medications that can cause muscle problems. Caution with rifampin, which reduces plasma concentrations of Isentress.

Tips: Isentress continues to be a 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 switched patients off Fuzeon and on to Isentress. Several studies showed good results with this strategy. To join a once-a-day Isentress study, consult your doctor or visit www.benchmrk.com and click on QDMRK. 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 such 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 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

Isentress (raltegravir) was approved (one tablet twice daily) for use in combination with other antiretroviral drugs in the treatment of HIV infection in 2007. It is approved only for those who have failed other antiretroviral therapy. Raltegravir is the first drug approved in a new class of antiretrovirals—integrase inhibitors. The HIV integrase enzyme inserts the virus DNA into the host DNA. An antiretroviral agent inhibiting the action of this enzyme should have great value in the treatment of HIV infection (even beyond what we know now), and health care providers are excited by the potential of this drug. While the long term adverse effects of raltegravir are not known, it currently appears to be fairly well tolerated. Reports of significant depression with the use of the drug await further verification. We have noted some patients with dizziness (we have not seen depression) with the drug, but have not verified this. Efficacy of raltegravir in HIV-infected individuals naïve to therapy has been demonstrated, but it is not yet approved for this use. Some of us haven't waited for this official approval! —Frank M. Graziano, M.D., Ph.D.

ACTIVIST

Isentress, formerly known as MK-0518, is the first FDA-approved drug in this novel class. After reverse transcription of HIV viral RNA into DNA occurs, HIV DNA integrates into a healthy CD4+ T-helper cell's nucleus, and thus its DNA. Integrase inhibitors work by blocking the viral enzyme that assists in this process. Isentress' initial indication is for the treatment-experienced with multiple drug resistance. Isentress when taken with optimized background therapy (OBT: at least one other fully active drug) has been shown to work well and side effects seem minimal. Isentress does not require Norvir boosting, quickly lowers viral load, and has relatively few drug-drug interactions. The great hope for this drug is that it will work to lessen resistance to other drug classes. But therein lies the paradox. Resistance to the integrase class can develop quickly if not combined with other active drugs. The challenge: which drugs? New and noteworthy: Isentress recently received FDA-approved review status for treatment-naïve patients. Hopefully, there will be an indication for initial therapy with treatment naïves by this summer. —Morris Jackson

INTERACTIONS

DRUG INTERACTIONS CHART

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

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

Nucleoside Reverse Transcriptase Inhibitors (also called nucleoside analogs, NRTIs, or nukes)	
Potential drug class interactions	None.
Combivir (Retrovir and Epivir)	See Epivir and zidovudine (Retrovir). Do not take zidovudine, Epivir, Epivir-HBV, Epzicom, Trizivir, Emtriva, Truvada, or Atripla while taking Combivir, since all or part of these medications are already in Combivir or have equivalent medications.
Emtriva (emtricitabine, or FTC)	No significant drug interactions. Do not take Truvada, Atripla, Epivir, Epivir-HBV, Epzicom, Combivir, or Trizivir while taking Emtriva, since they contain Emtriva or medication equivalent to it.
Epivir (lamivudine, or 3TC)	No significant drug interactions. Do not take Epivir-HBV, Epzicom, Combivir, Trizivir, Truvada, or Atripla while taking Epivir, since they contain Epivir or medication equivalent to it.
Epzicom (Epivir and Ziagen)	See Epivir and Ziagen. Do not take Combivir, Epivir, Epivir-HBV, 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 AZT)	Do not take with Combivir or Trizivir, since zidovudine is already in these medications. Amphotericin B, Benemid, Biaxin, dapsone, Depakote, doxorubicin, flucytosine, ganciclovir, hydroxyurea, interferon-alpha, Mycobutin, pentamidine, phenytoin (Dilantin and others), ribavirin, rifampin, sulfadiazine, Valcyte, and Zerit.
Trizivir (Epivir, Retrovir, and Ziagen)	See Epivir, Retrovir, and Ziagen. Do not take zidovudine (Retrovir), Epivir, Epivir-HBV, Ziagen, Emtriva, Truvada, or Atripla while taking Trizivir, since all or part of these medications are already in Trizivir or have equivalent medications.
Truvada (Viread and Emtriva)	See Emtriva and Viread. Do not take with Emtriva, Viread, Atripla, Epivir, Epivir-HBV, Combivir, Epzicom, or Trizivir, since all or part of these medications are already in Truvada or have equivalent medications.
Videx & Videx EC (didanosine, or ddI)	Alcohol, cimetidine, dapsone, ganciclovir, HIV protease inhibitors, hydroxyurea, itraconazole, ketoconazole, methadone, pentamidine, Rescriptor, Retrovir, ribavirin, Viread, and Zerit.
Viread (tenofovir)	Do not take with Truvada or Atripla, since Viread is in these medications. Hepsera, Kaletra, Norvir, Reyataz, Videx and Videx-EC.
Zerit (stavudine, or d4T)	Amphotericin B, dapsone, foscarnet, ganciclovir, pentamidine, Valcyte, Videx and Videx-EC, and zidovudine (AZT, Retrovir).
Ziagen (abacavir sulfate)	Do not take with Epzicom or Trizivir, since Ziagen is already in these medications. Alcohol.

