THE ROAD TO SUCCESS

FINANCIAL ASSISTANCE
FOR YOUR MEDS

TRENDS IN HIV TREATMENT AND CARE
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This page intentionally left blank.
You can spend your valuable time each week surfing the Internet for the latest results of HIV research and clinical trials, FDA approvals or changes to drug labels, reports on state and federal funding, and even which celebrity has donated time, talent, energy, or money to the fight against AIDS—or you can subscribe to **POSITIVELY AWARE**’s weekly **E-NEWS**.

It’s easy! Just go to [www.positivelyaware.com](http://www.positivelyaware.com), click on “Subscribe” and enter your email address.
Life with HIV can be an odd journey. You’ve been uprooted from the life you’ve known, and suddenly plopped down in the midst of a new set of circumstances. How to convey that on a magazine cover? As art director of PA, the answer was obvious: The Wizard of Oz.

It’s all about the yellow brick road. Look closely at our cover; you’ll see that Dorothy and friends are on a road made up of HIV meds. Creating an optimistic image that links HIV treatment to a better life with HIV is the continuation of a theme begun with last year’s Drug Guide, in which our Singing in the Rain-inspired cover featured pills as rain drops.

Any journey can seem daunting if traveling solo. But whatever your situation as someone who is HIV-positive, you’re not alone on this journey, and this issue of POSITIVELY AWARE, our 16th annual HIV Drug Guide, is your roadmap. —Rick Guasco
INSIDE

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The 16th Annual HIV Drug Guide
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AND OTHER RESOURCES, GO TO HIV.WALGREENS.COM/CHART
ONLINE

ONLY ON POSITIVELYAWARE.COM

Class distinction
An explanation of the different classes of HIV drugs.
www.positivelyaware.com/2012/12_02/class.shtml

DHHS treatment guidelines
Recommended treatment guidelines from the Department of Health and Human Services.
www.positivelyaware.com/2012/12_02/guidelines.shtml

DIGITAL EDITION
Read the print version of POSITIVELY AWARE on your computer.
http://issuu.com/positivelyaware

SCAN THIS QR CODE
WITH YOUR iPHONE OR OTHER SMARTPHONE TO ACCESS THE 16TH ANNUAL HIV DRUG GUIDE, OR GO TO positivelyaware.com/drugguide

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FOLLOW US ON FACEBOOK AND ON TWITTER (@POSWARE)

MARCH+APRIL 2012 7
Ms. Saltmarsh, I thank you and POSITIVELY AWARE for such a well written article that gives another voice to the work we are doing. It is bittersweet to see that what we are doing is not only bringing awareness to health disparities, but also to the phobias and stigmas that are still prevalent within today's society. Our hope is that this will help bring awareness to the need for providing quality health care services not only to MSM and Muslims, but to all who are in need.

—Labelsnj33
VIA POSITIVELYAWARE.COM

Unfortunately, I see those who (claim to) practice Islam as being largely inflexible. Some of the leaders within Islamic communities are downright superstitious and backwards.

For example, I’ve heard the Sodom and Gomorrah story being taught to youngsters as an example of a city that was the lowest place on earth, because God considers homosexuality to be the lowest thing one can do. This is not only ridiculous in terms of logic, but entirely inaccurate. By scriptural accounts, the city was destroyed because people were inhospitable, uncaring, and because there weren’t any good people in it. (Obviously there were hetero people there, or the city wouldn’t have survived for long.) Nevertheless, this is the trash that’s being taught.

Since at least a couple of kids in each classroom will grow up to be gay, I find it incredibly cruel to promote such perspectives—and yet the abuse continues, both within Islamic communities and in Christian institutions. (Mormons are about as blind as Muslims in this regard.)

With such heavy indoctrinations from such an early age, I don’t see religious tolerance coming any time soon.

—spectrewriter
VIA POSITIVELYAWARE.COM

Another reader responds to spectrewriter’s comment:

We’ve heard the same garbage from “Christians” like Fred Phelps and yet we all know Christians who are very accepting of LGBT people. Queer Muslims and our LGBT-friendly Muslim friends are opening a dialogue within our ummah that is admittedly about 40 years behind our Christian and Jewish brothers and sisters, but with their examples to learn from, we can catch up quickly. I’ve been happily surprised at how widely I’ve been accepted as a gay Muslim by straight Muslim friends. I realize that is a small pocket within a largely homophobic milieu, but there is discernable progress and enough historical precedent to show that prejudice will melt away on both sides.

—Jackfertig
VIA POSITIVELYAWARE.COM

Keeper of the faith
Thanks, Jeff, for continuing to sound the horn for all of us.

—Greg Knepper
VIA POSITIVELYAWARE.COM

Smart food
I wanted to compliment POSITIVELY AWARE for this very important issue out of the closet, so to speak, and into the streets. Having known the brothers in this article for several years now, I am very happy to see them take the steps to bring enlightenment to the MSM/HIV community and that being Muslim does not keep them from facing discrimination based on their sexual orientation and their status. Looking forward to working with these brothers in the near future.

—Imam Daayiee Abdullah
MASJID AN-NURAL ISSLAAH; WASHINGTON, DC

Discovering ‘Hidden People’

Great article, Ms. Saltmarsh, and it helps push this very important issue out of the closet, so to speak, and into the streets. Having known the brothers in this article for several years now, I am very happy to see them take the steps to bring enlightenment to the MSM/HIV community and that being Muslim does not keep them from facing discrimination based on their sexual orientation and their status. Looking forward to working with these brothers in the near future.

—Imam Daayiee Abdullah
MASJID AN-NURAL ISSLAAH; WASHINGTON, DC

IN BOX

Most talked about stories
IN THE JANUARY+FEBRUARY ISSUE

OF COMPASSION AND HOPE
THE HIDDEN PEOPLE
KEEPING THE FAITH

8 MARCH+APRIL 2012
AWARE for Nelson Vergel’s superb article, “Outsmarting HIV With Healthy Eating.” This was without a doubt the most practical, easy-to-understand article I’ve seen on this topic to date. As an HIV provider I am frequently asked for nutrition advice by my patients. I thought I was fairly informed, but this filled in many of my gaps in real-world practical advice. I would encourage all HIV patients (and their loved ones, support network, and providers) to read his article.

—Chad Zawitz, MD

Of compassion and hope
Great job with the January+February issue. I loved the range of articles about faith-based responses to the AIDS crisis, especially the African American churches and Islam. I wrote my Doctor of Ministry dissertation on a Hindu interfaith AIDS ministry, The River Fund, out of Sebastian, Florida (www.riverfund.org), with outreach in New York City and Atlanta, as well as an orphanage in Uganda. The LIFE program that TPAN offers is run by Shanti, as you may know. Shanti started as an HIV/AIDS hospice/service agency in San Francisco with a non-sectarian Eastern religious philosophy about loving compassion and care.

In faith and fellowship.
—Rev. Vilius Rudra Dundzila, PhD, DMin

Working together
I have followed TPAN and POSITIVELY AWARE for a number of years. Your magazine is one of the most consistently informative, and I continue to enjoy reading it.

Our program, Yoga of the Breath for People Living with HIV (www.hiv.artofliving.org), is one that changes the quality of people’s lives—from the newly diagnosed to those who have been living with HIV and on ART for years. The changes are not only in the mental/emotional sphere, but physiological as well.

Perhaps we can work together to serve the HIV community.

Continue to do the excellent work that you do.
—Francesca A. Jackson, DC

YOGA OF THE BREATH FOR PEOPLE LIVING WITH HIV

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A model, photographer, or author’s HIV status should not be assumed based on their appearance in POSITIVELY AWARE, association with TPAN, or contributions to this journal.

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FOR THE FIRST TIME IN THE HISTORY OF HIV, an “AIDS-free generation” is emerging as a viable possibility. However, the HIV/AIDS funding that would make it a reality has become more and more precarious.

THIS YEAR MARKS TPAN’S 25TH ANNIVERSARY—no matter the challenges we face, our commitment is steadfast and we are filled with optimism that is rooted in experience and fueled by our achievements thus far.

IN 2011, TPAN SERVED A RECORD NUMBER OF clients and implemented new programs, including Visual Arts and L.I.F.E. (Learning Immune Function Enhancement). However, many of our programs are un- or under-funded. In order to continue to provide the services and programs that meet the changing needs of our clients, your support means more than ever—we couldn’t do it without you!

Go to www.tpan.com for more information.
TPAN is the proud publisher of POSITIVELY AWARE.
The road to success

JUST LIKE MOST JOURNEYS IN LIFE, THE ROAD TO success in treating HIV is often paved with failure, false starts, and detours.

Recently I decided to change my entire HIV medication regimen, even though I had been on the same successful regimen for over seven years. I had been thinking about it, and discussing it with my doctor, for several years before finally arriving at the decision to switch my meds.

I had been, and still am, on a unique combination of a boosted protease inhibitor, along with a non-nuke. I had developed resistance to all of the nukes years ago as a result of sequential monotherapy, replacing one failing medication with only one other new medication, something you would not do today. My doctor told me that he would never make the same treatment decisions now as he did then, but we just didn’t know any better at the time. Plus, our options were limited to those medications that were then available.

I eventually settled in with a treatment regimen that worked, and worked well. It was a powerful combination—I maintained an undetectable viral load and high CD4 count for seven years—so needless to say, I had some trepidation about switching. You know the old saying, if it ain’t broke, don’t fix it.

But along with those great numbers came some other numbers that weren’t so great—namely, high LDL cholesterol (the bad kind), low HDL cholesterol (the good kind), high blood pressure (which is thankfully being controlled by medication), and more recently, high triglycerides. So now, a new medication is being added for that.

Of course, we can never be sure if all of those conditions are a direct result of the meds, some of them could be from the HIV, or just getting older. But what I haven’t mentioned are the side effects that I had put up with for all those years. Diarrhea, GI upset, insomnia, fatigue. And that’s just for starters. However, I learned to live with the side effects. I found ways to try to minimize them, and ultimately grew to accept the fact that it was the price I had to pay for staying alive.

So as others around me began switching to or starting on some of the newer medications that were more tolerable and much easier to take, I wondered to myself, should I change, too? I didn’t want to switch simply for the sake of switching. And there was the possibility, however remote, that the virus could “break through” and come roaring back. Did I even want to take that chance?

Or did I want to stick with what worked, what I knew—what was comfortable? I know myself well enough to know that my tendency is to stick with known, comfortable quantities, but I was also ready to improve my quality of life.

I knew one thing for sure, I felt very strongly about the need to preserve certain classes of drugs that I have never used, namely integrase inhibitors, and, to a lesser extent, entry inhibitors. I realize that I am extremely fortunate to even have this option, as some of my friends are out of options and don’t have that luxury.

So my strategy was first, I would continue to preserve those drug classes for future use, if and when they are needed. Next, based on results from past resistance tests and my treatment history, I would switch out my current boosted protease inhibitor for one that was more tolerable, that I could take once a day instead of twice, and which required less Norvir for boosting. Lastly, if I remained undetectable after the first switch, I would then switch out the older non-nuke for the newer one, which would hopefully result in fewer side effects.

Well, I’m happy to say that my switch was a complete success—at least, so far. And the best thing is? I am sleeping better now than I have for years.

What’s the moral of this story, you ask? I think one of the most interesting and telling points of my own personal journey is that, as someone who follows treatment developments and research more closely than most people would care to, it still took me years to finally decide to switch. I put up with intolerable side effects, partly out of fear, but mostly because I had gotten, well, comfortable. In this case, I learned that sometimes choosing to go beyond my “comfort zone” is a good thing and I’m glad I did.

Everyone’s story is different, and what works for one person may not work for another. You and your body are unique. So are your treatment choices and decisions. I’m not advocating that if you have side effects or other issues with your current regimen that you should definitely change your treatment. But I encourage you to talk to your doctor, do your homework (by reading this HIV Drug Guide!), and think about what you want most out of life, and our meds’, fullest potential.

Take care of yourself, and each other.
HIV-RELATED EXCESS BELLY FAT.

YOU’VE WORKED TO CONTROL YOUR HIV. NOW, TIME TO WORK ON YOUR

Important Risk Information

Do not use EGRIFTA® if you:

• Have pituitary gland tumor, pituitary gland surgery, or other problems related to your pituitary gland
• Have or have had a history of active cancer (either newly diagnosed or recurrent)
• Are allergic to tesamorelin or any of the ingredients in EGRIFTA®, including mannitol or sterile water
• Are pregnant or become pregnant

Before using EGRIFTA®, tell your healthcare provider if you:

• Have or have had cancer
• Have diabetes
• Are breastfeeding or plan to breastfeed
• Have kidney or liver problems
• Have any other medical condition
• Take prescription or non-prescription medicines, vitamins, or herbal supplements

EGRIFTA® may cause serious side effects, including:

• Serious allergic reaction. Stop using EGRIFTA® and get emergency help right away if you have any of the following symptoms: rash over your body, hives, swelling of your face or throat, shortness of breath or trouble breathing, fast heartbeat, feeling of faintness or fainting
• Swelling (fluid retention). EGRIFTA® can cause swelling in some parts of your body. Call your healthcare provider if you have an increase in joint pain, or pain or numbness in your hands or wrist (carpal tunnel syndrome)
• Increase in glucose (blood sugar) intolerance and diabetes
• Injection-site reactions, such as redness, itching, pain, irritation, bleeding, rash, and swelling. Change (rotate) your injection site to help lower your risk for injection-site reactions

The most common side effects of EGRIFTA® include:

• Joint pain
• Numbness and pricking
• Pain in legs and arms
• Nausea
• Swelling in your legs
• Vomiting
• Muscle soreness
• Rash
• Tingling
• Itching

EGRIFTA® will NOT cure HIV or lower your chance of passing HIV to others.

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 Consumer Brief Summary of EGRIFTA® on following page.

Ask your healthcare provider if EGRIFTA®, the first and only FDA-approved medicine for HIV-related excess belly fat, may be right for you.

For more information, visit www.egrifta.com or call the AXIS Center at 1-877-714-AXIS (2947).
YOU’VE WORKED TO CONTROL YOUR HIV. NOW, TIME TO WORK ON YOUR HIV-RELATED EXCESS BELLY FAT.

In two separate clinical trials of HIV-infected people with lipodystrophy, each lasting 6 months, EGRIFTA® reduced HIV-related excess belly fat by an average of 18% in the first trial, and 14% in the second trial. This reduction in excess belly fat resulted in an approximate 1-inch reduction in waist size. Individual results may vary. On average, patients on EGRIFTA® did not lose weight.

Like HIV, HIV-related excess belly fat is a chronic condition. In clinical studies:
- People who used EGRIFTA® continuously for 1 year maintained their results over this time period
- People who stopped taking EGRIFTA® after 6 months had their HIV-related excess belly fat come back

EGRIFTA® is believed to work with your own body to produce natural growth hormone to reduce your excess belly fat.

**Indication:**
EGRIFTA® is a daily injectable prescription medicine to reduce the excess abdominal fat in HIV-infected patients with lipodystrophy.

**Limitations of use:**
- The impact and safety of EGRIFTA® on cardiovascular health has not been studied
- EGRIFTA® is not indicated for weight-loss management
- It’s not known whether taking EGRIFTA® helps improve compliance with antiretroviral medications
- EGRIFTA® is not recommended to be used in children

**Important Risk Information**
**Do not use EGRIFTA® if you:**
- Have pituitary gland tumor, pituitary gland surgery, or other problems related to your pituitary gland
- Have or have had a history of active cancer (either newly diagnosed or recurrent)
- Are allergic to tesamorelin or any of the ingredients in EGRIFTA®, including mannitol or sterile water
- Are pregnant or become pregnant

**Before using EGRIFTA®, tell your healthcare provider if you:**
- Have or have had cancer
- Have diabetes
- Are breastfeeding or plan to breastfeed
- Have kidney or liver problems
- Have any other medical condition
- Take prescription or non-prescription medicines, vitamins, or herbal supplements

**EGRIFTA® may cause serious side effects, including:**
- Serious allergic reaction. Stop using EGRIFTA® and get emergency help right away if you have any of the following symptoms: rash over your body, hives, swelling of your face or throat, shortness of breath or trouble breathing, fast heartbeat, feeling of faintness or fainting
- Swelling (fluid retention). EGRIFTA® can cause swelling in some parts of your body. Call your healthcare provider if you have an increase in joint pain, or pain or numbness in your hands or wrist (carpal tunnel syndrome)
- Increase in glucose (blood sugar) intolerance and diabetes

**The most common side effects of EGRIFTA® include:**
- Joint pain
- Numbness and pricking
- Pain in legs and arms
- Nausea
- Swelling in your legs
- Vomiting
- Muscle soreness
- Rash
- Tingling
- Itching

EGRIFTA® will NOT cure HIV or lower your chance of passing HIV to others.

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

*Please see Consumer Brief Summary of EGRIFTA® on following page.*

**Ask your healthcare provider if EGRIFTA®, the first and only FDA-approved medicine for HIV-related excess belly fat, may be right for you.**

For more information, visit [www.egrifta.com](http://www.egrifta.com) or call the **AXIS Center at 1-877-714-AXIS (2947).**
Consumer Brief Summary for EGRIFTA® (tesamorelin for injection)

EGRIFTA® (eh-GRIF-tuh) (tesamorelin for injection) for subcutaneous use

Read the Patient Information that comes with EGRIFTA® before you start to take it and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is EGRIFTA®?
• EGRIFTA® is an injectable prescription medicine to reduce the excess in abdominal fat in HIV-infected patients with lipodystrophy. EGRIFTA® contains a growth hormone-releasing factor (GRF)
• The impact and safety of EGRIFTA® on cardiovascular health has not been studied
• EGRIFTA® is not indicated for weight-loss management
• It is not known whether taking EGRIFTA® helps improve compliance with antiretroviral medications
• It is not known if EGRIFTA® is safe and effective in children. EGRIFTA® is not recommended to be used in children

Who should not use EGRIFTA®?
Do not use EGRIFTA® if you:
• have pituitary gland tumor, pituitary gland surgery, or other problems related to your pituitary gland
• have or have had a history of active cancer (either newly diagnosed or recurrent)
• are allergic to tesamorelin or any of the ingredients in EGRIFTA®. See the end of this leaflet for a complete list of ingredients in EGRIFTA®
• are pregnant or become pregnant. If you become pregnant, stop using EGRIFTA® and talk with your healthcare provider. See “What should I tell my healthcare provider before using EGRIFTA®?”

What should I tell my healthcare provider before using EGRIFTA®?
Before using EGRIFTA®, tell your healthcare provider if you:
• have or have had cancer
• have diabetes
• are breastfeeding or plan to breastfeed. It is not known if EGRIFTA® passes into your breast milk. The Centers for Disease Control and Prevention (CDC) recommends that HIV-infected mothers not breastfeed to avoid the risk of passing HIV infection to your baby. Talk with your healthcare provider about the best way to feed your baby if you are taking EGRIFTA®
• have kidney or liver problems
• have any other medical condition

Tell your healthcare provider about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. EGRIFTA® may affect the way other medicines work, and other medicines may affect how EGRIFTA® works. Know the medicines you take. Keep a list with you to show your healthcare provider and pharmacist when you get a new medicine.

How should I use EGRIFTA®?
• Read the detailed “Instructions for Use” that comes with EGRIFTA® before you start using EGRIFTA®. Your healthcare provider will show you how to inject EGRIFTA®
• Use EGRIFTA® exactly as prescribed by your healthcare provider
• Inject EGRIFTA® under the skin (subcutaneously) of your stomach area (abdomen)
• Change (rotate) the injection site on your stomach area (abdomen) with each dose. Do not inject EGRIFTA® into scar tissue, bruises, or your navel
• Do not share needles or syringes with other people. Sharing of needles can result in the transmission of infectious diseases, such as HIV

What are the possible side effects of EGRIFTA®?
EGRIFTA® may cause serious side effects including:
• Serious allergic reaction. Some people taking EGRIFTA® may have an allergic reaction. Stop using EGRIFTA® and get emergency help right away if you have any of the following symptoms:
  – a rash over your body
  – hives
  – swelling of your face or throat
  – shortness of breath or trouble breathing
  – fast heartbeat
  – feeling of faintness or fainting
• Swelling (fluid retention). EGRIFTA® can cause swelling in some parts of your body. Call your healthcare provider if you have an increase in joint pain, or pain or numbness in your hands or wrist (carpal tunnel syndrome)
• Increase in glucose (blood sugar) intolerance and diabetes. Your healthcare provider will measure your blood sugar periodically
• Injection-site reactions. Change (rotate) your injection site to help lower your risk for injection-site reactions. Call your healthcare provider for medical advice if you have the following symptoms around the area of the injection site:
  – redness
  – itching
  – pain
  – swelling
  – irritation
• The most common side effects of EGRIFTA® include:
  – joint pain
  – pain in legs and arms
  – swelling in your legs
  – muscle soreness
  – tingling, numbness, and pricking

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of EGRIFTA®. For more information, ask your healthcare provider or pharmacist.

Keep EGRIFTA® and all medicines out of the reach of children.

General information about the safe and effective use of EGRIFTA®:
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use EGRIFTA® for a condition for which it was not prescribed.

Do not give EGRIFTA® to other people, even if they have the same symptoms you have. It may harm them.
Do not share your EGRIFTA® syringe with another person, even if the needle is changed.
Do not share your EGRIFTA® needles with another person.

This Patient Information leaflet summarizes the most important information about EGRIFTA®. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about EGRIFTA® that is written for healthcare professionals.

For more information about EGRIFTA®, go to www.EGRIFTA.com or contact the AXIS Center toll-free at 1-877-714-2947.

What are the ingredients in EGRIFTA®?
Active ingredient: tesamorelin
Inactive ingredients: mannitol and Sterile Water for Injection

EMD Serono

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WHAT LIES AHEAD

Trends in HIV treatment and care

BY JOEL GALLANT, MD, MPH

2012 PROMISES A NUMBER OF CHANGES AND ADVANCES in the way we treat and prevent HIV infection. There is growing enthusiasm for widespread use of antiretroviral therapy (ART), regardless of CD4 count, both for treatment and prevention. New drugs and co-formulations are coming this year that will expand treatment options and simplify drug regimens, especially for initial therapy. At the same time, political and economic realities may prevent us from being able to implement broad-scale treatment and prevention efforts, and the coming of generic drugs, while cost-saving, may put limits on our choices of antiretroviral drugs.

WHEN TO START
San Francisco and New York City now recommend ART for everyone with HIV, regardless of CD4 count and viral load. Current U.S. treatment guidelines already come close to that aggressive standard. They recommend ART for anyone with a CD4 count below 500, and say that everyone else should consider treatment. Treatment is also recommended at any CD4 count for people with additional conditions, including pregnancy, HIV-associated nephropathy (HIVAN), hepatitis B or C, older age, high viral load, rapid CD4 decline, and high risk for heart disease.

In the minds of many HIV experts, ART is now the “default”—recommended unless there’s a good reason not to treat. Reasons why not to treat? People who aren’t ready or willing to start should wait until they are. Some people have no way to pay for treatment, an increasingly common scenario even in the United States. We don’t know what to do with “elite controllers”—people whose viral loads are already undetectable without therapy. Assuming normal and stable CD4 counts, it would be hard to show a benefit to starting ART in those individuals.

How did we get to this point, where ART is recommended for virtually everyone else? First, we’re recognizing that HIV isn’t just a disease of immunosuppression due to CD4 decline. Untreated HIV has consequences even for people with high CD4 counts, due to the inflammation and immune activation caused by ongoing replication of the virus. Shutting off viral replication may help to
reduce the long-term risk of conditions such as heart disease, cognitive decline, loss of bone density, and malignancies by reducing HIV-associated inflammation.

We also know that treating people with HIV lowers their risk of infecting others. In fact, the HPTN 052 study demonstrated that ART was 96% effective at preventing transmission to negative partners, a far greater efficacy than we’ve seen with any other form of prevention so far, including condoms, circumcision, microbicides, vaccines—probably even “abstinence.” Put simply, if everyone with HIV were on treatment with an undetectable viral load, we would see virtually no new cases.

Evidence of the benefit of early ART is clear, but the decision to treat early must also consider the cost of therapy, in order to weigh the costs against the benefits. Once-daily regimens are now the norm; a growing number of single-tablet regimens (STRs) are becoming available; tolerability and safety are high. Weighing the financial cost against the benefits is more complicated, since it involves economics and politics rather than science. This is where the prevention benefits of ART become so important. Some people may be unwilling to pay for universal ART for individuals, but if universal treatment can slow or even stop the epidemic, perhaps they’ll see it as money well spent. (At least, that’s what they should be thinking!)

**THE INITIAL REGIMEN**

Things are good with respect to initial ART, and there’s promise for continued improvement. We now have two single-tablet regimens available, Atripla and Complera, with the “Quad” pill coming soon, and additional co-formulated products and STRs in development. Before long, there may be an STR for almost everyone starting therapy, regardless of which nucleoside analog backbone they’re using and whether they’re starting ART using a non-nucleoside reverse transcriptase inhibitor, protease inhibitor, or integrase inhibitor. The co-formulations are likely to benefit treatment-experienced people too, either by allowing use of an STR or by reducing pill burden. For example, taking Norvir as a separate “booster” won’t be necessary when the new booster, cobicistat, is approved and combined with Reyataz and Prezista. There’s also the possibility that we’ll begin to see use of Selzentry or other CCR5 antagonists as part of first-line regimens. People with high CD4 counts who haven’t started ART are more likely to have R5-tropic virus, the kind that’s required for use of this class of agents. The availability of less expensive tropism assays and once-daily CCR5 antagonists may make this an appealing strategy in the future.

The coming of generics is the wild card. The generic versions of Zerit, Videx, Retrovir, and Combivir have had little impact because they’re not preferred drugs, but when Sustiva goes generic, everything could change. With a preferred agent potentially costing a fraction of the cost of its brand name equivalent, it may be hard to justify paying more for the shiny new STRs. Will people have to go back to taking 3-pill regimens to save money, while the STRs languish on pharmacy shelves? Only time will tell. The coming of generic ART is clearly a mixed blessing: On the one hand, who can complain about cheaper HIV drugs at a time when thousands of Americans are on waiting lists for treatment? On the other hand, a move from an STR to a 3-pill mixture of generic and brand name drugs will feel like a step in the wrong direction.

**BEYOND FIRST-LINE THERAPY**

The pipeline for new antiretroviral agents is focused on first-line treatment for one obvious reason: that’s where the money is. The efficacy and tolerability of current therapy means that most people do well on their initial regimens and stay on them for a long period of time. Drug companies are far more interested in developing drugs for the large first-line therapy market than for the small number of people with highly resistant virus who are waiting for new drugs.

But there are still people with highly resistant virus, and who’s to say we won’t see the emergence of resistance to integrase inhibitors and other new agents in the future? Fortunately, there are a few drugs still being developed for treatment-experienced patients, including drugs with novel mechanisms of action, such as the elusive attachment inhibitors (drugs that block the first stage of viral entry).

**BEYOND ART**

In the past, I rarely talked about anything “beyond ART,” because there was so little to say. That has changed in recent years. While no one should volunteer for a bone marrow transplant to be cured of HIV, the experience of “the Berlin patient” tells us that cure is conceivable, and the topic of cure has been a much bigger focus of scientific conferences and research spending than in years past. We’ve even seen some corporate interest in this area: for example, Sangamo BioSciences is attempting to modify human CD4 cells to make them uninfectable using zinc finger nuclease technology. We’re still a long way from a cure, but it’s moved from the realms of science fiction to science.

I should also mention what I’ll call “ARP” (for “antiretroviral prevention”). There’s now strong evidence that antiretroviral agents can be taken by HIV-negative people, either orally (as pills) or topically (as microbicides) to prevent infection. While many argue that condoms do the job for far less money, our 50,000 new cases per year tell us that our current approaches aren’t working. If people who won’t wear condoms would take pills or use microbicides to stay negative, that’s money well spent. The unanswered questions have to do with finances and implementation: Who will pay for biomedical forms of prevention, and who will provide it?

**THE FUTURE OF HIV CARE**

We may be approaching an important turning point in the way HIV care is delivered, and the uncertainty is both promising and scary. If fully implemented, the Affordable Care Act may improve health care for a large number of uninsured Americans. However, it could also threaten the quality of HIV care if it leads to weakening of the Ryan White CARE Act, the source of a network of HIV centers providing high quality, multidisciplinary medical and social services to people with HIV throughout the country. Even
privately insured people benefit from Ryan White, since they may get their care at HIV centers of expertise that wouldn’t exist without the program. Ideally, the Ryan White program should serve as a model for what medical care could be like for all Americans. But policymakers could ignore that, instead transitioning HIV care to Medicaid-funded clinics with little or no HIV expertise, at a time when the already underfunded Medicaid program is targeted by budget cutters in Washington.

CONCLUSIONS
It’s an exciting time in the history of the HIV epidemic, with outstanding treatment options that keep getting better, and prevention breakthroughs that could have a major impact on the future of the epidemic. However, we’re also in the middle of a global financial crisis, and more importantly, a political crisis, in which a large proportion of citizens reject virtually any form of government spending and believe that every dollar they earn is their own to keep. Of course it’s not about the money; it’s about having the right priorities and political will. Though costly, ART is a highly cost-effective way to treat HIV infection and prevent its spread. We spend far more money on foolish things, with little to show for our spending.

I wish I could conclude by saying that the future of the HIV epidemic will be guided purely by science and sound, evidence-based health care policy, but that may not be the case. Far too much depends on economics and politics, which we’ll be hearing a lot about in 2012.

FIND YOUR HIV DRUG IN THE GUIDE

Nucleoside reverse transcriptase inhibitors (NRTIs)

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Integrase inhibitors (INSTIs)

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PK enhancer

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positivelyaware.com/drugguide
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Everyone has to begin somewhere when learning about HIV, and if you have questions about your treatment, be sure to check with your care provider, pharmacist, or local HIV/AIDS service organization. Medications that are included in the HIV Drug Guide are only those drugs in the U.S. that are either FDA approved and currently on the market, are now (or soon to be) available through an expanded access program (EAP), or are expected to be FDA approved in the coming year.

Drugs are color-coded by class and are listed alphabetically by brand name (capitalized) or generic name (lower case) if not yet FDA approved. The brand name is listed first, then the generic name (scientific designation), and any abbreviations. Example: Isentress is the brand name, raltegravir is the generic name, and RAL is the abbreviation. Remember that even though every drug has a generic name, not all are available in generic form. When a drug is available as a generic, it will be indicated in the “Standard dose” section of the drug’s page.

New this year: when a drug is available in generic form, or when it is part of a multi-drug combination, it will be referred to by its generic name. Example: Retrovir, also known as AZT, is available in generic form as zidovudine. Therefore, on the Combivir page, it is referred to as zidovudine since it is part of Combivir. However, you should still look for the Retrovir page to find information on zidovudine. Note: In the doctor’s comments on each drug page, the drugs are sometimes referred to by their most commonly known abbreviation.

Drugs used to treat HIV should be taken in combination, using medications from two or more different classes of drug. To learn more about how the different drug classes work, go to www.positivelyaware.com/2012/12_02/class.shtml.

A fixed dose combination (FDC) combines two or more drugs in one tablet or capsule, such as Epzicom (lamivudine/abacavir). A single-tablet regimen (STR) contains several drugs from different drug classes and is a complete regimen in one pill, such as Atripla (efavirenz/emtricitabine/tenofovir). Atripla and Complera are two single-tablet regimens that are now available, with approval of another STR, the “Quad,” expected sometime during 2012.

The Average Wholesale Price (AWP) is used by pharmacies and other buyers to negotiate the amount they pay for drugs. The AWP is included as a way to compare what you would pay out-of-pocket if you do not have drug insurance coverage.

Our special pullout drug chart allows you to easily pinpoint dosing information and food and liquid requirements for each medication. The side effect and drug interaction charts make it easier to identify some of the more common side effects and interactions. Always refer to the individual drug pages, package insert, or talk to your physician or pharmacist for complete information.

Paying for your medications can often be a challenge, but there are programs that can help cover all or part of the costs. For a complete list of HIV drug co-pay and patient assistance programs, see page 77.

The HIV treatment guidelines are established by a panel of experts in conjunction with the Department of Health and Human Services (DHHS). The guidelines should be used by both physicians and patients to help inform treatment decisions. They’re available as a downloadable PDF at www.aidsinfo.nih.gov or go to www.positivelyaware.com/2012/12_02/guidelines.shtml.

Finally, remember that all treatment decisions should be made in partnership with your health care provider. Knowledge is power, and armed with the right tools—the most up-to-date, accurate information—you can learn to take control of not only the virus, but also of your health care and the quality of your life.
Talk with your doctor about ways to help protect your immune system.

HIV treatment is now recommended for everyone with a T-cell count of 500 or less and should be considered when T-cells are higher than 500, according to the DHHS* and the IAS-USA†, along with other factors. Starting treatment early may help protect your immune system and vital organs. Today’s medicines may have fewer, more manageable side effects. They may help you live a longer, healthier life. Receive helpful information about living with HIV that you should know. Call toll free 1-888-447-1728, or visit TREATHIVNOW.COM.

*DHHS = Department of Health and Human Services †IAS-USA = International AIDS Society USA. ©2012 Gilead Sciences, Inc. All rights reserved. UN11783 01/12
Potential side effects and toxicity
See the individual drugs contained in Combivir, Epivir, and Retrovir, for details. Fatigue, myopathy (muscle damage), and flare-up of hepatitis B upon stopping (due to the withdrawal of lamivudine). The zidovudine in Combivir has been associated with alteration of various cells in the blood through bone marrow suppression, resulting in anemia (low red blood cell counts) and/or neutropenia (low white blood cell counts), particularly during the first three months of therapy in people with advanced HIV. Zidovudine is also associated with lipoatrophy (fat loss of the arms, legs, face, and/or buttocks—sometimes called “AZT butt”). The lipoatrophy could be irreversible or fat could take a long time to rebuild after your regimen is changed. See chart on page 70 for potential drug class side effects.

Potential drug interactions
Also see the individual drugs contained in Combivir, Epivir, and Retrovir, for more information. Do not take Combivir with Atripla, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Retrovir, Trizivir, or Truvada, since all or part of these medications are already in Combivir or they have equivalent medications. Zerit cannot be taken with Combivir, as it can limit effectiveness of the zidovudine part of Combivir.

More information
May be taken with food to decrease potential nausea associated with zidovudine. One head-to-head study against Truvada (emtricitabine and tenofovir) found greater toxicity with Combivir, due to anemia (see Retrovir). Last year, the HIV treatment guidelines from the Department of Health and Human Services (DHHS) downgraded Combivir from “alternative” to “acceptable” dual nuke background for people taking antiviral therapy for the first time, citing twice-daily dosing and greater toxicity than Truvada or Epzicom. Anyone taking zidovudine might consider taking Combivir even if you are already resistant to the lamivudine component. Resistance to lamivudine makes HIV less fit to replicate. It also slightly improves the antiviral activity of zidovudine and tenofovir (Viread), and for that reason, some doctors keep lamivudine onboard in combination with those drugs after M184V resistance develops. Thanks to extensive data, Combivir continues to be preferred to Truvada for pregnant women who are taking therapy for the first time, according to the treatment guidelines. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
In the early years of the HAART era, Combivir was the most commonly used nucleoside “backbone” in what was often referred to as the “cocktail.” Since then it’s lost its luster: it’s taken twice a day and has the disadvantages of zidovudine (AZT) toxicity (see Retrovir). As a result, it’s been largely replaced by the safer and better tolerated once-daily coformulations, Truvada and Epzicom. Because the patents have expired on both AZT and 3TC (Epivir), Combivir is now available in generic form, but who cares? —JOEL GALLANT, MD, MPH

Activist’s comments
Although no longer the backbone of choice, Combivir represents a pivotal point in the history of regimens: fewer pills, less often, fewer side effects (for most folks). This set the tone for future regimens to ease up on the pill burdens, and a focus on finding less toxic formulas. It’s still quite useful in prevention of mother-to-child transmission in many parts of the world. Combivir can still be a good backup plan for those unable to take other nucleoside backbones, so it continues to have a place in the antiretroviral arsenal, but is clearly not a major player in the future of HIV treatment. —JOEY WYNN
**Emtriva**

**BRAND NAME**

**emtricitabine**, or **FTC**

**GENERIC NAME**

**CLASS:** Nucleoside reverse transcriptase inhibitor (nucleoside, NRTI, or nuke)

**MANUFACTURER:** Gilead Sciences, Inc. | www.gilead.com, (800) GILEAD-5 (445-3235)

**AWP:**
- $504.37 / month for 200 mg capsules;
- $110.38 for 170 mL solution (10 mg/mL)

**STANDARD DOSE:** One 200 mg capsule once a day, with or without food, with no dietary restrictions. The dosing needs to be adjusted for children and people who have decreased kidney function. It is also available as an oral solution for children three months and older and adults who are not able to swallow the capsules. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

**Potential side effects and toxicity**

Very tolerable. Side effects (rarely seen) may include headache, diarrhea, nausea, and rash. Flare-up of HBV (hepatitis B) in people co-infected with HBV has occurred when Emtriva was discontinued because it also treats HBV (see “More information”). Skin discoloration (darkening of the skin on the palms and the soles of the feet) can occur, but is generally mild and otherwise harmless. See chart on page 70 for potential drug class side effects.