Non-Nucleoside Reverse Transcriptase Inhibitors (also called non-nucleoside analogs, NNRTIs, or non-nukes)	
Potential drug class interactions	HIV protease inhibitors; methadone.
Intelence (etravirine, or TMC-125)	Aptivus/Norvir, Kaletra, Lexiva/Norvir, Norvir, Reyataz/Norvir, Selzentry, Sustiva, Viramune, and unboosted (without Norvir, or in rare cases, Rescriptor) PIs.
Rescriptor (delavirdine)	Agenerase, amlodipine, certain amphetamines and antiarrhythmic drugs, Biaxin, birth control pills, carbamazepine (Tegretol and others), Cialis, Crixivan, dapsone, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), felodipine, fluticasone (Advair, Flonase, Flovent), immunosuppressants, Invirase, Kaletra, Levitra, Lexiva, methadone, lovastatin, midazolam, Mycobutin, nifedipine, Norvir, phenobarbital, phenytoin (Dilantin and others), pimozide, Propulsid, quinidine, Reyataz, rifampin, simvastatin, St. John's wort, trazodone, triazolam, Viagra, Viracept, Vytorin, warfarin, and Xanax (alprazolam).
Sustiva (efavirenz)	Do not take with Atripla, since Sustiva is already in Atripla. Bepridil, Biaxin, birth control pills, carbamazepine (Tegretol and others), Crixivan, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), Invirase, itraconazole, Kaletra, Lexiva, Lipitor, methadone, midazolam, Mycobutin, Norvir, pravastatin, Reyataz, rifampin, phenobarbital, phenytoin (Dilantin and others), pravastatin, simvastatin, St. John's wort, triazolam, Vfend, and warfarin.
Viramune (nevirapine)	Biaxin, birth control pills, calcium channel blockers (Adalat, Norvasc, Procardia, and others), carbamazepine (Tegretol and others), clonazepam, Cordarone, disopyramide, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), ethosuxomide, flucanozole, HIV protease inhibitors, immunosuppressants, Kaletra, ketoconazole, lidocaine, methadone, midazolam, Mycobutin, prednisone, rifampin, St. John's wort, triazolam, and warfarin.
Dual-class Fixed Dose Combination	
Atripla (Sustiva/Truvada)	See Sustiva and Truvada (Emtriva/Viread). Do not take Sustiva, Emtriva, Truvada, Viread, Epivir, 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, and tuberculosis drugs.
Aptivus (tipranavir) (must be taken with Norvir)	Aptivus/Norvir interacts with many other drugs, so it is important to tell your health care professional all the medications you are taking. See the manufacturer package insert for the most complete list. Birth control pills, calcium channel blockers (Adalat, Norvasc, Procardia, and others), carbamazepine (Tegretol and others), Cialis, Crestor, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), disulfirum (Antabuse), Flagyl, fluconazole, fluticasone (Advair, Flonase, Flovent), other HIV protease inhibitors, immunosuppressants, itraconazole, ketoconazole, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam (oral), Mycobutin, Paxil, phenobarbital, phenytoin (Dilantin and others), pimozide, pravastatin, quinidine, rifampin, Rythmol, simvastatin, St. John's wort, Tambocor, trazodone, triazolam, valproic acid, Viagra, vitamin E, Vfend, Videx, warfarin, Ziagen, zidovudine, and Zoloft.
Crixivan (indinavir sulfate)	Birth control pills, calcium channel blockers (Adalat, Norvasc, Procardia, and others), carbamazepine (Tegretol and others), Cialis, coffee or alcohol (and other diuretics), Cordarone, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), fluticasone (Advair, Flonase, Flovent), garlic supplements, grapefruit juice, itraconazole, immunosuppressants, ketoconazole, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam, Mycobutin, phenytoin (Dilantin and others), phenobarbitol, pimozide, pravastatin, Rescriptor, Reyataz, rifampin, Rythmol, simvastatin, St. John's wort, Sustiva, Tambocor, trazodone, triazolam, warfarin, Viagra, Viramune, and Vytorin. See drug page for more interactions.