**Potential drug interactions**

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

**More information**

Emtriva is similar to Epivir; both treat HBV and have the same resistance profile for HIV and HBV. However, unlike Epivir, Emtriva remains in blood cells for a longer interval. Emtriva is known to be very effective against chronic hepatitis B (although the manufacturer has not applied for FDA approval for this treatment). If you have HIV and HBV and you have Hep B needs treatment but your HIV doesn’t, you should be treated for both. You should never be treated only for HBV without treatment for HIV. Emtriva and Viread both work against HBV and HIV and can be used together as the NRTI backbone to increase activity and avoid HBV resistance, but there are other HBV treatments available that can be combined with HIV meds. If you are co-infected with HIV and HBV and you stop Emtriva, your HBV may reactivate and you may experience signs and symptoms of acute HBV. You should be closely monitored by your physician. If your HIV develops resistance to Epivir or Emtriva, it does not mean that your HBV is also resistant to them. Emtriva is available as a combination tablet with Viread (tenofovir), which is called Truvada. Truvada is the only NRTI combination on the preferred list of the U.S. HIV treatment guidelines for the NRTI component of first-time therapy. Drug resistance that the virus develops against Emtriva, the M184V mutation, makes the virus less fit to replicate. It also slightly improves the antiviral activity of Tenofovir (zidovudine) and Viread, and for that reason, some doctors keep Emtriva on board in combination with those drugs after M184V resistance develops. In 2006, Emtriva was combined with Sustiva (efavirenz) and Viread (tenofovir) in one pill, which is known as Atripla. Emtriva oral solution should be kept in the refrigerator. If kept at room temperature, the oral solution should be used within three months. See package insert for more complete information on potential side effects and interactions.

**Doctor’s comments**

Few people take Emtriva itself; it’s almost always combined with tenofovir in the form of Truvada, with tenofovir and efavirenz in the form of Atripla, or with tenofovir and rilpivirine in the form of Complera (with more co-formulations on the way). The characteristics of FTC are similar to those of 3TC (Epivir): it has the same resistance profile and is also safe and extremely well tolerated. The main difference between the two drugs is that FTC tends to be combined with tenofovir, while 3TC is usually taken in combination with AZT (Retrovir), abacavir (Ziagen), or both. Aside from the convenience of the co-formulations, there may be other reasons why these combinations make sense. Both tenofovir and FTC have similar half-lives, which are longer than those of other nucleoside analogs. This means they hang around longer in the blood and in CD4 cells. Combining two drugs with similar half-lives may help to prevent resistance if doses are missed or treatment is interrupted. Indeed, we seem to see less tenofovir resistance when tenofovir is combined with FTC than when it’s combined with 3TC, a consideration that may become relevant now that 3TC is going generic.

—JOEL GALLANT, MD, MPH

**Activist’s comments**

The “Quiet Giant” of the ARV world, the “son of 3TC” is much better than its dad. This beauty (FTC) is a great tool. It makes the virus “less fit,” meaning less able to multiply and produce lots of harmless mutations, so it isn’t as harmful as wild types. From personal experience, I have never heard anyone complaining about side effects from Emtriva, though it’s hard to tell, as it is usually blended in with other drugs in compounds like Truvada, or once-daily single tablet regimens like Atripla or Complera. Long half life means it stays in the system longer. Because of its activity against hepatitis B virus, people should check with their doctors before using this drug to prevent HBV cross resistance or “flare-ups” when stopping the medication. —JOEY WYNNE
Potential side effects and toxicity
Very tolerable. Side effects (though rarely seen) may include headache, nausea, vomiting, diarrhea, fever, fatigue, hair loss, insomnia, malaise (general ill feeling), nasal symptoms, and cough. See chart on page 70 for potential drug class side effects.

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

More information
One benefit is that the drug resistance 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. The mutation also slightly improves the antiviral activity of Retrovir and Viread, and for that reason, some doctors keep Epivir onboard in combination with those drugs after M184V resistance develops. Epivir is also approved for the treatment of hepatitis B virus (HBV), under the brand name Epivir-HBV, which has a lower dose than Epivir (Epivir-HBV is used only in people without HIV), but if you have HIV and HBV, you will need to take full-dose Epivir along with a complete regimen to treat HIV and HBV. If you have HIV and HBV and your hep B needs treatment but your HIV doesn’t, you should be treated for both. You should never be treated only for HBV without treatment for HIV. Epivir and Viread both work against HBV and HIV and can be used together as the NRTI backbone to increase activity and avoid HBV resistance, but there are other HBV treatments available that can be combined with HIV meds. Make sure you are taking Epivir at HIV doses—always ask your doctor or pharmacist. If you are co-infected with HIV and HBV and you stop Epivir, your HBV may reactivate and you may experience signs and symptoms of acute HBV. You should be closely monitored by your physician. If your HIV develops resistance to Epivir, it doesn’t mean that your HBV is also resistant to it. Epivir is also available in three combination products: Combivir, with zidovudine, taken one tablet twice a day; Epzicom, with abacavir, taken one tablet once daily; and Trizivir with zidovudine and abacavir, taken one tablet twice a day. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
In the early ’90s the approval of 3TC (Epivir) was a big shot in the arm to the tired nucleoside class. Adding it to other nucleoside analogs after they’d stopped working seemed to revive them for awhile, and if you started 3TC and AZT together, resistance was delayed. We later learned that the 3TC mutation, M184V, could delay the emergence of thymidine analog mutations (TAMs, the mutations in your virus that you got from taking AZT or d4T [stavudine]) or partially reverse the resistance that they caused. During the early years of the HAART era, 3TC became a component of virtually every antiretroviral regimen, and even today, most people taking either AZT or abacavir are also taking 3TC using a co-formulation. 3TC is extremely well tolerated and very safe with long-term use. Resistance to 3TC occurs quickly if the viral load isn’t completely suppressed, and while there are some resistance advantages to having an M184V mutation, it’s still better not to have it, allowing 3TC to retain its full antiviral activity.
—JOEL GALLANT, MD, MPH

Activist’s comments
The earlier (and weaker) version of a nucleoside with a kick, this drug along with AZT made for a reduction in the number of pills and helped as a backbone for many combinations in the ’90s. This drug still has a useful purpose, especially in financially limited settings as generics came to market, so it keeps its place on the list of drugs we can use to combat HIV. —JOEY WYNN
**Potential side effects and toxicity**

The most common side effects of Epzicom are the same as the individual drugs it contains—see Epivir (lamivudine) and Ziagen (abacavir). Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir (see Ziaugen page). A simple and inexpensive blood test for HLA-B*5701 (a genetic marker) can identify people at high risk for this reaction and virtually eliminate HSR. About 90% of HSR occurs within the first six weeks of treatment. Symptoms of HSR usually worsen, very slowly, with every dose. If treatment is stopped because of this serious reaction, you can never take products containing abacavir, such as Epzicom or Trizivir, again (called “re-challenging”). Re-challenging could cause a rare life-threatening 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 fever; muscle ache; malaise (general ill feeling); severe nausea, vomiting, diarrhea, or abdominal pain; severe tiredness; respiratory symptoms (cough, difficulty breathing, and sore throat); and possible rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. Hypersensitivity might be confused with flu during flu season, but remember that HSR worsens with every dose. Check with your doctor if you have any side effects after taking this medicine—don’t just stop! Some observational studies seem to indicate that abacavir may increase the risk of cardiovascular events, including heart attacks, in people with greater risk factors (such as smoking, diabetes, high blood pressure, and drug use). One possible explanation was found—people with kidney problems were put on abacavir in order to avoid tenofovir, which has potential for kidney toxicity, and those people already had a strong risk for heart problems. The FDA conducted an analysis of 26 randomized clinical trials that evaluated abacavir. This analysis did not show an increased risk of heart attacks associated with the use of abacavir. Last year, DHHS HIV treatment guidelines added the statement, “to date, no consensus has been reached either on the association of [abacavir] use with MI [myocardial infarction, or heart attack] risk or a possible mechanism for the association.” People who have high risk for heart disease are monitored more closely and the decision to stop or never start a regimen containing abacavir is up to you and your provider. See chart on page 70 for potential drug class side effects.

**Potential drug interactions**

See the individual drugs contained in Epzicom, Epivir and Ziagen, for more information. Do not take Epzicom with Atipla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Trizivir, Truvada, or Ziagen, since all or part of these medications are already in Epzicom or have equivalent medications. Alcohol can increase the levels of abacavir and therefore increase the possibility of side effects.

**More information**

Currently, U.S. HIV treatment guidelines recommend Truvada over Epzicom as the preferred backbone for the NRTI component of an HIV drug combination for first-time therapy. Epzicom is listed as an alternative NRTI backbone. Study ACTG 5202 reported that for those people who started treatment with a viral load of more than 100,000, Epzicom was “significantly less effective at controlling HIV” in the regimens tested. Moreover, time to a serious adverse event was sooner in the people taking Epzicom. These efficacy and safety findings were not confirmed in a manufacturer-sponsored study, HEAT, another large study comparing Epzicom and Truvada. Still, in HIV therapy, there is always use for an alternative choice of drugs. The DHHS guidelines state, “Pending additional data, [Epzicom] should be used with caution in individuals who have plasma HIV RNA [viral load] greater than 100,000 copies/mL, as well as in persons at higher risk for cardiovascular disease. However, Epzicom remains a good alternative dual-NRTI option for some treatment-naive patients.” Remember, too, that Truvada has its own side effect and drug interaction issues, although it’s famed for its tolerability. The HLA-B*5701 test should never be used to diagnose HSR. Do not use a skin patch test to confirm HSR. Regardless of the results, it is important to monitor the potential for this reaction. If HSR is suspected or cannot be ruled out, products containing abacavir should be discontinued. The incidence of HSR was the same between Epzicom once-daily and Ziaugen 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. The lamivudine portion of Epzicom is also used to treat the hepatitis B virus (HBV); see Epivir page. If you are co-infected with HIV and HBV and you stop Epzicom, your HBV may reactivate and you may experience signs and symptoms of acute HBV. You should be closely monitored by your physician. See package insert for more complete information on potential side effects and interactions.

**Doctor’s comments**

Epzicom is the safe, well-tolerated, once-daily co-formulation of abacavir (Ziagen) and 3TC (Epivir). It’s generally viewed as the best alternative to Truvada when tenofovir can’t be used (usually for reasons having to do with the kidneys). The issues of abacavir hypersensitivity (see Ziaugen) apply to Epzicom as well, so an HLA-B*5701 test should always be ordered before taking this drug. Epzicom appears to be somewhat less effective than Truvada in people with viral loads above 100,000. For reasons discussed elsewhere, we also tend to avoid Epzicom in people who are at high risk of coronary heart disease. —Joel Gallant, MD, MPH

**Activist’s comments**

A combination of abacavir and lamivudine, Epzicom was a convenient once-a-day improvement over Combivir, or so we thought. Complications, side effects, and risk of coronary issues have made this far less prescribed than in prior years. As it fades out of favor, it leaves us with a mediocre backup tool for those failing all of the latest greatest therapies. —Joey Wynn
Potential side effects and toxicity

May include headache, fever and chills (more common in children), muscle soreness, fatigue, nausea, and fingernail discoloration. Zidovudine (Retrovir) has been associated with alteration of various cells in the blood through bone marrow suppression, resulting in anemia (low red blood cell counts), which can make you feel short of breath and tired, and/or neutropenia (low white blood cell counts), which can increase your risk for getting colds and other infections, particularly during the first three months of therapy in people with advanced HIV. Potential exists for severe anemia requiring blood transfusion, erythropoietin injections, or hospitalization when used on its own or particularly if used in combination with hydroxyurea. Your provider may check your blood in the first 4-6 weeks after you start zidovudine and will look for anemia and neutropenia. Zidovudine is associated with lipatrophy (fat loss of the arms, legs, face, and/or buttocks—sometimes called “AZT butt”). The lipatrophy could be irreversible or fat could take a long time to rebuild after your HIV regimen is changed. See chart on page 70 for potential drug class side effects.

Potential drug interactions

Do not take with Combivir or Trizivir, since zidovudine is already in these medications. Biaxin and rifampin (under various brand names) may decrease zidovudine blood levels. Do not take with the cancer treatment doxorubicin, Benemid (probenecid), Dilantin (phenytoin), and Depakote (valproic acid) may increase blood levels and decrease clearance of zidovudine, but no dosing adjustments are recommended. Zidovudine and Zerit (stavudine) should never 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, fluycytosine, sulfadiazine, interferon-alpha, and ribavirin (Rebetol). Ribavirin (used with interferon to treat hepatitis C) may decrease the efficacy of zidovudine and increase the risk of lactic acidosis and should not be used together. For patients taking zidovudine, measure hemoglobin once a week after starting other medications that can cause anemia until hemoglobin has stabilized. Notify your health care provider if you’re experiencing pain and/or swelling in the legs, worsening or shortness of breath, increases in blood pressure, dizziness, or loss of consciousness, extreme tiredness, or blood clots in hemodialysis vascular access ports. Methadone can increase zidovudine levels but no dose adjustments are recommended. Monitor for adverse effects.

More information

Zidovudine is rarely used nowadays, though it remains the go-to medication for pregnancy and infants after birth, to prevent mother-to-child transmission. The not-so-good news for people adding zidovudine—the fatigue and the potential anemia, but it is still a very good HIV mediation with many years of data behind it and a good option for people who have developed resistance to some of the newer first-line HIV medications. You can start taking erythropoietin (Procrit or Epogen) for some anemias, but that’s adding another drug if you have other options. Taking with food may minimize upset stomach. Zidovudine 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. Thanks to extensive data, zidovudine is a preferred drug for pregnant women who are taking therapy for the first time, according to U.S. HIV treatment guidelines. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments

Retrovir (AZT) was the first drug approved for the treatment of HIV, and while its benefits were modest and temporary, it did make a difference for many people. It enjoyed two revivals, first with the approval of Combivir (AZT plus 3TC) and later with the approval of Trizivir (AZT plus 3TC plus abacavir). However, the use of AZT in any form has declined with the approval of safer, more convenient, and more effective alternatives. AZT must be taken twice a day and can cause anemia, nausea, fatigue, and lipatrophy. In fact, while AZT may not cause lipatrophy as often or as quickly as Zerit (d4T) does, there’s some evidence that lipatrophy caused by AZT may be less reversible. Because of its long history of safety in pregnancy, AZT remains a preferred nucleoside for pregnant women, though there is growing comfort with the use of other agents.

—Joel Gallant, MD, MPH

Activist’s comments

The grandfather of HIV drugs, it has morphed over the years to stay relevant. The only real application for AZT these days is for use in mother-to-child transmission prevention, as it is safe for pregnancy. AZT is probably still in wide use in other countries, as less costly generics are available in most markets. AZT has been relegated to second or third string for most prescribers. To be fair, it remains one of the few effective antivirals that cross the blood/brain barrier, achieving CNS penetration, which makes it useful for those with neuropsychological problems. —Joey Wynn

Retrovir

BRAND NAME

zidovudine, or AZT, or ZDV

GENERIC NAME

CLASS: Nucleoside analog reverse transcriptase inhibitor (nucleoside analog, NRTI, or nuke)—fixed dose combination
MANUFACTURER: ViiV Healthcare | www.viivhealthcare.com, (877) 844-8872
AWP: $555.12 (generic $309.89) / month for 300 mg tablets, $71.34 (generic $56.42) for 240 mL of 10 mg/mL syrup

STANDARD DOSE: One 300 mg tablet twice a day (12 hours apart); two 100 mg capsules three times a day (8 hours apart) also available; with or without food, with no dietary restrictions. Clear, strawberry-flavored liquid available for infants four weeks of age and up; dose is weight-based. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. If your kidney function is less than 15 mL/min or you are on dialysis, your dose will need to be adjusted. Used in pregnancy and for newborns to prevent HIV transmission from mother to child. Generic is available.
Potential side effects and toxicity
The most common side effects of Trizivir are the same as those of the drugs it contains—see Epivir, Retrovir, and Ziajen. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir; see Ziajen page. A simple and inexpensive blood test for HLA-B*5701 (a genetic marker) can identify people at high risk for this reaction and virtually eliminate HSR. The HLA-B*5701 test should never be used to diagnose HSR. Do not use a skin patch test to confirm HSR, as the skin test is only used as a research tool. Regardless of the results, it is important to monitor the potential for this reaction. If HSR is suspected or cannot be ruled out, products containing abacavir should be discontinued. If treatment is stopped because of this serious reaction, you can never take products containing abacavir, such as Epzicom or Trizivir, again (called “re-challenging”). Re-challenging can cause a rare life-threatening 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 worsen, very slowly, with every dose. Symptoms usually, but not always, include some combination of fever; muscle ache; severe nausea, vomiting, diarrhea, or abdominal pain; severe tiredness; respiratory symptoms (cough, difficulty breathing, and sore throat); and possible rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. Hypersensitivity might be confused with flu during flu season, but remember that HSR worsens with every dose. Check with your doctor if you have any side effects after taking this medicine—don’t just stop! Some observational studies seemed to indicate that abacavir may increase the risk of cardiovascular events, including heart attacks, in people with greater risk factors (such as smoking, diabetes, high blood pressure, and drug use). One possible explanation was found—people with kidney problems were put on abacavir in order to avoid Viread (tenofovir), which has potential for kidney toxicity and those people already had a strong risk for heart problems. The FDA conducted an analysis of 26 randomized clinical trials that evaluated abacavir. This analysis did not show an increased risk of heart attacks associated with the use of abacavir. Last year, DHHS HIV treatment guidelines added the statement, “to date, no consensus has been reached either on the association of [abacavir] use with MI [myocardial infarction, or heart attack] risk or a possible mechanism for the association.” People who have high risk for heart disease are monitored more closely and the decision to stop or never start a regimen containing abacavir is up to you and your provider. Other side effects associated with Trizivir may include headache, nausea, upset stomach, and fatigue. May be taken with food to decrease potential nausea associated with zidovudine. The zidovudine in Trizivir has been associated with alteration of various cells in the blood through bone marrow suppression, resulting in anemia (low red blood cell counts) and/or neutropenia (low white blood cell counts), particularly during the first three months of therapy in people with advanced HIV. Zidovudine is also associated with lipoatrophy (fat loss in the arms, legs, face, and/or buttocks—sometimes called “AZT butt”). The lipoatrophy could be irreversible or fat could take a long time to rebuild after changing your regimen. See chart on page 70 for potential drug class side effects.

Potential drug interactions
See the drugs contained in Trizivir—Epivir, Retrovir (zidovudine, AZT), and Ziajen. Trizivir is the only triple combination NRTI that has been studied in a randomized, controlled study, which has shown it to be inferior to the standard treatment of two NRTIs plus Sustiva. U.S. treatment guidelines recommend that Trizivir should only be used if other options are not available due to toxicities or drug interactions associated with other HIV regimens. Trizivir contains Epivir, which is used to treat the hepatitis B virus (HBV). If you are co-infected with HIV and HBV and you stop Trizivir, your HBV may reactivate and you may experience signs and symptoms of acute HBV. You should be closely monitored by your physician. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
In the early years of the HAART era, when people were suffering on effective but complex and toxic regimens like Combivir plus Crixivan, Trizivir appeared like a breath of fresh air. Just one pill twice a day, with no need to watch the clock or time your meals, and no kidney stones, diabetes, dry skin, cracked lips, or ingrown toenails to worry about. Sure, some people developed abacavir hypersensitivity reactions (see Ziajen), and many had the usual zidovudine (AZT) side effects (see Retrovir). But compared to what we had before, it seemed almost too good to be true. Well, it was. This “triple-nuke” regimen was shown to be less effective than a regimen containing Sustiva, both at high and low viral loads, and its use declined rapidly after that. Today, if you had some reason to be taking AZT, 3TC, and abacavir, it would make sense to take them in the form of Trizivir. But taking Trizivir alone is no longer recommended.

—JOEL GALLANT, MD, MPH

Activist’s comments
Although it gave us a sneak peak at therapies to come, this hopeful “one pill, twice a day” triple combination therapy failed to make the mark. Now widely ignored, it is left in the past chapters of history. It helped propel the consumer demand for therapies with less pill burden, but failed to reduce the toxicities less.

—JOEY WYNN
Truvada

BRAND NAME

emtricitabine / tenofovir, or FTC / TDF

GENERIC NAME

CLASS: Nucleoside/nucleotide reverse transcriptase inhibitor (nucleoside/nucleotide, NRTI, or nuke)—fixed dose combination

MANUFACTURER: Gilead Sciences, Inc. | www.gilead.com, (800) GILEAD-5 (445-3235

AWP: $1,427.09 / month

STANDARD DOSE: For adults and pediatric patients 12 years or older and weighing more than 77 pounds, one tablet (200 mg emtricitabine / 300 mg tenofovir) once a day, with or without food, with no dietary restrictions. Dosing frequency needs to be adjusted for people with decreased kidney function and Truvada should not be used if the kidney function is less than 30 mL/min or if on dialysis. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

Potential side effects and toxicity

See the individual drugs contained in Truvada—Viread and Emtriva. Overall, fairly well tolerated, however, individuals may experience diarrhea, nausea, vomiting, and gas. Skin discoloration on palms and soles may also occur. The Viread in Truvada is associated with decreases in bone mineral density (BMD). BMD monitoring should be considered in people who have a history of pathologic bone fracture or are at risk for osteopenia or osteoporosis. The effects of calcium supplements with or without vitamin D have not been studied, but their use may be beneficial. Calcium and vitamin D levels can be checked by your provider to assess the need for these supplements. Less common side effects include kidney toxicities and low blood phosphate.

Potential drug interactions

See the individual drugs contained in Truvada—Viread and Emtriva. Do not take with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Trizivir, Truvada, or Viread, since all or part of these medications are already in Truvada or have equivalent medications. Truvada increases levels of Videx EC, so use with caution and monitor. Tenofovir decreases the concentration levels of Reyataz. In addition, Reyataz and Kaletra increase tenofovir concentrations. The reason for these interactions is unknown. It is recommended that patients taking Reyataz and Truvada should be monitored for Truvada-associated adverse events. When taken with Truvada, it is recommended that Reyataz 300 mg is taken with Norvir 100 mg (all as a single daily dose with food). Reyataz without Norvir should not be taken with Truvada. No dose adjustment is needed when used with Kaletra. Avoid taking Truvada with current or recent use of kidney-toxic drugs.

More information

Currently, DHHS HIV treatment guidelines recommend Truvada over Epzicom as the only preferred medication for the NRTI component for first-time therapy. Study ACTG 5202 reported that while both Epzicom and Truvada reduced viral load, for those people who started treatment with a viral load of more than 100,000, Epzicom was “significantly less effective at controlling HIV” in the regimen tested. Moreover, time to a serious adverse event was sooner in the people taking Epzicom. Remember, however, that Truvada has its own side effect and drug interaction issues, although it’s famed for its tolerability. Kidney function must be monitored before and during treatment with Truvada and it may not be a good option for patients with underlying kidney problems. GS-7340, a pro-drug (substance that becomes activated after entering the body) of tenofovir, is being developed. The pro-drug has the same mechanism of action, but is expected to provide greater effectiveness at a dose 10 times lower than that used for Viread. A tablet containing Emtriva and GS-7340 has been developed and is being studied. This would be Emtriva with GS-7340 instead of tenofovir. Truvada is combined with efavirenz to form Atripla and is also in the new Complera, another triple regimen in one pill. Truvada is also in advanced Phase 3 study in a quadruple formula with two of Gilead’s investigational drugs: elvitegravir, an integrase inhibitor (same class as Isentress), and the drug booster cobicistat (GS-9350); see the “Quad,” page 56. Gilead has applied for FDA approval of Truvada as HIV prevention, which is called PrEP (for pre-exposure prophylaxis). Truvada PrEP is controversial, with some people rooting for it and others worried that it will be used incorrectly, among other concerns. At any rate, Truvada can already be used off label (not an FDA approved use) for prevention. Although the effect of supplementation with calcium and vitamin D has not been studied, such supplementation may be beneficial for all patients, according to the FDA. See package insert for more information on potential side effects and interactions.

Doctor’s comments

Truvada is now the preferred nucleoside backbone for initial regimens according to DHHS and IAS-USA guidelines, based on studies showing that it’s more effective and safer than Combid, and more effective at high viral loads than Epzicom. When combined with efavirenz (Sustiva), it is used in the form of Atripla, the first approved single-pill regimen and, combined with rilpivirine, it forms Complera, the second approved single-pill regimen. People taking Truvada need to be monitored for kidney toxicity (see Viread), and those who already have kidney disease may need to take Truvada less frequently than once a day, or better yet, avoid it altogether. The bone issues seen with tenofovir (see Viread) also apply to Truvada.

—JOEL GALLANT, MD, MPH

Activist’s comments

The little train that could! Who knew that this combination would become the blockbuster it is today? Part of the majority of regimens prescribed today, it is (for many people) easy to take, with few side effects for the average person. Its only downside is that there are no comparable alternatives for those who need to avoid the possibility of kidney toxicity and possible bone loss reported by some. I’ve been on this for a decade, before the two components were in one pill and I can’t imagine having to stop taking it. Only adding the final drug to it could make it better, and guess what? There are now two once-daily single tablet regimens with this super couple in it—Atripla and Complera both contain Truvada. Getting it down to one pill once a day is the gold standard now. —JOEY WYNN

30 MARCH+APRIL 2012 FOR THE LATEST INFORMATION ON TRUVADA, GO TO positivelyaware.com/truvada
**Videx EC and Videx**

**BRAND NAME**

**didanosine, or ddl**

**GENERIC NAME**

**CLASS:** Nucleoside reverse transcriptase inhibitor

(nucleoside, NRTI, or nuke)

**MANUFACTURER:** Bristol-Myers Squibb | www.bms.com, (800) 321-1335

**AWP:** $425.00 / month for Videx EC 400 mg capsules

(generic didanosine $329.00 / month)

**STANDARD DOSE:** One 400 mg enteric-coated Videx EC, delayed-release capsule once a day for people who weigh 132 pounds or more. Dose needs to be adjusted for those weighing less than 132 pounds; kidney function less than 60 mL/min; and when combined with Viread, Truvada, or Atripla. Take strictly on an empty stomach (unless taking with Viread), one hour before or two hours after food or drink, except water. Approved for children weighing at least 44 pounds. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Capsules must be swallowed whole. Videx is also available as a buffered powder for oral solution. Generic Videx EC (didanosine EC) is available.

**Potential side effects and toxicity**

Peripheral neuropathy (tingling, burning, numbness, or pain in the hands or feet) may go away once Videx EC is stopped, but can be painful and permanently debilitating if not treated in time or if you continue to use Videx EC after symptoms of neuropathy start. It occurs more frequently when Videx EC is used with Zerit or in people with more advanced HIV. Upset stomach, diarrhea, headache, and, more rarely, pancreatitis (inflammation of the pancreas), have also been reported. 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. Recent post-marketing surveillance has reported cases of non-cirrhotic portal hypertension (increased blood pressure in the vessels that connect to and from the liver) associated with the use of Videx EC. Symptoms (elevated liver enzymes, enlarged spleen, blood in vomit, and fluid collection in abdomen) may begin months to years after starting Videx EC. Routine doctor visits and lab tests will assist in early detection and prompt discontinuation of Videx EC. 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. People with a history of peripheral neuropathy, pancreatitis, or heavy alcohol use should avoid Videx EC. Body fat redistribution/accumulation has also been reported with Videx EC. See chart on page 70 for potential drug class side effects.

**Potential drug interactions**

Should not be taken with Viread (tenofovir), if possible. However, if co-administration is necessary, use tenofovir with caution and close monitoring, since Videx EC levels are increased with tenofovir (a medication also found in Atiprila, Complera, and Truvada). Videx EC dose should be decreased to 250 mg daily for patients weighing more than 132 lbs. and 200 mg daily for those weighing less. Adjust dose of Videx EC when taking Viread, Truvada, Atripla, or Complera to avoid Videx-related toxicity, including neuropathy and pancreatitis. The combined use of Videx and Retrovir (zidovudine), Zerit, or hydroxyurea may increase risk of peripheral neuropathy. Videx EC taken with Zerit increases the risk of facial wasting and/or lactic acidosis. Combining Videx EC with Zerit, hydroxyurea, alcohol, ganciclovir, valganciclovir, or intravenous (not inhaled) pentamidine may increase risk of pancreatitis. Do not take with ribavirin or allopurinol. Also, ganciclovir substantially increases Videx EC levels, and is generally recommended not to be taken together. If there is no alternative to ganciclovir, use it with caution and monitor for Videx EC toxicity. Videx powder in oral solution should be taken on an empty stomach one hour before or two hours after protease inhibitors, Tagamet (cimetidine), ketoconazole, itraconazole, and dapsone, and one hour apart from Rescriptor. Videx EC capsules 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). Methadone decreases Videx powder concentrations significantly and should not be used together, but if necessary, the Videx EC capsule formulation should be used.

**More information**

Videx EC is rarely used. Videx EC compared to Zerit may have lower risk of peripheral neuropathy, but the rate found in clinical trials was still 12-34%. This is hardly an issue anymore, since Zerit is even more rarely used (if ever). Swallow the capsules whole. The enteric coating reduces diarrhea compared to the previous formulation. If you have reduced kidney function, you may require a lower dose. Notify your doctor right away if peripheral neuropathy is suspected. See package insert for more complete information on potential side effects and interactions.

**Doctor’s comments**

Videx (ddl), approved in 1991, was our second antiretroviral drug. People often used it after AZT stopped working. Later it was added to AZT in our primitive attempts at early combination therapy. It was a complicated drug to take, requiring twice-daily dosing on an empty stomach, and sometimes involving the use of powder formulations or the mixing of crushed tablets with antacids to improve tolerability. The new EC (enteric coated) formulation eliminates those problems, but this is no longer a drug with much of a purpose. Its resistance patterns overlap with the better tolerated tenofovir and abacavir, and it causes neuropathy, pancreatitis, and probably lipoatrophy. More recently, questions have been raised about whether ddl might cause non-cirrhotic portal hypertension, an uncommon but serious and potentially fatal liver condition that doesn’t get better after you stop taking the drug. —JOEL GALLANT, MD, MPH

**Activist’s comments**

Is there anyone out there still on this drug? There may be a handful of folks still using this, but it is mainly a relic of HIV treatment history. Too many toxic side effects for me to tolerate it back in the day, but Jeff Taylor said it best in last year’s rundown: "The fact that it’s rarely used anymore can work in its favor, making it a useful add-on drug to salvage regimens for patients who’ve exhausted all other options.” Other than that, I can’t see much use.

—JOEY WYNN

FOR THE LATEST INFORMATION ON VIDEX EC AND VIDEX, GO TO positivelyaware.com/videx

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Viread
BRAND NAME

tenofovir disoproxil fumarate (tenofovir), or TDF
GENERIC NAME

CLASS: Nucleotide reverse transcriptase inhibitor (nucleotide, NRTI, or nuke)
AWP: $926.09 / month

STANDARD DOSE: One 300 mg tablet once a day, with or without food, with no dietary restrictions. Dosing frequency needs to be adjusted for people with decreased kidney function. One 150 mg, 200 mg, or 250 mg once a day for children ages 2 or older. Oral powder formulations. Dosing frequency needs to be adjusted for people with decreased kidney function. One

Potential side effects and toxicity
Overall, fairly well tolerated; however, diarrhea, nausea, vomiting, and gas are the most common side effects of Viread. Decreases in bone mineral density (BMD) have been observed with the use of Viread. BMD monitoring should be considered in people who have a history of pathologic bone fracture or are at risk for osteopenia or osteoporosis. Creatinine clearance (CrCl) should be assessed before initiating treatment with Viread. CrCl and serum phosphorus should be monitored more often in patients at risk. Less common side effects of Viread, occurring with undetermined incidence, include kidney toxicities and low blood phosphate. 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. Viread is indicated for the treatment of chronic hepatitis B in adults. It should never be used alone to treat hepatitis B in people who have HIV. See chart on page 70 for potential drug class side effects.

Potential drug interactions
Do not take with Atripla, Complera, or Truvada since tenofovir is in these medications. Viread should not be used in combination with Hepsera. Videx levels are increased with Viread; therefore, use with caution and monitor closely when taking Videx with Atripla, Complera, Truvada, or Viread to avoid Videx-related toxicity. Videx EC dose should be decreased to 250 mg daily for patients who weigh more than 132 pounds (60 kg) and 200 mg daily for those less than 132 pounds. See “More Information.” 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 taking Reyataz and Viread should be monitored for Viread-associated adverse events. When Reyataz is taken with Viread, it is recommended that Reyataz 300 mg is taken with Norvir 100 mg (all as a single daily dose with food). Unboosted Reyataz (without Norvir) should not be taken with Viread. No dose adjustment is needed when used with Kaletra. Avoid using Viread with current or recent use of kidney-toxic drugs. Viread levels are increased with Incivek; monitor closely for Viread side effects.

More information
Viread (tenofovir) combined with emtricitabine, also available in Truvada, is considered the preferred NRTI combination by U.S. HIV treatment guidelines for first-time therapy. GS-7340, a pro-drug (substance that becomes activated after entering the body) of tenofovir is being developed. The pro-drug has the same mechanism of action, but is expected to provide greater effectiveness at a dose 10 times lower than that used for Viread. A tablet containing emtricitabine and GS-7340 has been developed and is being studied. GS-7340 is metabolized differently and is less likely to affect the kidneys, but still has activity against hepatitis B. Its lower dose also makes co-formulations with other drugs more possible. Last year Gilead entered into an agreement to develop a fixed dose combination of its emtricitabine along with GS-7340 and Janssen Therapeutics’ protease inhibitor Prezista (darunavir). The body clears most of Viread through the kidneys and dose adjustment is recommended for those with impaired kidney function. Serious kidney problems have been rare and most have been in those with pre-existing kidney disease or taking kidney-toxic drugs. Results this year from a large observational study found a greater risk of kidney toxicity with tenofovir. However, the characteristics of kidney toxicity with Viread are still being defined. The manufacturer recommends that individuals with impaired kidney function should be monitored closely, especially people with advanced HIV disease, high blood pressure, and diabetes, even in those who did not start out with kidney disease. Like Epivir and Emtriva, Viread has activity against hepatitis B, and it is FDA approved for hep B therapy. Viread is used by itself for hep B treatment, but should not be used alone by people with hep B and HIV. If you have HIV and HBV and your hep B needs treatment but your HIV doesn’t, you should be treated for both. If your HIV develops resistance to tenofovir and/or emtricitabine, it doesn’t mean that your hepatitis B is also resistant to them. If you are co-infected with HIV and HBV and you stop tenofovir, you may experience signs and symptoms of acute HBV. You should be closely monitored by your physician. Five-year data on co-infected people found sustained suppression of hep B and a reduction in liver fibrosis and a reversal of cirrhosis. Overall, 88% of patients saw improvement in their overall liver histology. Viread may have prolonged activity against hepatitis B even when resistant to Epivir. The FDA noted that supplementation with calcium and vitamin D may be beneficial for all patients taking Viread. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
Because of its safety and effectiveness, the combination of tenofovir and FTC, in the form of Truvada, or, when combined with efavirenz as Atripla, has become the preferred nucleoside combination in both the DHHS and IAS-USA guidelines. Tenofovir is also co-formulated with FTC and rilpivirine to make Complera, and we’re expecting additional tenofovir-containing co-formulations soon. In most cases, an initial antiretroviral regimen should include tenofovir unless there’s a good reason to use something else. Tenofovir’s main flaw is kidney toxicity: it can reduce kidney function, and can also cause wasting of phosphate in the urine, leading to bone problems. However, these are toxicities that can be detected using simple and standard lab tests, and they’re uncommon, especially in people taking tenofovir with efavirenz as part of an initial regimen. Kidney toxicity may be somewhat more common when tenofovir is combined with protease inhibitors, but these are still widely used, recommended regimens. The other concern is bone: It’s now clear that there’s a mild and transient loss of bone density whenever you start antiretroviral therapy, but the loss of bone may be somewhat more pronounced in people taking tenofovir.