Protease Inhibitors (PIs) Continued	
Invirase (saquinavir) (must be taken with Norvir)	Aptivus/Norvir, Biaxin, birth control pills, Cialis, Cordarone, Crestol, Crixivan, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), dapsone, fluticasone (Advair, Flonase, Flovent), garlic supplements, Kaletra, Lanoxin, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam, Mycobutin, Nizoral, Norvir, pimozide, pravastatin, quindine, rifampin, Rescriptor, Reyataz, Rythmol, simvastatin, St. John's wort, Sporanox, Sustiva, Tambocor, trazodone, triazolam, Viracept, Viagra, Viramune, and Vytorin.
Kaletra (lopinavir/ritonavir)	Biaxin, birth control pills, carbamazepine (Tegretol and others), certain calcium channel blockers, Cialis, Cordarone, digoxin, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), Flagyl, fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, itraconazole, Lescol, Levitra, Lexiva, Lipitor, lovastatin, Mepron, methadone, midazolam, Mycobutin, nifedipine, pimozide, phenobarbital, phenytoin (Dilantin and others), pravastatin, rifampin, Retrovir, Rythmol, simvastatin, St. John's wort, steroids (especially Decadron), Sustiva, trazodone, triazolam, Uroxatral, Viagra, Videx, Viramune, Vytorin, warfarin, and Ziagen.
Lexiva (fos-amprenavir calcium)	Birth control pills, certain calcium channel blockers, Cialis, Crestor, disulfirum (Antabuse), ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), Flagyl, fluticasone (Advair, Flonase, Flovent), Kaletra, Lipitor, Lescol, Levitra, lovastatin, pimozide, pravastatin, Rescriptor, Rythmol, methadone, midazolam, Mycobutin, rifampin, simvastatin, St. John's wort, steroids (especially Decadron), Sustiva, Tambocor, trazodone, triazolam, Viagra, and warfarin.
Norvir (ritonavir)	See the manufacturer package insert for the most complete list. Alcohol, Biaxin, birth control pills, Cialis, Cordarone, disulfiram (Antabuse), Ecstasy, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), Flagyl, fluticasone (Advair, Flonase, Flovent), garlic supplements, GHB, immunosuppressants, Lescol, Levitra, Lipitor, lovastatin, midazolam, pimozide, pravastatin, rifampin, Rythmol, simvastatin, St. John's wort, Tambocor, tobacco, trazodone, triazolam, Uroxatral, and Viagra.
Prezista (darunavir)	Altoprev, Advicor, Biaxin, birth control pills, calcium channel blockers (Norvasc, Procardia, and others), carbamazepine, Cialis, Cisapride, Crestor, ergot alkaloids (Cafergot, D.H.E. 45, Ergomar, ergonovine, methylergonovine, Migranal), fluticasone (Advair, Flonase, and Flovent), immunosuppressants, Invirase, itraconazole, Kaletra, ketoconazole, Levitra, Lipitor, lovastatin, methadone, Mevacor, midazolam (oral), nifedipine, Paxil, pimozide, phenobarbital, phenytoin, pravastatin, rifabutin, rifampin, Simcor, simvastatin, St. John's wort, trazodone, triazolam, Vfend, Viagra, Vytorin, warfarin, and Zoloft.
Reyataz (atazanavir sulfate)	Antacids (including Axid, Rolaids, Tums, Mylanta, Pepcid, and Zantac), bepridil, birth control pills, calcium channel blockers (Adalat, Norvasc, Procardia, and others), Cialis, Crixivan, Camptosar, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, itraconazole, ketoconazole, Lescol, Levitra, lidocaine, Lipitor, lovastatin, midazolam (oral), Mylanta, phenytoin (Dilantin and others), pimozide, pravastatin, proton-pump inhibitors (Aciphex, Nexium, Prevacid, Prilosec-OTC), quinidine, rifabutin, rifampin, simvastatin, St. John's wort, Sustiva, triazolam, trazodone, Vfend, Viagra, Videx and Videx-EC, Viread, Vytorin, and warfarin. See drug page for more.
Viracept (nelfinavir)	Birth control pills, carbamazepine (Tegretol and others), Cialis, Cordarone, Crixivan, ergot alkaloids (Cafergot, D.H.E. 45, Methergine, Wigraine), fluticasone (Advair, Flonase, Flovent), garlic supplements, Invirase, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam, Mycobutin, phenobarbital, phenytoin (Dilantin and others), pravastatin, Prilosec-OTC, rifampin, simvastatin, St. John's wort, triazolam, trazodone, Viagra and Vytorin.
Entry Inhibitors	
Fuzeon (enfuvirtide, or T-20)	None found to be clinically significant.
Selzentry (maraviroc)	Invirase, Kaletra, ketoconazole, Norvir, Reyataz, rifampin, and Sustiva.
Integrase Inhibitor	
Isentress (raltegravir)	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 Paul Djuricich, R.Ph., 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 health care providers, including your pharmacist, since small reactions may become serious. There may also be management techniques for the side effect. Visit http://www.acria.org/index.php?q=publications/educational-booklets/side-effects.