—JOEL GALLANT, MD, MPH

Activist’s comments
One half of the “super couple” that makes up Truvada, this mighty drug has the potential to be around for decades more. Time will tell if the potential issues with bone density and kidney function will take their toll on this drug. It’s hard to imagine this drug falling out of favor, but hey, every King of the Mountain has his day! —JOEY WYNN

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Zerit
BRAND NAME

stavudine, Or d4T
GENERIC NAME

CLASS: Nucleoside reverse transcriptase inhibitor
(nucleoside, NRTI, or nuke)
MANUFACTURER: Bristol-Myers Squibb | www.bms.com, (800) 321-1335
AWP: $493.38 (generic $411.16) / month for 40 mg capsules

STANDARD DOSE: One 40 mg capsule twice a day for people weighing 132 pounds or more, or one 30 mg capsule twice a day for people weighing less; with or without food, with no dietary restrictions. It is FDA approved in children from birth on. Zerit is also available in 15 mg, 20 mg, 30 mg, and 40 mg capsules, and a powder for oral solution; check for food restrictions. Dose reduction needed in people with kidney problems. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Generic is available.

Potential side effects and toxicity
Headache, diarrhea, nausea, rash, and peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet) are the most common side effects. Peripheral neuropathy is more common in people who have more advanced HIV or are taking other medications that can cause peripheral neuropathy. It goes away once stavudine is stopped, but can be painful and permanently debilitating if stavudine is not stopped as soon as neuropathy is noticed. Caregivers of young children should be instructed regarding noticing and reporting peripheral neuropathy. Additive lipoatrophy (facial wasting) and mitochondrial toxicities can occur when combined with Videx EC. Adverse reactions and serious laboratory abnormalities in children were similar in type and frequency to those seen in adults. Pancreatitis (inflammation of the pancreas) can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting, and blood in the urine. Risks for pancreatitis include higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Stop all HIV medications and see a health care provider right away. Your physician will check for pancreatitis by doing blood tests. People with a history of peripheral neuropathy, pancreatitis, or heavy alcohol use should avoid stavudine. Lipoatrophy, fat loss in the face and limbs (arms and legs) and, to a lesser degree, lipohypertrophy (such as “buffalo hump” and increased abdominal fat) has been associated with stavudine. Stavudine and zidovudine (Retrovir) are the HIV drugs most implicated by studies as causing lipoatrophy. Stavudine also seems to be implicated in blood lipid (fat) increases, particularly triglycerides. See chart on page 70 for potential drug class side effects.

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

More information
Stavudine is rarely used in the U.S., due to its toxicity and the availability of newer HIV 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 stavudine 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. Stavudine is associated with facial wasting, peripheral neuropathy, and pancreatitis, and many leading HIV advocates are adamant that it should be avoided because of these serious, and relatively common, toxicities. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
I can’t think of any reason to use this toxic drug anymore. Even resource-limited countries, where it has been used widely because of its low cost, are trying to move away from d4T. It can cause neuropathy, lipoatrophy, lactic acidosis, and hepatic steatosis (fatty infiltration of the liver). The originally approved dose (40 mg twice a day) was clearly too high, but while d4T might be safer at lower doses, why bother?
—Joel Gallant, MD, MPH

Activist’s comments
A very old drug, not used in the United States anymore, and with a list of toxic side effects a mile long; I would steer clear from this one. Unfortunately, it is still used in developing countries, as generics make it a financially attractive agent for cash-strapped governments trying to provide therapies for their populations. —Joey Wynn
Potential side effects and toxicity
Approximately 5–8% of people who took abacavir experienced hypersensitivity reaction (HSR, an allergic-like reaction). A simple and inexpensive blood test for HLA-B*5701 (a genetic marker) can identify patients at risk for this reaction and virtually eliminate HSR. If the HLA-B*5701 test is positive, this means that you will likely have the HSR if you start taking abacavir, and an allergy to it should be entered in your medical record even if you have never taken abacavir in the past. If you start abacavir without having the HLA-B*5701 test done, you should be monitored closely the first 6 weeks or so (HSR occurs usually within the first 6 weeks). If you develop the HSR reaction, treatment with abacavir will be stopped and you can never take abacavir or any other product containing abacavir, such as Epzicom or Trizivir, again (called “re-challenging”). Re-challenging can cause a rare life-threatening 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 of HSR usually worsen, very slowly, with every dose. People who think they are experiencing HSR must be evaluated by an experienced HIV provider right away before they stop taking abacavir. Symptoms resolve quickly (24–48 hours) after permanent discontinuation. Symptoms usually, but not always, include some combination of fever; muscle ache; malaise (general ill feeling); severe nausea, vomiting, diarrhea, or abdominal pain; severe tiredness; respiratory symptoms (cough, difficulty breathing, and sore throat); and possible rash. Symptoms are listed on the patient information sheet and warning card that you receive each time you fill your prescription. You should keep the warning card with you. HSR might be confused with flu during flu season, but remember that HSR worsens with every dose. Check with your doctor if you have any side effects after taking this medicine—don’t just stop! See “More information.” More common side effects may include nausea, vomiting, diarrhea, fatigue, headache, fever, rash, trouble sleeping, unusual dreams, and anorexia (loss of appetite). Some observational studies seemed to indicate that abacavir may increase the risk of cardiovascular events, including heart attacks, in people with greater risk factors (such as smoking, diabetes, high blood pressure, and drug use). One possible explanation was found—people with kidney problems were put on abacavir in order to avoid Viread (tenofovir), which has potential for kidney toxicity and those people already had a strong risk for heart problems. The FDA conducted an analysis of 26 randomized clinical trials that evaluated abacavir. This analysis did not show an increased risk of heart attacks associated with the use of abacavir. Last year, DHHS HIV treatment guidelines added the statement, “to date, no consensus has been reached either on the association of [abacavir] use with MI [myocardial infarction, or heart attack] risk or a possible mechanism for the association.” People who have high risk for heart disease are monitored more closely and the decision to stop or never start a regimen containing abacavir is up to you and your provider. See chart on page 70 for potential drug class side effects.

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

More information
The manufacturer recommends that people with symptoms of acute respiratory disease consider HSR even if another diagnosis such as pneumonia, bronchitis, or flu is possible. Do not use a skin patch test to confirm HSR. Dose adjustment is needed in people with mild liver disease and the oral solution will need to be used in these patients. There are no data in people with moderate/severe liver disease and therefore it should not be used in those individuals. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
Ziagen is a well-tolerated drug that is typically combined with 3TC (see Epzicom), or less commonly with 3TC and AZT (see Trizivir). While it has few side effects, it can cause a potentially dangerous hypersensitivity reaction (HSR) in some people. Fortunately, we now have a blood test, HLA B*5701, that accurately predicts who will develop this reaction and who won’t. The test should always be ordered before starting abacavir, and people with a positive test should never take abacavir in any of its forms (Ziagen, Epzicom, or Trizivir). There is controversial evidence linking abacavir with an increased risk of heart attack. This evidence comes from several large observational studies, but the association hasn’t been seen in several other large studies, and no one knows what the mechanism of the association would be. Experts disagree on whether abacavir increases cardiac risk or not, but most agree that until we know for sure, it’s best to avoid the drug in people with coronary heart disease or multiple risk factors for heart disease. The comparison of Ziagen and Viread for initial therapy is discussed under Epzicom and Truvada. —JOEL GALLANT, MD, MPH

Activist’s comments
Starting out as a popular once-daily drug, Ziagen has also fallen out of favor. Like so many pop singers and boy bands in the music industry, this drug came out with much fanfare, and ended up in the doghouse. A potentially fatal hypersensitivity reaction was reported, as well as several clinical trials identifying abacavir as possibly increasing the risk of cardiac events for some people. With all of these limitations and potentially dangerous possibilities, this drug is usually passed over for far less worrisome options. —JOEY WYNN
**Edurant**

**BRAND NAME**

**rilpivirine hydrochloride (rilpivirine), or RPV**

**GENERIC NAME**

**CLASS:** Non-nucleoside reverse transcriptase inhibitor (non-nucleoside, NNRTI, or non-nuke)

**MANUFACTURER:** Janssen Therapeutics | (877) JANSSEN (526-7736), www.janssenthoughertics.com

**AWP:** $804.39 / month

**STANDARD DOSE:** One 25 mg tablet once daily with a meal of at least 400 calories. Take missed dose as soon as possible with a meal, unless it is closer to the time of your next dose. Do not double up on your next dose.

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### Potential side effects and toxicity

Insomnia, headache, rash, and depressive disorders (depression, negative thoughts, and suicidal thoughts or actions). When looking at pooled data of the two Phase 3 studies (ECHO and THRIVE), Edurant had significant tolerability advantages when compared to Sustiva. There were lower rates of discontinuation due to side effects. Edurant also has a favorable lipid profile when compared to Sustiva. There were minimal increases in LDL (“bad” cholesterol), total cholesterol, and triglycerides. See chart on page 70 for potential drug class side effects.

### Potential drug interactions

Non-nukes interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with Complera, which already has Edurant in it. Do not take with Sustiva, Atripla, Intellence, or Rescriptor. Antacids should be taken two hours before or at least four hours after an Edurant dose. H2 receptor antagonists, such as Pepcid, Tagamet, and Zantac, should be taken 12 hours before or four hours after an Edurant dose. Proton pump inhibitors, such as Nexium, Prevacid, and Prilosec, should not be taken. Cannot be taken with the anti-seizure medications carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the anti-TB drugs rifabutin, rifampin, and rifapentine; or the herb St. John’s Wort. Do not take with more than one injectable dose of the steroid dexamethasone; repeated topical use is okay. Clinically monitor the anti-fungals fluconazole (Diflucan), itriconazole (Sporonox), ketoconazole (Nizoral), and itraconazole (Sporanox), posaconazole, and Vfend; dose-adjustment for these medications may be needed. Use azithromycin when possible instead of the antibiotics Biaxin, erythromycin, and troleandomycin (Tao). Methadone levels are reduced slightly and patients should be monitored for symptoms of withdrawal. Should be used with caution when taken with medications with a known risk of Torsade de Pointes or QT prolongation (these are abnormal heart rhythms and can make the heart stop).

### More information

Approved by the FDA in 2011 for adults who have not taken HIV medications before, as a stand-alone medication and in a fixed dose pill with Truvada (one pill, once-a-day regimen—see Complera) as well. Studies ECHO and THRIVE showed that Edurant is non-inferior (a term used in scientific research that means the drug is no worse nor better than those it’s compared to) to Sustiva in efficacy—84% vs. 82% of patients achieved a viral load of less than 50 copies/mL (undetectable) and CD4 count increases of 190 vs. 172 when comparing Edurant and Sustiva, respectively. Although individuals were less likely to stop treatment due to side effects on Edurant vs. Sustiva, they were more likely to experience virologic failure on Edurant (9% vs. 4.8% for Sustiva at 48 weeks), and their HIV was more likely to develop drug resistance mutations when compared to Sustiva. Of those with virologic failure, a new NRTI resistance mutation was developed by 68% vs. 32% and a new NNRTI resistance mutation was developed by 63% vs. 54% respectively. More cross-resistance to Intellence, Sustiva, and Viramune was seen with Edurant treatment failures than with Sustiva failures. These findings can be explained in part by looking at an individual’s baseline viral load and their adherence to medication. With the combination of high viral load (more than 100,000 copies/mL) and poor adherence, individuals in the study were three times more likely to experience virologic failure with Edurant when compared to Sustiva. The 25 mg Edurant dose was selected because the 75 mg and 150 mg doses studied were associated with a risk of abnormal heart rhythm (prolonged QT interval). While its tolerability and safety profiles are advantages for Edurant, the greater potential for virologic failure and cross-resistance to the other NNRTIs compared to Sustiva puts Edurant at a disadvantage for first-time treatment, since people may not be able to switch to another NNRTI if their HIV develops NNRTI resistance mutations with Edurant. For proper absorption, it must be taken with a meal that you chew. Nutritional drinks, even high-calorie protein shakes or products like Ensure, won’t be enough. Taken with a meal. The amount of fat doesn’t matter. Meal examples include two slices of whole wheat toast with peanut butter, fresh fruit, and orange juice; a roast beef sandwich on a hard roll with mayo and cheese; and two cups of spaghetti with marinara sauce and a slice of bread. Edurant is a tiny pill about the size of a baby aspirin. While Sustiva is associated with a risk of birth defects, Edurant is Pregnancy Category B (found safe in animal studies), but no studies in humans have been conducted, and Edurant should be used in pregnancy only if the potential benefit justifies the potential risk. (Most HIV medications are Pregnancy Category B.) See package insert for complete information on potential side effects and drug interactions.

### Doctor’s comments

Edurant was approved for initial therapy by the FDA in 2011, followed by approval of Complera, a single-tablet combination of rilpivirine, tenofovir, and FTC. The combination of Edurant plus two NRTIs was shown to be better tolerated than Atripla in two large clinical trials. Overall results were similar, but Atripla was somewhat more effective in people with viral loads above 100,000, and there was more virologic failure and resistance, including cross-resistance to Intellence, in people who took Edurant. Current guidelines list Edurant-based regimens as “alternatives” to the preferred regimens. Edurant must be taken with a full meal and should not be taken with drugs that reduce stomach acid.

—JOEL GALLANT, MD, MPH

### Activist’s comments

A refreshing addition to the HIV arsenal, Edurant is a tiny pill! I haven’t heard anyone complaining of side effects yet, and most importantly, there’s been a mass migration of folks who can’t tolerate Atripla and kept having the vivid dreams. I’ve had friends switch and they are thrilled—with no side effects (yet) and labs improving for them, they’re content. Clearly not for all, and in combination, this once-daily therapy is just what the doctor ordered for many! Edurant has a niche in the rainbow of needs and situations for the people who need specialized HIV therapy.

—JOEY WYNN
**IntelenCe**  
**BRAND NAME**

**etraVirine, or ETR**  
**GENERIC NAME**

**CLASS:** Non-nucleoside reverse transcriptase inhibitor  
(non-nucleoside, NNRTI, or non-nuke)

**MANUFACTURER:** Janssen Therapeutics (800) JANSSEN (526-7736),  
www.intelence-info.com

**AWP:** $1,033.99 / month

**STANDARD DOSE:** One 200 mg tablet, or two 100 mg tablets, twice a day, with food. People unable to swallow pills can dissolve tablets in water. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

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**Potential side effects and toxicity**

IntelenCe is generally tolerable. The most common side effects include nausea, rash, and peripheral neuropathy. Drug label warns of hypersensitivity (allergic-like) reactions, which sometimes occur with liver failure, and fatality due to Stevens-Johnson Syndrome, erythema multiforme, and toxic epidermal necrolysis (TEN), all skin disorders. These are very rare side effects. The FDA advised, “Discontinue IntelenCe immediately if signs or symptoms of severe skin reactions or hypersensitivity reactions develop (including, but not limited to, severe rash or rash accompanied by fever, malaise [general ill feeling], fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis [eye inflammation], facial edema [swelling], hepatitis, and eosinophilia [increased levels of the white blood cells called eosinophils, a sign of an allergic reaction].” In addition, levels of liver enzymes called transaminases should be monitored. Rash is associated with all of the current non-nukes. See chart on page 70 for potential drug class side effects.

**Potential drug interactions**

Non-nukes interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. IntelenCe should not be taken with Sustiva, Viramune, Rescriptor, or full-dose (600 mg twice daily) Norvir (IntelenCe levels are lowered with each of these). It should not be taken with unboosted (without Norvir) PIs, or with Aviptuvirus/Norvir, Reyataz/Norvir, or Lexiva/Norvir. It can, however, be taken with Prezista/Norvir, Kaletra, and Invirase/Norvir. It can be taken with the integrase inhibitor Isentress. Taking it with Selzentry requires a Selzentry dose adjustment to 600 mg twice daily when used without a boosted PI. Adjust Selzentry dose to 150 mg twice daily if taken with both IntelenCe and Prezista 600 mg/ Norvir 100 mg twice a day. In people who’ve failed therapy with other NNRTIs, IntelenCe should not be taken only with NRTIs. Do not take with Dilantin (phenytoin), phenobarbital, rifampin, Tegetrol (carbamazepine), and the herb St. John’s wort. Use with caution when combined with antifungals (fluconazole and voriconazole). Monitor the effectiveness of Coumadin (warfarin) and adjust dose if needed. Alternatives to Plavix should be considered when used with IntelenCe. Biaxin (clarithromycin) may be used in cases of MAC (a form of tuberculosis), in which alternatives like azithromycin should be considered. Do not take IntelenCe with Mycobutin if you’re on a Norvir-boosted PI. If you’re not, Mycobutin dose should be 300 mg once daily. No interaction was found between IntelenCe and acid suppressants (Prolosec, Zantac, and others). IntelenCe can be safely combined with methadone. IntelenCe can also be safely combined with Viagra, Cialis, and Levitra, though a higher dose of these drugs may be needed to achieve the same clinical effect.

**More information**

IntelenCe is a very important addition to the NNRTI class. The older NNRTIs can develop resistance quickly, and with only one mutation in the virus. In fact, some individuals in the U.S. are newly infected with an NNRTI-resistant virus. The second-generation NNRTI IntelenCe was developed to have a higher genetic barrier to drug resistance. It is not approved for people taking HIV therapy for the first time, although that use is still being explored and small studies to date have shown good efficacy and safety in comparison to Sustiva-based regimens. It has shown significant viral load reduction in people with drug resistance to Sustiva or Viramune, although it may work better in Sustiva failures (where the HIV mutation K103N is more likely present, and which does not affect IntelenCe activity). In patients who have experienced virologic failure on an NNRTI-containing regimen, do not use IntelenCe in combination with only a nucleoside backbone. Janssen has another NNRTI for treatment-naive people (first time on HIV therapy); see Edurant. Some physicians are prescribing IntelenCe once daily to increase adherence, although not FDA approved, based on supportive data. Some patients complain of hard-to-swallow large chalky pills. Those unable to swallow the tablets can stir them in a glass of water until the tablets are completely dissolved and then drink the solution. Rinse the glass with water a few more times and swallow the rinse each time to make sure you get the full dose. The new 200 mg tablets are also dispersable, and decrease pill burden. Comparative studies between the 100 mg and 200 mg tablets showed a high rate of patient preference for the 200 mg tablets because they were easier to swallow. See package insert for more complete information on potential side effects and interactions.

**Doctor’s comments**

IntelenCe is a true “second-generation” agent, in that it often works after Viramune or Sustiva have failed. There are some exceptions: People who continued to take NNRTIs (especially Viramune) long after their virus had developed NNRTI resistance may have cross-resistance to IntelenCe. But IntelenCe will be active for the majority, and fortunately, it’s a safe and well-tolerated drug, which has recently been made simpler by the approval of a 200 mg tablet, which is taken twice a day. IntelenCe tablets can be a little chalky, and people who aren’t good at quickly swallowing pills sometimes complain that they start to dissolve before they’ve been swallowed. One way of dealing with this is to dissolve them in water, and then drink the water with your other pills. Taking the entire dose once a day is probably okay because of the long half-life of the drug, but it hasn’t been studied or approved for once-daily dosing. IntelenCe is usually combined with a boosted protease inhibitor, but can’t be given with all of them because of drug interactions. It’s been best studied in combination with Prezista/Norvir.

—JOEL GALLANT, MD, MPH

**Activist’s comments**

One of the newer non-nukes, IntelenCe is useful, but an “also ran” for me. It will go down in history as the “just in time” life preserver for many people. It was a new option along with Isentress and Prezista for many salvage clients needing a new “breath of life” in their therapies. Along with most of the newer agents, it has a low pill burden, few side effects (most notably rash), and is still effective when other non-nukes have bit the dust. Without the vivid dreams/CNS problems of Sustiva, and lacking the lipid problems too, it has enough useful characteristics to stay in play for a few years to come. —JOEY WYNN
Rescriptor
BRAND NAME
delavirdine, or DLV
GENERIC NAME

CLASS: Non-nucleoside reverse transcriptase inhibitor
(non-nucleoside, NNRTI, or non-nuke)
MANUFACTURER: ViiV Healthcare | www.viivhealthcare.com, (877) 844-8872
AWP: $381.89 / month for 200 mg tablets

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. Take with or without food, but again, avoid grapefruit juice. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

Potential side effects and toxicity
Most common side effects are 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 one to three weeks after starting Rescriptor. If you experience blistering, mouth lesions, conjunctivitis (redness or inflammation of the eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever, or malaise (general ill feeling), you should stop the medication, and seek medical attention right away. See chart on page 70 for potential drug class side effects.

Potential drug interactions
Non-nukes interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. You should not take Rescriptor with Halcion (triazolam), migraine medicines in any form, OraP (pimozide), oral Versed (midazolam), Xanax (alprazolam), or the herb St. John’s wort. Do not use Mevacore, Vitorin, or Zocor cholesterol (lipid) lowering meds; suggested alternatives are Lescol (fluvastatin), Lipitor (atorvastatin), and Pravacol (pravastatin). Liver enzymes should be checked regularly if you are on these cholesterol meds, as they can increase risk for liver toxicity with Rescriptor.

Rescriptor needs stomach acid in order to be absorbed correctly. Over-the-counter antacids, like Tums or Maalox, decrease absorption of Rescriptor, so take it one hour apart from these remedies. Other acid-reducing drugs (like Zantac, Tagamet, and Prilosec) may also reduce absorption of Rescriptor—try not to take them together for long periods of time. People with low stomach acid should take Rescriptor with acidic beverages (orange or cranberry juice, etc.) to increase acidity. Certain amphetamines and antiarrhythmic drugs should not be used with Rescriptor—therefore, inform your health care provider if you have a history of heart or blood pressure problems. Dose adjustment may be needed when taken with Biaxin (clarithromycin) if you have decreased kidney function. Rescriptor should be used with caution with Procardia or Adalat (nifedipine), Norvasc (amlodipine), Plendil (felodipine), Coumadin (warfarin), and quinidine. Use caution with anti-convulsants: Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Mycobutin (rifabutin) and Rifadin (rifampin), used to treat tuberculosis, increase Rescriptor levels.

Rescriptor is not recommended with either rifampin or Mycobutin. Rescriptor increases levels of protease inhibitors Crixivan, Lexiva, Invirase, Kaletra, Norvir, and Viracept, as well as immunosuppressants (including transplant drugs), birth control pills (ethinyl estradiol), and methadone, so caution is advised if using together. Cialis, Levitra, and sildenafil (Viagra) levels are increased by Rescriptor; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Also, increased levels of trazodone can occur with Rescriptor and therefore should be used with caution. Increased levels of the inhaled and nasal sprays that contain fluticasone, a steroid for asthma or allergies (found in Advair, Flonase, and Flovent) can occur with Rescriptor which can result in Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes), and therefore should not be used unless no other options are available.

More information
Very rarely used due to its three-times-a-day dosing, it has not been compared to the newer NNRTIs and the studies done with Rescriptor included the older NRTIs (Retrovir, Videx, Hivid, EpiVir) with only 45% of patients achieving a viral load of less than 400 copies/mL. Research demonstrates that smaller doses of Rescriptor increase blood levels of some protease inhibitors, making it unique among the NNRTIs. Some people who cannot tolerate Norvir (ritonavir) are successfully using Rescriptor instead to boost their protease inhibitor. Studies of this use, however, have not been published. A new booster medication for HIV drugs is on the way; see cobicistat. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
It’s the rare patient who takes Rescriptor anymore, not that it was ever a widely used drug. It may be less potent than other NNRTIs, was never extensively studied, and has to be taken three times a day. It was sometimes used in patients with unusual NNRTI mutations that caused resistance to Viramune and Sustiva but not to Rescriptor, but most of those patients are now taking Intensit. As with any NNRTI, Rescriptor can cause rash. It has drug interactions that are different from those of other NNRTIs: It increases levels of protease inhibitors rather than decreasing them. It was once suggested as an alternative PI booster for that reason, but no one was excited about taking a booster three times a day. —JOEL GALLANT, MD, MPH

Activist’s comments
I’ve never met a single person on this drug, and I don’t have much to say about it. Relegated to the dark dusty corners of the HIV regimen history books, I guess. Next! —JOEY WYNN
Sustiva
BRAND NAME

efavirenz, or EFV
GENERIC NAME

CLASS: Non-nucleoside reverse transcriptase inhibitor
(non-nucleoside, NNRTI, or non-nuke)

MANUFACTURER: Bristol-Myers Squibb | www.sustiva.com; (800) 321-1335

AWP: $729.99 / month for 600 mg tablets

STANDARD DOSE: One 600 mg tablet, once a day, typically at bedtime, on an empty stomach or with a light, low-fat snack. Is also available in smaller 50 mg and 200 mg capsules. Approved for children 3 years and older. Strawberry/mint flavored solution available for children under expanded access program. Take missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose.

Potential side effects and toxicity
Central nervous system (CNS) or psychiatric symptoms (dizziness, insomnia, impaired concentration, drowsiness, abnormal dreams, hallucinations, severe depression, suicidal thoughts or actions, aggressive behavior, paranoic reactions, and manic reactions). These symptoms typically diminish within four weeks. Patients with a history of drug or alcohol use, psychiatric illness, or who are taking psychiatric medications may be at an increased risk for these reactions. Other side effects may include rash, nausea, vomiting, diarrhea, fever, and increased liver enzymes. These symptoms may occur early and generally resolve within two to four weeks. Rash is more common, and more severe, in children, as are low levels of some blood cells. May raise levels of triglycerides and cholesterol. May lead to false positive urine tests for use of marijuana, but more specific tests can differentiate between marijuana and Sustiva. Women taking Sustiva should not become pregnant or breast-feed. See “More information.” Increases in liver enzymes in people with hepatitis B and/or C may occur and should be monitored. Use with caution in people with mild liver impairment; not recommended for people with moderate or severe liver impairment. See chart on page 70 for potential drug class side effects.

Potential drug interactions
Non-nukes interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with Atipra, Compliera, Edurant, Intellence, Rescriptor, or Viramune. Do not take the following medications with Sustiva: midazolam, triazolam, pimozone, bepridil, or Biaxin, or the herbs St. John’s wort and Gingko biloba. Sustiva may affect Coubamid (warfarin) levels. Sustiva decreases metha- done levels; dose adjustment may be necessary to avoid withdrawal symptoms. Increase Kaletra to three tablets twice daily with food (recommended) when taken with Sustiva in treatment-experienced people. Kaletra cannot be taken once daily with Sustiva. Monitor liver enzymes closely if Sustiva and Norvir are used together. Reyataz once-daily dose should be higher (400 mg) and also boosted with Norvir when taken with Sustiva, but treatment-expe- rienced people should not take this combination at all. With once-daily Lexiva, boost with 300 mg Norvir. Rifampin decreases Sustiva levels, so increase the Sustiva dose to 800 mg once daily for people weighing 110 pounds or more. Rifabutin can be used as an alternative to rifampin but double the dose. When taken with anticonvulsants Dilantin, phenobarbital, or Tegretol, periodic monitoring of blood levels of anticonvulsants and Sustiva should be done or alternative anti-seizure medications considered. Effectiveness of birth control pills may be decreased; consider the use of additional or alternative contraceptive methods. The maintenance dose of Noxafil, Sporanox, and Vfend should be increased to 400 mg every 12 hours and the Sustiva dose should be decreased to 300 mg once daily using the capsule formulation. Levels of immunosuppressants (used in transplants, specific types of arthritis, and autoimmune conditions) can be decreased and should be monitored when starting or stopping Sustiva. When taking Sustiva with Zolof, Lipitor, pravastatin, simvastatin, and diltiazem, their dosages may need to be adjusted. The levels of bupropion and sertraline are lowered; titrate dose based on clinical response. Sustiva can decrease levels of buprenorphine. No dose adjustment is recommended, but monitor for withdrawal symptoms. Sustiva can decrease the effects of Malarone; consider alternative drug. Avoid taking Sustiva with the hepatitis C drug Victrelis (boceprevir), as Sustiva lowers Victrelis concentrations.

More information
According to current guidelines for adults and adolescents, Sustiva is the preferred NNRTI drug for NNRTI-based regimens. Avoid driv- ing or operating heavy machinery for a few hours after dose. Some people adjust to Sustiva by taking Ativan or Ambien to sleep for the first few weeks, though you may feel even more groggy the next morning. If you can’t sleep, ask about switching the timing of your dose little by little until you’re taking it in the daytime. Based on the HIV pregnancy registry, very few infants born to women who have become pregnant while on efavirenz have had birth defects. Most birth defects occurred when exposure to efavirenz was in the first trimester. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
Ten years after its approval in 2002, Sustiva (as well as Atipria, the combination of efavirenz, tenofovir, and emtricitabine) remains a pre-ferred drug in all treatment guidelines. Besides its excellent potency and long-term safety, it also has a very long half-life, which makes it forgiving of missed or delayed doses (not that you would ever miss or delay a dose!). Its flaws, however, include “neuropsychiatric” side effects (dizziness, vivid dreams or nightmares, difficulty concentrating, and mood changes) and allergic rashes, all of which are common during the first few weeks, though they generally go away without having to stop the drug. Once you’ve been on Sustiva for three to four weeks, it’s usually smooth sailing, though it can raise lipid levels. When starting Sustiva or Atipria, take it in the evening on an empty stomach (at least two hours after dinner) to minimize side effects. Start it on a weekend or on an evening when you have nothing important to do for the next few mornings. In most cases, things get better with each dose, so stick with it. But if you don’t feel like your normal self after a month on Sustiva or Atipria, it’s time for a change. Some people may have persist-ent neurologic side effects, including depres- sion. It’s easy to become resistant to Sustiva, so don’t stop this drug unless you’re replacing it with something else. Sustiva can cause birth defects; pregnant women should avoid it during the first trimester. —JOEL GALLANT, MD, MPH

Activist’s comments
Sustiva is the king of the non-nukes! This powerhouse has major benefits and major downsides. Convenient once-daily dosing of Sustiva has been studied more than any other drug, and has beaten the best of them in terms of durability and effectiveness. All is not rosy though, as the downside is pretty scary for those with side effects. It can cause vivid dreams, nightmares, depression, out of range levels for lipids, cholesterol, and even risk of possible bone problems down the road make this drug not suitable for everyone. It has meal restrictions and definitely cannot be taken by women who are pregnant or thinking about having children. —JOEY WYNN
Viramune XR and Viramune

BRAND NAME

CLASS: Non-nucleoside reverse transcriptase inhibitor (non-nucleoside, NNRTI, or non-nuke)

MANUFACTURER: Boehringer Ingelheim | www.viramunexr.com, (800) 274–8651

AWP: $632.68 for XR / month, $133.02 for 240 mL suspension (50 mg/5 mL)

STANDARD DOSE: One 200 mg IR (immediate release) tablet once daily for two weeks, then full dose of one 400 mg once daily for Viramune XR or one 200 mg tablet twice daily for Viramune, with or without food, with no dietary restrictions. Viramune is frequently prescribed as two 200 mg tablets once daily, although once-daily dosing is not FDA approved with the IR formulation. Viramune XR once daily is approved only for adults. Dose for children 15 days or older is 150 mg/m² once daily for 14 days, then 150 mg/m² twice daily thereafter, not to exceed 400 mg daily. Take missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose. If you interrupt therapy for more than seven days, you will need to restart with 200 mg IR daily for 14 days, followed by 400 mg XR daily or 200 mg IR twice daily. For dialysis patients, an additional dose of 200 mg IR is required after each dialysis. A 50 mg/5 mL oral suspension is also available.

Potential side effects and toxicity

Most common side effects include headache, nausea, vomiting, fever, and rash (reduced with 14-day lead-in dosing). Severe rash, including Stevens-Johnson syndrome, while rare, can be life-threatening; notify your health care provider immediately. Seek medical attention right away if you experience blistering, mouth sores, conjunctivitis (redness or inflammation of the eye, or pink eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever, or malaise (general ill feeling). Do not increase dose if rash develops during dose escalation or if it is accompanied by the conditions listed above. Once-daily lead-in dose should not exceed 28 days. An alternative drug should be considered at this time. An increase in liver enzyme levels has been observed and in rare instances, hepatitis has developed. In such cases, it may be necessary to stop taking Viramune (either formulation) until liver function returns to normal. Permanently discontinue it if abnormalities return. Rarely, severe and life-threatening liver damage, including fatal cases, has occurred. Women with CD4 counts greater than 250 T-cells, including pregnant women have the highest risk of serious liver damage, though men with more than 400 T-cells are also at risk. The package insert says Viramune or Viramune XR should not be started in these groups unless the benefit outweighs the risk. The highest risk period is within the first six weeks of treatment, but patients should be monitored closely for the first 18 weeks. See chart on page 70 for potential drug class side effects.

Potential drug interactions

Non-nukes interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with Atripla, Complera, Edurant, Intelence, Rescriptor, Reyataz, Sustiva, or St. John’s wort. Rifampin should not be used with Viramune; Mycobutin (rifabutin) is the recommended alternative to rifampin for tuberculosis treatment. Use with caution with midazolam, triazolam, cisapride, fluconazole, or Cordarone, lidocaine or disopyramide, ethosuximide, clonazepam, calcium channel blockers (Procardia and others), immunosuppressants (including transplant drugs), and Coumadin (warfarin). Do not use with Biaxin or Nizoral. Viramune decreases methadone levels; dose adjustment may be necessary to avoid withdrawal symptoms. Can reduce levels of protease inhibitors; dose adjustment may be needed if they are taken together. Kaletra should be increased to three tablets twice a day in treatment-experienced people. Use caution with anti-convulsants: Dilantin, phenobarbital, and Tegretol. Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception. During the first six weeks of therapy, prednisone should be avoided; it can cause increased severity and incidence of rash.

More information

The once-daily Viramune XR was FDA approved in 2011, but many providers already prescribe once-daily dosing with the old formulation. The regular Viramune (IR) formulation may go generic (nevirapine) this year. Monitor liver function and signs of rash during first six months. Do not ignore yellowing of your eyes or skin, as this may be a sign of a severe liver effect. Studies show that nevirapine 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. Viramune should not be used for PEP (post-exposure prophylaxis). Viramune has been shown to have a positive impact on triglycerides and cholesterol levels. When taken 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 taken alone. The use of at least one other HIV drug helped to cut down the incidence of resistance. Single- or double-dose Viramune may be used for babies born to HIV-positive mothers. Mothers should not breast-feed their infants while taking Viramune. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments

Viramune is a component of the vast majority of first-line regimens worldwide, in part because of the low cost of generic nevirapine. It has not been as popular in the United States, however, in part because of the stronger clinical data with Sustiva, but also because of its greater early toxicity. It’s listed as an “acceptable” NNRTI in the DHHS guidelines and an “alternative” in the IAS-USA guidelines. Viramune can cause skin rashes and liver toxicity during the first few weeks, which can be severe and even life-threatening. The risk is greatest when it’s started in people with high CD4 counts: above 250 in women and above 400 in men. Below those CD4 thresholds, the risk is low, and the long-term safety is excellent, with less lipid elevation than with Sustiva. Viramune should be started at half-dose (200 mg once daily) and increased to the full dose (400 mg twice daily) after two weeks only if there is no rash or liver enzyme elevation. Viramune XR, a new 400 mg single tablet, once-daily formulation, was approved last year. Compared to Sustiva, resistance to Viramune is somewhat more likely to cause cross-resistance to Intelence.

—JOEL GALLANT, MD, MPH

Activist’s comments

The softer, gentler none-nuke, Viramune is now a “once-daily” XR (extended release) formula. This reformation helped this drug maintain some market share from moving over to the generic version. Clinical studies showed that people who were undetectable on another regimen could safely switch to Viramune. Many in Florida have switched safely to this lipid-friendly drug (better at maintaining normal levels of cholesterol and triglycerides), so this drug has a niche for those who can’t tolerate Sustiva-based regimens or Atripla. However, with so many new drugs with fewer pills and fewer side effects, I have a feeling this drug’s day as a mainstay are numbered.