Nucleoside Reverse Transcriptase Inhibitors (also called nucleoside analogs, NRTIs, or nukes)	
Potential drug class side effects	Pancreatitis (inflammation of the pancreas), enlarged, fatty liver, and lactic acidosis.
Combivir (Retrovir and Epivir)	See Epivir and Retrovir.
Emtriva (emtricitabine, or FTC)	A very tolerable drug, but side effects may include headache, diarrhea, nausea and rash. Darkening of the skin on the palms and the soles of the feet has also been reported.
Epivir (lamivudine, or 3TC)	A very tolerable drug, but side effects may include headache, nausea, vomiting, diarrhea, fever, fatigue, hair loss, insomnia, malaise (general ill feeling), nasal symptoms, cough, peripheral neuropathy, low white blood cell count, anemia, and pancreatitis.
Epzicom (Epivir and Ziagen)	See Epivir and Ziagen.
Retrovir (zidovudine, or AZT)	Headaches, fever, chills, muscle soreness and/or damage, fatigue, nausea, lipodystrophy, fingernail discoloration, anemia, and neutropenia (low white blood cell count).
Trizivir (Epivir, Retrovir, and Ziagen)	See Epivir, Retrovir, and Ziagen.
Truvada (Viread and Emtriva)	See Viread and Emtriva. Abdominal distension/pain.
Videx & Videx EC (didanosine, or ddI)	Peripheral neuropathy, upset stomach, diarrhea, headache, pancreatitis (inflammation of the pancreas), eye changes and optic neuritis, increased uric acid levels, insomnia, and body fat redistribution.
Viread (tenofovir)	Overall fairly well tolerated; however, side effects may include nausea, diarrhea, vomiting, flatulence (gas), bone changes, kidney toxicities, and low blood phosphate.
Zerit (stavudine, or d4T)	Peripheral neuropathy, facial wasting, mitochondrial toxicities, lipodystrophy, headache, chills/fever, malaise, insomnia, anxiety, depression, rash, upset stomach, diarrhea, abdominal pain, and blood lipid increases. Peripheral neuropathy noted in children.
Ziagen (abacavir sulfate)	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 drug class side effects	Rash.
Intelence (etravirine, or TMC-125)	Rash, diarrhea, nausea, and headache.
Rescriptor (delavirdine)	Headache, nausea, vomiting, diarrhea, fatigue, elevated liver enzymes, itchy skin or rash, and body fat accumulation or redistribution.
Sustiva (efavirenz)	Central nervous system (CNS) and psychiatric symptoms. Rash, nausea, vomiting, diarrhea, fever, insomnia, and increases in triglycerides, good cholesterol (HDL), and liver enzymes. False positive tests for marijuana. Birth defects.
Viramune (nevirapine)	Headache, nausea, vomiting, fever, rash, Stevens-Johnson syndrome, increase in liver enzymes, liver damage, and drug-induced hepatitis.