—JOEY WYNN

FOR THE LATEST INFORMATION ON VIRAMUNE AND VIRAMUNE XR, GO TO positivelyaware.com/viramune
Aptivus
BRAND NAME

tipranavir, or TPV
GENERIC NAME

CLASS: Protease inhibitor (PI)
MANUFACTURER: Boehringer Ingelheim | www.aptivus.com, (800) 542-6257
AWP: $1,420.09 / month; $419.84 for 95 mL bottle of solution

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 formulations available for children ages 2 years and older. Must take with food when using Norvir tablets; no food restrictions with Norvir capsules, but preferably taken with food to improve Norvir tolerability. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

Potential side effects and toxicity
Aptivus contains a sufa component, so use cautiously in patients with sufa allergies. Mostly gastrointestinal-related: mild diarrhea, nausea, vomiting, abdominal pain, and fatigue. Other side effects may include headache, fever, dry mouth, and dizziness. Rash, including sensitivity to the sun, has occurred (most commonly among children). Some patients who developed rash also had one or more of the following: joint pain or stiffness, throat tightness, generalized itching, muscle aches, fever, redness, blisters, or peeling skin. Women taking birth control pills may be at higher risk for rash. If a severe rash occurs, Aptivus should be discontinued. Stop using Aptivus if rash appears with the symptoms of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Aptivus can lower blood levels of Intence. Zidagen, Vidi EX, and Retrovir (zidovudine) and they should not be combined. Take Vidi EX and Aptivus two hours apart. Aptivus should not be taken with other protease inhibitors because it greatly lowers their blood levels. Lowest level of Aptivus is increased 45% with Fuzeon, but dose adjustments are not recommended. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception. Methadone doses may need to be increased. Buprenorphine/naloxone (Suboxone) can decrease Aptivus levels significantly; consider monitoring Aptivus levels, but dose adjustments are not recommended. 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 (warfarin). Tegretol, Dilanthin (phenytoin), or phenobarbital may increase Aptivus levels, so alternate seizure medications should be used and monitoring of Aptivus levels is recommended. Caution should be used with valproic acid, which may be less effective due to decreased concentrations. Use caution when taking itraconazole or fluconazole. Rifampin should not be used; reduced dose and frequency of Mycobutin is the recommended alternative for the treatment of TB. Use with caution with bosentan, salmeterol, immunosuppressants (including transplant drugs), and colchicine (lower colchicine dose). Norvir and Aptivus capsules contain alcohol (but should not be enough to trigger relapse); so be cautious with Antabuse (disulfiram) or Flagyl. Oral solution contains vitamin E; do not take additional vitamin E beyond that found in a multivitamin. Antacids can decrease levels of Aptivus. Aptivus should be taken two hours before or one hour after antacids. Aptivus decreases Prilosec (omeprazole) concentrations and Prilosec dose may need to be increased. Use of the hepatitis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

Potential drug interactions
PIs interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist of the medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with alfuzosin, Revatio, T ambocor, Vii tidz, Cordarone (amiodarone), Quinidine, or the herb St. John’s wort. Do not use Advicor, Altoprev, Norvir, or the discontinued Agenerase, for example, may have Prezista cross-resistance but will still respond to Aptivus. For that reason, it’s always important to make the choice of a second-line PI based on resistance testing.

—JOEL GALLANT, MD, MPH

Doctor’s comments
Aptivus is a “second-generation” PI, meaning that it’s often active against PI-resistant virus. However, it is not widely used, mainly because of the availability of Prezista, which is safer, better tolerated, and is active against a wider range of PI-resistant virus. Aptivus causes more lipid elevation and liver toxicity than other PIs, possibly because it requires a higher boosting dose of Norvir (200 mg twice a day). However, there are some situations in which Aptivus is a better choice than Prezista. People who developed resistance to Lexivita or the discontinued Agenerase, for example, may have Prezista cross-resistance but will still respond to Aptivus. For that reason, it’s always important to make the choice of a second-line PI based on resistance testing.

—JOEL WYNN

Potential drug interactions
PIs interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist of the medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with alfuzosin, Revatio, T ambocor, Vii tidz, Cordarone (amiodarone), Quinidine, or the herb St. John’s wort. Do not use Advicor, Altoprev, Norvir, or the discontinued Agenerase, for example, may have Prezista cross-resistance but will still respond to Aptivus. For that reason, it’s always important to make the choice of a second-line PI based on resistance testing.

More information
Due to its drug resistance profile, drug interactions, higher pill burden, and the need for refrigeration if the indoor temperature is too hot, Aptivus is not as popular as other PIs. It is only FDA approved for treatment-experienced patients. Take with food to minimize stomach problems. It actually lowers the blood levels of Norvir, so you may not see as many of the GI side effects. Refrigerate capsules before opening, though Aptivus can be stored at room temperature (up to 77°F), but must be used within 60 days. See package insert for details.

—JOEL GALLANT, MD, MPH

Activist’s comments
I hate to be brief, but this drug has a limited value in the HIV arsenal in this age of newer, less toxic pills. I don’t know anyone on this drug at this time, and I don’t think it is still being prescribed, unless there’s someone with a long history of taking ARVs and who is in a deep salvage situation. The increased Norvir boosting is enough to send you back to the days of high dose Norvir’s GI upsets and metallic tongue tastes. Next! —JOEY WYNN
Crixivan

**BRAND NAME**

**indinavir sulfate (indinavir), or IDV**

**GENERIC NAME**

**CLASS:** Protease inhibitor (PI)

**MANUFACTURER:** Merck and Co. | www.merck.com, (800) 850-3430

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

**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: 800 mg with 100 mg Norvir or 800 mg with 200 mg Norvir (all doses taken with food and with plenty of water to avoid kidney sludge or stones). Avoid grapefruit juice and vitamin C (more than one gram a day). Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Drink lots of non-caffeinated fluids throughout the day. See chart on page 71 for potential drug class side effects.

**Potential side effects and toxicity**

Headache, fatigue or weakness, malaise (general ill feeling), nausea, diarrhea, stomach pain, loss of appetite, yellowing of skin/eyes, changed skin color, dry mouth/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. Crixivan has also been associated with hemolytic anemia (premature destruction of red blood cells) and it should be stopped once the anemia is diagnosed. See chart on page 71 for potential drug class side effects.

**Potential drug interactions**

PIs interact with many other drugs. See the package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with alfuzosin, Revatio, Tambocor (flecainide), Rythmol (propafenone), Cordarone (amiodarone), oral Versed (midazolam), triazolam, rifampin, pimozone, garlic supplements, or the herb St. John’s wort. Do not use Advicor, Altopen, Livalo, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects from these medications. Not recommended in combination with Reyataz. Reduce Crixivan to 600 mg every eight hours when taken with Rescriptor. Itraconazole (200 mg twice a day), or ketoconazole (200 mg once a day). The dose of Mycobutin should be reduced to 150 mg daily or 300 mg three times a week and Crixivan dose increased to 1,000 mg every eight hours or use Norvir-boosted dose when taken together. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception. Additional monitoring may be required when taking Coumadin (warfarin) or calcium channel blockers (such as Norvasc, Procardia, and others). Use caution with anti-convulsants: Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Crixivan may decrease levels of methadone and methadone may need to be increased, but withdrawal rarely occurs. Also, increased levels of trazodone can occur with Crixivan. Increased levels of the inhaled and nasal sprays with fluticasone (found in Advair, Flonase, and Flovent) can occur with Crixivan; use only if the benefits outweigh the risks, and monitor for signs of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometime diabetes). Alternatives should be considered, particularly for long-term use. Use with caution bosentan, salmeterol, immunosuppressants (including transplant drugs), and colchicine; use lower dose of colchicine. Use of the hepatitis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

**More information**

Very rarely used. Drink at least 48 oz. of fluids daily, preferably water or clear liquids (soda pop doesn’t count!) to decrease the chances of kidney stones. Don’t forget to drink more water in summer or with increased sweating. Large amounts of coffee or alcohol can increase risk of stones due to increased dehydration. Stones may continue after stopping Crixivan. Store in original container and keep dry. See package insert for more complete information on potential side effects and interactions.

**Doctor’s comments**

Crixivan deserves our undying gratitude for having saved many lives in the late ’90s, but it’s now a drug of purely historical importance. Side effects included kidney stones or kidney failure, diabetes, lipid changes, dry skin, chapped lips, ingrown toenails, and possibly body-shape changes (the dreaded “Crix belly,” for example). When taken without Norvir boosting, its dosing schedule was unforgiving and complex: when boosted by Norvir, it just became more toxic. Avoid it.

—JOEL GALLANT, MD, MPH

**Activist’s comments**

This miracle drug will go down in history as a game changer. People went from just staying alive to living with HIV. Although at the time, it was too many horse pills, too much water to drink, and still all kinds of side effects, but we dealt with it. Today, it is very rarely used, only by those still on it from back in the day who think “if it ain’t broke, don’t fix it!” I convinced someone three months ago to switch off of it to a newer regimen, and he thanked me two months later, as it really was a difficult regimen, both in managing side effects and pill burden. Thanks, Crixivan, you’ll always be remembered for that crossroads. —JOEY WYNN
**Potential side effects and toxicity**

Most common are diarrhea, abdominal discomfort, vomiting, and nausea. Drug label warning states that Invirase/Norvir may change the electrical activity of the heart, which may lead to abnormal heart rhythms called prolonged QT or PR intervals. People with underlying heart conditions, who have heart rate or heart rhythm problems, or low potassium or magnesium levels, are at greater risk. Symptoms may include lightheadedness and fainting. A medication guide is now required with a prescription. See chart on page 71 for potential drug class side effects.

**Potential drug interactions**

PIs interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Viramune, Sustiva, and Mycobutin (rifabutin) decrease Invirase levels. Not recommended to be used with Aptivus/Norvir or Prezista. Should be used with caution and may require dose adjustment with Reyataz (additive effect on QT and PR interval prolongation may occur). Rescriptor, Crixivan, Norvir, Viracept, and Kaletra all significantly increase Invirase concentrations. No dosage change when taken with Kaletra, but additive effect on QT and PR interval prolongation may occur. Do not take with alfuzosin, Revatio, Tambocor (flecainide), Rythmol (propafenone), Biaxin (clarithromycin), dexamethasone, Cordarone (amiodarone), oral Versed (midazolam), Halcion (triazolam), Orap (pimozide), Lanzoxin (digoxin), quinidine, trazodone, Tykosyn (doxeflilide), lidocaine (systemic), garlic supplements, or the herb St. John’s wort. Colchicine levels may be increased and dose reduction is necessary. Do not use Advicer, Altopen, Livalo, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor, Lipitor, and Pravacol (pravastatin), but should be used with caution and started at the lowest dose possible; you should be monitored closely for increased side effects from these medications. Cannot be taken with rifampin. Rifabutin can be used as alternative, but its dose needs to be decreased. Methadone doses may need to be increased. Invirase increases levels of fluticasone (active component of Advair, Flonase, and Flovent); use only if the benefits outweigh the risks, and monitor for signs of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Alternatives should be considered, particularly for long-term use. Use calcium channel blockers with caution. Monitor digoxin levels; digoxin dose may need to be decreased. Use caution with anti-inflammatory agents (carbamazepine, phenobarbital, and Dilantin (phenytoin)) as these medications will decrease Invirase levels. Invirase may increase dapson levels. Invirase may alter Coumadin levels; additional monitoring may be required. Do not take with birth control pills as Invirase reduces the level of the hormone ethinyl estradiol. 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. PriLOSE, Prevacid, or any other PPI (medications used to treat acid reflux or heartburn) increase Invirase levels, therefore monitor for possible side effects from Invirase if taken together. Use with caution with bosentan, salmeterol, and immunosuppressants (including transplant drugs). Refer to the package insert for the complete guide to the drug interactions. Use of the hepatitis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

**Doctor's comments**

Saquinavir has a long and confusing history. In the form of Invirase, it was the first approved PI, but it had limited appeal because of poor absorption and low drug levels. Then came Fortovase, which was better absorbed but had more gastrointestinal side effects. The combination of Fortovase plus Norvir (initially using high doses of both drugs) was highly effective but not easy to take. Since the boosting effect of Norvir eliminated the absorption concerns with Invirase, Fortovase was eventually retired and Invirase made a small comeback, combined with lower, better tolerated doses of Norvir. In fact, it would still be a reasonable combination if it weren’t for the availability of once-daily boosted PIs (Prezista and Reyataz) that use half the daily dose of Norvir. The FDA also recently issued a warning about potentially serious EKG changes with Invirase. Saquinavir will be the first PI to go generic, though it seems unlikely that this will increase its use much, at least in the United States. —JEOl Gallant, MD, MPH

**Activist’s comments**

I believe Invirase was the first protease inhibitor, so it will have a place in the history books. “Back in the day” it had a place, though a small one—with all the meal restrictions and complications from side effects, it never really stood out in my book. All the formulations saquinavir went through just made it more difficult to keep track of where it stood in the rankings. Some folks believe it will make a comeback with the generic version, but I doubt it. However, it may get yet another life when it goes generic in developing countries, as they need to develop stronger regimens.

—JOey Wynn

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**Invirase**

**Brand Name**

**Protease inhibitor (PI)**

**Manufacturer:** Genentech | www.genentech.com, (800) 626-3553

**AWP:** $1,112.09 / month for 500 mg tablets

**STANDARD DOSE:** Two 500 mg film-coated tablets with 100 mg Norvir two times a day with food, or within two hours of a meal for patients over 16 years old. Must be taken with Norvir. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

**saquinavir, or SQV**

**Generic Name**

**CLASS:**

**MANUFACTURER:**

**AWP:**
Potential side effects and toxicity
Diarrhea is the most common and can be severe, but may be less severe with the tablets. Rash, nausea, vomiting, stomach pain, headache, muscle weakness, and elevated liver enzymes (a sign of liver damage—this may be more common in people with hepatitis B or C). See chart on page 71 for potential drug class side effects.

Potential drug interactions
Pls interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with alfuzosin, Revatio, Tambocor, Rythmol, Cordarone, oral Versed (midazolam), Halcion, Incivek, rifampin, pimozone, garlic supplements, or the herb St. John’s wort. Do not use Advicor, Altoprev, Livalo, Mevacor, Simcor, Vytorin, or Zocor for the treatment of high cholesterol. Alternatives are Crestor, Lescol, Vytorin, or Zocor for the treatment of high cholesterol. Estrogen are Crestor, Lescol, Lipitor, and Pravacol, but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects from these medications. Oral solution contains alcohol, so do not use with Antabuse or Flagyl. Use calcium channel blockers (such as Norvasc and Procardia) with caution. Dosage of methadone may need to be increased. Because of high pill burden, physicians usually prescribe three tablets a day with a day of the 200/50 mg dose when using with Sustiva or Viramune. Current guidelines state the Kaletra dose should total 500 mg lopinavir and 125 mg ritonavir twice daily when used with Sustiva or Viramune. Not recommended to be taken with Lexiva. Kaletra may lower lev-Els of Retrovir (zidovudine) and Ziaqen. Videx and Kaletra can be taken together, but without food. If Kaletra is taken with food, Videx should be taken an hour before or two hours after Kaletra. If taking Kaletra with Viread or combinations containing tenofovir, you should be monitored for side effects from tenofovir as Kaletra increases its levels. Rifabutin dosage should be reduced to 150 mg every other day (or 150 mg three times per week) when used with Kaletra. Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception. Mefpron levels may be reduced with Kaletra. Avoid Sporanox or Nizoral doses greater than 200 mg per day with Kaletra. Monitor for side effects when taken with Norvir. Decreases Vent levels. People with kidney impairment may require lower Biaxin doses with Kaletra. Blood levels of immunosuppressants should be monitored, because levels may increase. Kaletra may alter Coumadin (warfarin) levels; additional monitoring may be required. Steroids, especially Decadron, may decrease levels of Kaletra. Kaletra increases levels of fluticasone (found in Advair, Flonase, and Flovent), use only if the benefits outweigh the risks, and monitor for signs of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Kaletra increases levels of trazodone. Use caution with anti-convulsants Tegretol, phenobarbital, and Dilantin, as they may lower levels of Kaletra. Drug levels of bupropion are lowered; titrate dose based on clinical response. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Use with caution with bosentan, salmeterol, and colchicine. Kaletra can decrease the effects of colchicine. Kaletra can decrease the levels of Malarone. Use of the hepatitis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

More information
According to U.S. HIV treatment guidelines, the need for 200 mg a day of Norvir (contained in Kaletra) and the higher rate of gastrointestinal side effects compared to other PIs using 100 mg Norvir, make Kaletra an alternative for treatment-naive people. Four tablets once daily can increase side effects, especially diarrhea. Taking with food and anti-diarrheal medicine helps lessen diarrhea. Kaletra should not be taken once a day by children under 18. Kaletra solution cannot be given to premature babies until 14 days after their due date because it contains propylene glycol, which infants can not eliminate very well from their bodies. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
Kaletra transformed our use of HAART, ushering in the widespread use of Norvir-boosted PIs, not just for treatment-experienced patients, but for anyone using a PI. The advantages of boosting include less frequent dosing and a big barrier to resistance, especially if you have no PI resistance to start with. Kaletra was far easier and better tolerated than drugs like Crixivan, and more effective than Viracept, which was in common use at the time of its approval. It became the gold-standard PI and maintained that position for many years. However, Kaletra use has been declining, and it’s now considered a preferred PI only for pregnant women. It’s increasingly being replaced by Norvir-boosted Prezista and Reyataz, which can be taken once daily with just 100 mg per day of Norvir compared to 200 mg in a daily dose of Kaletra. These drugs cause less diarrhea and lipid elevation than Kaletra. Kaletra still has the advantage of being the only co-formulated PI, meaning that you don’t have to take Norvir as a separate tablet, though that’s likely to change soon with the imminent approval of cobicistat, a booster that can be more easily co-formulated with other PIs. —JOEL GALLANT, MD, MPH

Activist’s comments
Once the “lion” of the protease inhibitor class, Kaletra is no longer a preferred drug in DHHS treatment guidelines. Amazing clinical results for most helped it hold the title for quite some time, but the downsides started to weigh heavily as newer agents with fewer side effects came to market. Kaletra has interactions with many drugs, especially Viagra and some female contraceptives, plus it has the lipid problems of many of the older PIs. Pricing scandals and Abbott’s unwillingness to work with other companies to co-formulate their Norvir boosting agent with another’s drugs didn’t help with community sentiment about their products, although their co-pay cards are pretty easy to use. Kaletra remains one of the best treatments for pregnant women. Otherwise, mixed reviews at best in this day and age. —JOEY WYNN
Lexiva
BRAND NAME

fosamprenavir calcium (fosamprenavir), or FPV
GENERIC NAME

CLASS: Protease inhibitor (PI)
MANUFACTURER: ViiV Healthcare | www.viivhealthcare.com, (877) 844-8872
AWP: $947.12 / month for 60 tablets;
$133.20 for 225 mL oral suspension (50 mg/mL)

STANDARD DOSE: For people on a PI for the first time: two 700 mg tablets with either one 100 mg or two 100 mg Norvir, both once daily; or two 700 mg tablets (without Norvir), twice daily; or one 700 mg tablet with 100 mg Norvir, twice daily. For PI-experienced patients, one 700 mg tablet Lexiva with 100 mg Norvir, twice daily. Available for children ages 2 and older. For people with liver problems, the dose of Lexiva may need to be adjusted and Norvir may or may not be used depending on the degree of liver disease. A grape/bubblegum/peppermint-flavored oral suspension is also available. Can be taken with or without food, with no dietary restrictions, at any dose. Adults must take suspension without food. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

Potential side effects and toxicity
Because Lexiva contains a sulfa component, it should be used with caution in patients with allergies to sulfa drugs. The most common side effects may include nausea, rash, diarrhea, headache, and vomiting. Rash occurred in about 19% of patients, but severe rashes were uncommon. If you experience a rash, notify your doctor. For mild or moderate rashes, your doctor may choose to continue Lexiva, with close monitoring. Patients with hepatitis B or C should be monitored closely for the possibility of elevated liver enzyme levels. Dose adjustment is recommended for people with liver impairment. Side effects and laboratory abnormalities were similar when Lexiva was taken once or twice daily, with or without Norvir. See chart on page 71 for potential drug class side effects.