SIDE EFFECTS

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, and Immune Reconstitution Inflammatory Syndrome (IRIS).
Protease Inhibitors (PIs)	
Potential drug 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) (must be taken with Norvir)	Gastrointestinal-related—mild diarrhea, nausea, vomiting, and abdominal pain. Headaches, fever, fatigue, dry mouth, rash (including sensitivity to sun), dizziness, liver toxicity, and bleeding in the brain. Aptivus has a "sulfa" component, and should be used with caution in patients with allergies to sulfa drugs. Also see Norvir.
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, liver toxicity, kidney stones, increased bilirubin, itchy/dry skin, ingrown toenails, and hair loss.
Invirase (saquinavir) (must be taken with Norvir)	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 results. 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, alcohol intolerance, liver problems, increased muscle enzymes, and uric acid.
Prezista (darunavir)	Rash, diarrhea, nausea, headache, and common cold. Prezista contains a "sulfa" component 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 test results, including elevated levels of unconjugated bilirubin.
Viracept (nelfinavir)	Diarrhea, stomach discomfort, nausea, gas, weakness, and rash.
Entry Inhibitors	
Fuzeon (enfuvirtide, or 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)	Diarrhea, nausea, vomiting, headache, fever, abdominal pain, fatigue, weakness, dizziness, and lipodystrophy.

CURRENT DHHS TREATMENT GUIDELINES FOR FIRST TIME THERAPY

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 (once daily) Fosamprenavir + ritonavir (twice daily) Darunavir + ritonavir (once daily) Lopinavir/ritonavir (once or twice daily)	Tenofovir/emtricitabine [3]
Alternative (alphabetical order)	Nevirapine [2]	Atazanavir [4] (unboosted, once daily) Fosamprenavir (unboosted, twice daily) Fosamprenavir + ritonavir (once daily) Saquinavir + ritonavir (twice daily)	Abacavir/lamivudine [3] Didanosine + lamivudine [3] Zidovudine/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. November 3, 2008; 1–136. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed January 21, 2009; page 38, Table 6.*

GUIDELINES

PA ONLINE

JOIN US ON MYSPACE AT
WWW.MYSPACE.COM/POSITIVELYAWARE
ADD US AS YOUR FRIEND AND
CHECK OUT OUR COMMUNITY PARTNERS.

THE 2008 PA INDEX OF ARTICLES IS NOW AVAILABLE ONLINE AT WWW.POSITIVELYAWARE.COM.

Join in on our online Community Forum

The online Community Forum allows users to post and discuss topics of interest to them, in a safe and non-judgmental environment with other individuals who share similar interests. It features several exclusive chat rooms, including The Women's Forum, The Men's Locker Room, SmartSex Talk, and the newly added Drug Guide section (where you can share your experience with different drugs, side effects, and drug interactions).

The staff of TPAN and PA regularly monitor the activity of the various chat rooms within the Community Forum, and are available to answer any specific questions users may have, as well as to provide technical support.

You can also view exclusive online newsbriefs at www.positivelyaware.com, and stay in the know by subscribing to our bi-weekly PA E-mail Update.

PA ONLINE POLL

MARCH / APRIL 2009 POLL QUESTION

This month's question:

How long have you been living with HIV?

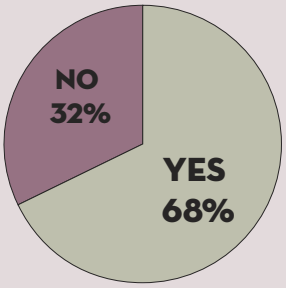
VOTE AT WWW.POSITIVELYAWARE.COM

STAY CURRENT WITH PA E-MAIL UPDATES

Sign-up today for our *Positively Aware* e-mail newsletter and receive regular updates on HIV treatment news and information.

Visit www.tpan.com or www.positivelyaware.com and click on Subscribe. Once you receive a confirmation e-mail, you can update your TPAN profile to include "*Positively Aware* Updates."

NOVEMBER / DECEMBER POLL RESULTS

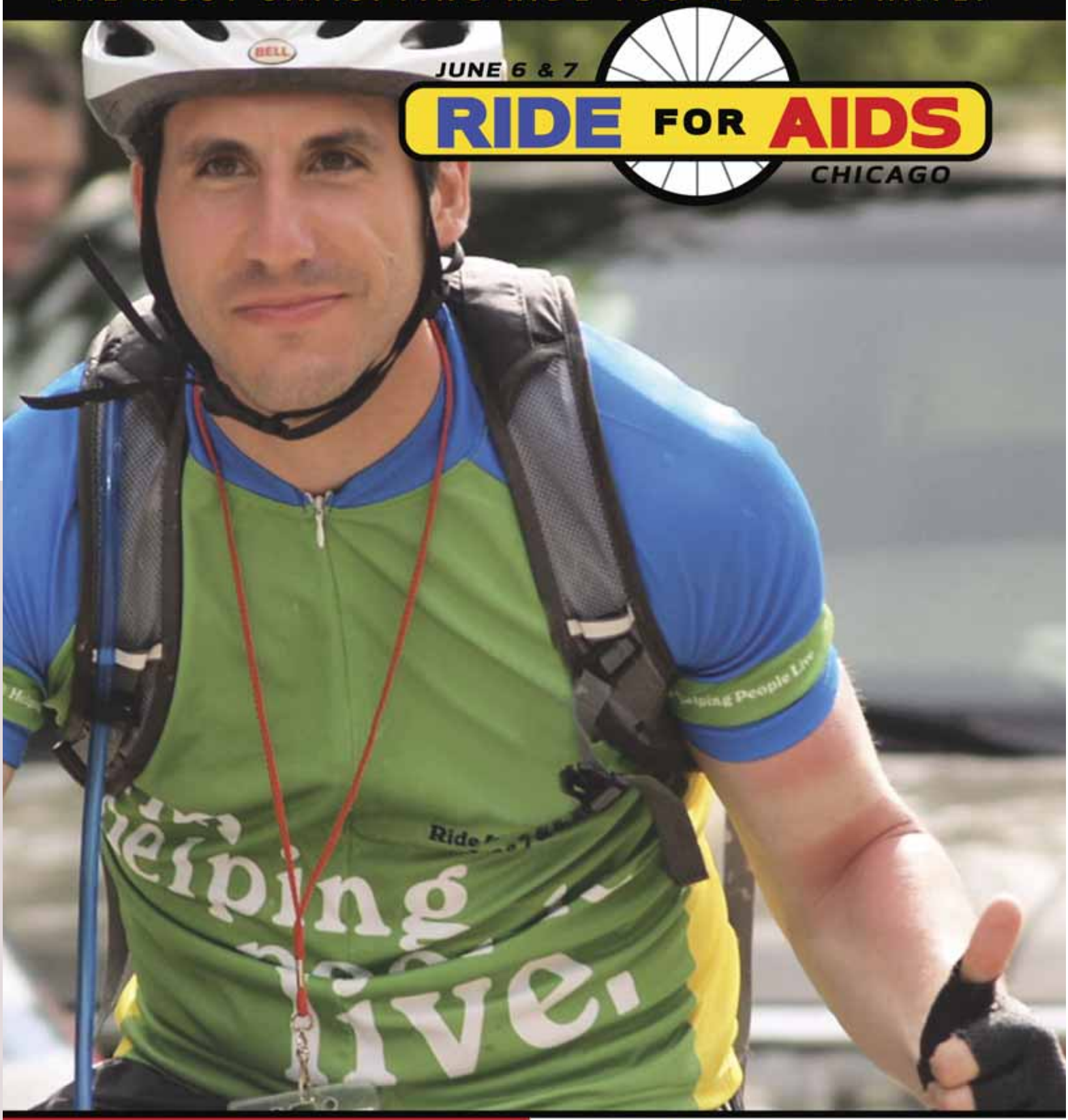


Have you ever had to stop or switch medications due to intolerable side effects?

COMMENTS

- Crixivan, because of kidney stones.
- Almost all of them—30 years of various medication has taken a major toll on my kidneys, my liver, and, god knows, my colon, let alone my spirit. Life with HIV/AIDS has been a lesson I never wanted.
- Diarrhea from hell and Imodium didn't help.
- Sustiva is very strong to some people. I am a small female, and only a few pounds over the children's dosage. My health care provider worked with me, now I am on 300 mg twice a day, and doing great.
- Too many times, each time suffering though new side effects.
- I have always followed my doctor's advice and suffered through the side effects. There were times he did mention that if the side effects did get too terrible to take, he would change the medication. He also mentioned that it is possible the new medications may have worse side effects. I trust my doctor when he said it was best to stay on the medications I was taking, since my numbers were improving. After all, while it has been 15 years since my diagnosis, I am still here.

THE MOST SATISFYING RIDE YOU'LL EVER HAVE.



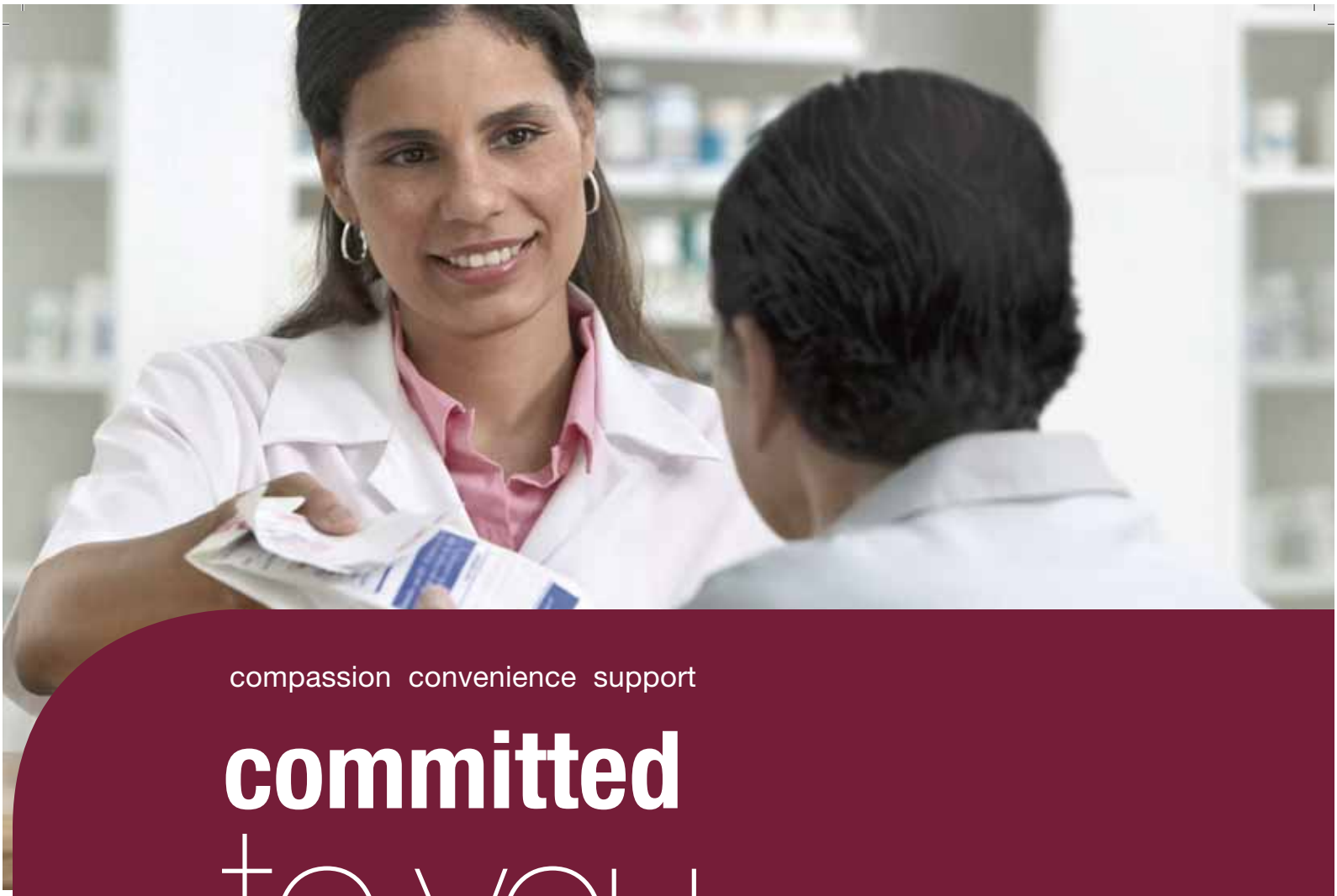
100% OF PLEDGES RETURNED TO BENEFICIARIES

REGISTER TODAY!
WWW.RIDEFORAIDS.ORG
773.989.9400

TEST POSITIVE AWARE NETWORK

with community partner

Better Existence with HIV



compassion convenience support

committed to you.

Walgreens
The Pharmacy America Trusts • Since 1901®

HIV.walgreens.com