Potential drug interactions
Pis interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Not recommended to be taken with Kaletra. When taken with Sustiva, boost once-daily Lexiva with 300 mg of Norvir. Do not take with alfuzosin, Revatio, Tambocor, Rythmol, oral Versed (midazolam), Halcion (triazolam), rifampin, Orap (pimozide), or the herb St. John’s wort. Should not be taken with Incivek (telaprevir), because levels of both Lexiva and telaprevir are decreased. Do not use Advicor, Altoprev, Livalo, Mevacor (lovastatin), Simcor, Vytorin, or Zocor (simvastatin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacor (pravastatin), but use with caution and start at the lowest dose possible: monitor closely for increased side effects from these medications. Calcium channel blockers (Norvasc, Procardia, and others) should be used with caution and careful monitoring. Lexiva should be taken two hours before H2 blockers (Zantac, Pepcid, and others). Lexiva can lower methadone concentrations. A dose adjustment of Mycobutin (rifabutin) will be needed when used in combination with Lexiva. Steroids, such as Decadron, can decrease levels of Lexiva. Increases levels of fluticasone (found in Advair, Flonase, and Flovent); use only if the benefits outweigh the risks, and monitor for signs of Cushings’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Alternatives should be considered, particularly for long-term use. Trazodone concentrations may increase; a lower dose of trazodone is recommended. Drug levels of Paxil are lowered; titrate dose based on clinical response. Use caution with anti-convulsants Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Lexiva may alter Coumadin (warfarin) levels; additional monitoring may be required. Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception methods. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis per 72 hours or 2.5 mg Levitra per 24 hours, or 25 mg Viagra per 48 hours. Use with caution with Biaxin (clarithromycin), bosentan, salmeterol, immunosuppressants (including transplant drugs), and cochicine (lower the dose). Use of the hepatis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

More information
Last year, U.S. HIV treatment guidelines dropped Lexiva in regimens not containing Norvir as an option for first-time therapy because of inferior potency and the potential for developing cross-resistance to Prezista, a recommended protease inhibitor for first-time treatment. The lower dose of Norvir may cause less of an increase in cholesterol and triglycerides, but there are 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. An analysis from a French cohort showed Lexiva was associated with an increased risk of heart attacks, heart disease, and stroke. A liquid formula of Lexiva is available. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
Before there was Lexiva, there was Agenerase, which came in enormous, suppository-sized capsules taken at large, stomach-filling doses. The approval of Lexiva, a “pro-drug” of Agenerase, was a big improvement and it had the most versatility of any PI. It could be taken with or without food, with or without Norvir boosting, and once or twice a day. However, a comparison of twice-daily Norvir-boosted Lexiva showed no advantages over Kaletra in terms of effectiveness, safety or tolerability, and Kaletra had the advantage of co-formulation. Later, a once-daily regimen of two tablets (1,400 mg) of Lexiva with 100 mg of Norvir was approved for people who hadn’t taken PIs before, but there weren’t any clear advantages of this combination over boosted Reyataz or Prezista, which had been more extensively studied. As a result, this worthy PI hadn’t been widely used. While it’s one of the few PIs that doesn’t have to be boosted, the use of unboosted Lexiva can lead to Prezista cross-resistance, and should therefore be avoided. —JOEL GALLANT, MD, MPH

Activist’s comments
Originally released in a form known as Agenerase, this drug is an “also ran.” It has no real advantage over sturdier regimens, and it was still linked to the Norvir booster problems; it simply never caught on. I guess there may be a few reasons for a handful of folks to use it, but I’m no fan of this one. On to better choices! —JOEY WYNN
Norvir	 ritonavir
BRAND NAME

CLASS: Protease inhibitor (PI)
MANUFACTURER: Abbott Laboratories | www.norvir.com, (800) 222–6885
AWP: $314.99 / month for 30 tablets;
$1,728.24 for 240 mL oral solution (80 mg/mL)

STANDARD DOSE: Almost never used at its approved dose (a lead-in dosing, then six 100 mg tablets twice daily). Do not crush or chew tablets, always swallow whole. Norvir is primarily used as a boosting agent for other PIs (increases the levels of other PIs so that they can be taken less often), at smaller doses of 100 to 400 mg, either once or twice a day with a meal. See drug label of the other PI. Always take Norvir at the same time as the other PI prescribed by your provider. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Approved for children ages one month and older. Liquid formulation available, but it tastes horrible.

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; and alcohol intolerance. Other potential side effects are liver problems, such as an increase in liver enzymes (AST, ALT, and GGT), hepatitis, jaundice (yellowing of skin), and increased muscle enzyme (CPK) and uric acid. People with hepatitis B or C may be at increased risk. See chart on page 71 for potential drug class side effects.

Potential drug interactions
PIs interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with alfuzosin, Revatio, Tambocor, Rythmol, Cordarone, oral Versed, Halcion, Rifadin, Orap, Vfend (voriconazole), garlic supplements, or the herb St. John’s wort. Do not use Advicor, Altopen, Livalo, Mevacor, Simcor, Vytorin, or Zocor for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects from these medications. Increases levels of fluoxetine (found in Advair, Fionase, and Flovent); use only if the benefits outweigh the risks, and monitor for signs of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Trazodone concentrations may increase; a lower dose of trazodone is recommended. Norvir and Adderall may decrease levels of methadone and methadone may need to be increased, but withdrawal rarely occurs. Use caution with anti-convulsants Tegretol (carbamazepine), phenobarbital, and Dilantin (phenytoin). Use calcium channel blockers (such as Norvasc, Procardia, and others) with caution. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viaggra per 48 hours. Effectiveness of birth control pills may be decreased; consider the use of alternative or additional contraception. 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. Biaxin (clarithromycin) levels can increase by up to 80%. Use with caution with bosentan, salmeterol, and immunosuppressants; lower colchicine dose. Use of the hepatitis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

More information
The real strength of Norvir is its use with other PIs as a boosting agent, allowing for a lower dose of both and, in many cases, less frequent dosing. A promising alternative to Norvir boosting called cobicistat is in research, and is expected to be approved this year (see cobicistat, page 57). In one study, similar efficacy, safety, and tolerability out to 48 weeks were seen with cobicistat- vs. Norvir-boosted Reyataz. Blood concentration is higher with Norvir tablets when taken with food (as required), and may cause more side effects. Stomach side effects are reduced by taking Norvir with high-fat foods (such as peanut butter)—however, some other HIV medicines should not be taken with high fat foods. You can mix liquid solution in ice cream, milk (especially chocolate), or pudding to hide Norvir-boosted Reyataz. Of those, I would never prescribe an unboosted PI other than Reyataz, and I do that only for my patients whom I refer to as “ritonophobes,” people who, perhaps because of a Pavlovian response to memories of high-dose Norvir, get nauseated just by looking at the bottle. Norvir now comes in a heat-stable tablet, so it no longer requires refrigeration. We’re expecting approval of cobicistat, a non-Norvir booster, later this year, which should allow for co-formulation with PIs like Reyataz and Prezista, and which will also be used to boost elvitegravir, a new integrase inhibitor.

Doctor’s comments
Norvir enjoyed very brief use as a PI in its own right, but the people who took it at its full, virtually intolerable dose of 600 mg twice a day didn’t enjoy it at all. The dose was then reduced to 400 mg twice a day taken with Invirase. That regimen’s claim to fame was that it wasn’t Crixivan and it wasn’t full-dose Norvir, but it was still tough to take. Now, it’s used only because of its interactions with the other PIs, at “booster” doses of 100-200 mg per day. This prolongs their half-lives, decreases dosing frequency, and reduces the risk of drug resistance. All PIs except Viracept can be boosted by Norvir, and the only PIs that can be given unboosted are Viracept and Reyataz. Of those, I would never prescribe an unboosted PI other than Reyataz, and I do that only for my patients whom I refer to as “ritonophobes,” people who, perhaps because of a Pavlovian response to memories of high-dose Norvir, get nauseated just by looking at the bottle. Norvir now comes in a heat-stable tablet, so it no longer requires refrigeration. We’re expecting approval of cobicistat, a non-Norvir booster, later this year, which should allow for co-formulation with PIs like Reyataz and Prezista, and which will also be used to boost elvitegravir, a new integrase inhibitor.

—JOEL GALLANT, MD, MPH

Activist’s comments
Norvir is the ultimate “Catch-22” of the HIV drug world. Originally a protease inhibitor itself in the earliest days, it was unrealistic to tolerate it, much less stay on it for long periods of time. Then Abbott finds a boosting feature, and voilà, a new reason to market the “almost dead” drug again! Now at much lower doses, it acts as a booster for other drugs. The company has made many mistakes over the years in regard to pricing and not working with other companies to co-formulate this drug. Patients wanting a once-a-day protease inhibitor will have to continue to deal with the uncomfortable side effects and be careful with the long list of drugs which interact with Norvir; even the booster amounts can cause reactions. I used to get super angry when doctors would say “mild” diarrhea is one of the few effects, as if any diarrhea is easy to deal with, especially when you’re out in public! Grrrrrrr. —JOEY WYNN

FOR THE LATEST INFORMATION ON NORVIR, GO TO positivelyaware.com/norvir

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Prezista
BRAND NAME

Protease inhibitor (PI)

MANUFACTURER:

Janssen Therapeutics | www.prezista.com, (877) JANSSEN (526-7736)

AWP:

$1,271.09 / month for 600 mg tablets, $1,482.99 for 400 mg tablets

STANDARD DOSE: 800 mg (two 400 mg tablets) with 100 mg Norvir once daily with food for first-time therapy and treatment-experienced adults without Prezista-related HIV resistance, or 600 mg (one 600 mg tablet) with 100 mg Norvir twice daily with food for those who have been on other HIV medications in the past and failed those medications and have at least one Prezista-related HIV drug resistance mutation. Prezista should never be taken without Norvir. 75 mg and 150 mg tablets available for children over six, dose based on weight. An oral suspension for children three years or older and adults who have difficulty swallowing pills is available. Please see the new package insert for specific directions on how to take the oral solution based on weight. As with the Prezista tablet, the oral solution needs to be taken with Norvir. Take a missed dose as soon as possible, but not if more than 12 hours past the once-daily dose (or six hours past the twice-daily dose). Do not double up on your next dose; take the next dose on schedule.

Potential side effects and toxicity
Prezista contains a sulfa component, and should be used cautiously by people with sulfa allergies. Prezista may cause mild to moderate rash (0.4% of people taking it), accompanied by fever and/or elevations of AST/ALT (liver enzymes) in some cases, but the most common side effects may include diarrhea, nausea, headache, rash, and abdominal pain. Liver function should be measured before starting therapy and should be monitored. Increased monitoring should be considered for people with underlying chronic hepatitis B or C, cirrhosis, or elevated levels of AST/ALT, especially during the first several months of therapy. No dose adjustment is necessary for those with mild to moderate liver disease, but Prezista/Norvir is not recommended for people with severe liver impairment. Severe rash, while very rare (in less than 0.1% of those taking it), can be life-threatening. Seek medical attention immediately. You may need to stop all medications. See chart on page 71 for potential drug class side effects.

Potential drug interactions
PIs interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Do not take with albufuzin, Revatio, oral Versed (midazolam), triazolam (Halcion), Ergomar, ergonovine, methylerygonovine, the herb St. John’s wort, cisapride, pimozone (Orap), and rifampin. Should not be taken with Incivex (telaprevir), because levels of both Prezista and telaprevir are decreased. Prezista may decrease levels of phenytoin (Dilanion), phenobarbital, and Tegretol; levels should be monitored. A reduced dose of rifabutin is recommended. Do not use Advicor, Altoprev, Mevacor, Simcor, Vytorin, or Zocor for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor, Lescol, and Lipitor, but should be used with caution and started at the lowest dose possible; you should be monitored closely for increased side effects from these medications. Pravacol (pravastatin) cannot be used with Prezista in the presence of liver impairment. 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). Vfend should not be used unless the benefits outweigh the risks. 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 calcium channel blockers, such as Norvasc and others, and beta-blockers, such as propanolol; clinical monitoring is recommended. A lower dose of trazodone and desipramine may be recommended. Close monitoring of INR levels required when using Coumadin (warfarin). Increases levels of fluticasone (found in Advair, Flonase, and Flovent); use only if the benefits outweigh the risks, and monitor for signs of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Alternatives should be considered, particularly for long-term use. Effectiveness of birth control pills may be decreased; consider the use of alternative or additional methods of contraception. No dose adjustment required with buprenorphine (Subutex or Suboxone) or methadone. Monitoring of antidepressant response is recommended with selective serotonin reuptake inhibitors (such as Paxil, Zoloft). Use with caution with bosentan, anticoagulants, and contraceptive; use lower dose of colchicine. Use of the hepatitis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

Prezista started out as the best of the “second-generation” PIs, showing excellent activity in most people with PI-resistant virus. Then it was shown to be more effective and more “resistant to resistance” than Kaletra in people who had taken PIs before but whose virus was susceptible to both drugs. A later study found that a once-daily dose of Prezista/Norvir had a number of advantages over Kaletra for first-line therapy, including less diarrhea, less lipid elevation, and better activity at higher viral loads. The latest development has been the approval of the once-daily dose for treatment-experienced patients who have no Prezista mutations. In short, you could say it’s the “PI for all seasons.” The main downside of Prezista is that it’s more likely than other PIs to cause an allergic rash, and, unlike the rash with Sustiva, a rash on Prezista often requires a switch to a different drug. Prezista must always be taken with Norvir, and with food. —JOEL GALLANT, MD, MPH

Activist’s comments
Prezista replaced Kaletra as ruler of the roost, even though Reyataz is nipping at its heels. It has fewer side effects than the older PIs, but it does still have many of the drug interactions common to the older drugs. Janssen earned kudos from the HIV advocacy community over their pricing policies. Easy access websites allow for PAPs and co-pay cards for those with insurance coverage. Oddly enough, for many of us who never saw CD4 increases with our undetectable viral loads over the years, this gem can really crank up the CD4 counts for us. One of my personal favorites!

—JOEY WYNN
Potential side effects and toxicity
Dizziness and lightheadedness; possible jaundice (yellowing of the skin or eyes), not related to liver damage, but report to your medical provider right away. Other side effects may include rash, kidney stones, and elevated liver enzymes, a sign of liver damage (more common in people with hepatitis B or C). Reyataz should not be taken by treatment-experienced patients on hemodialysis. Reyataz is the only PI that doesn’t increase lipid levels, but higher lipid levels may be seen if Reyataz is boosted with Norvir. See chart on page 71 for potential drug class side effects.

Potential drug interactions
PIs interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Medications used to treat acid reflux (GERD) and heartburn, like proton pump inhibitors (PPIs) and H2-receptor antagonists (H2RAs), can lower the levels of Reyataz. Treatment-experienced people cannot take Reyataz with PPIs. Treatment-naive people can take a PPI in a dose comparable to Prilosec OTC 12 hours before Reyataz/Norvir. H2RAs like Pepcid may be taken (no more than 20 mg twice a day if treatment-experienced or 40 mg twice a day if treatment-naive, or equivalent doses) at the same time as Reyataz/Norvir with food (before the H2RA has started to work) or at least 10 hours later. If taking with Viread or Truvada and an H2RA, you must take the 400 mg Reyataz/100 mg Norvir dose with food. When taking Reyataz without Norvir, dose can be taken at least two hours before and at least 10 hours after an H2RA. Reyataz should be taken two hours before or one hour after antacids (Rolaids, Tums, etc.). Do not take with alfuzosin, Revatio, rifampin, Camptosar, oral Versed, Halcion, pimozone, Crivixan, or St. John’s wort. Do not use Adcirca, Altopen, Livalo, Mavcor, Simcor, Vytoris, or Zocor. Alternatives are Crestor, Lescol, Lipitor, and Pravacol, but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects from these medications. Must be taken two hours before or one hour after Videx EC (unless taking Videx EC with Viread). Treatment-naive people should take 400 mg Reyataz/Norvir (100 mg) when taking with Sustiva, but treatment-experienced people should not take Reyataz with Sustiva. Viread decreases the levels of Reyataz and Reyataz increases Viread levels, which could increase adverse events. Monitor for Viread-associated adverse events. Reyataz can be taken unboosted with Epzicom if Norvir is not indicated or not tolerated. Use the heart medications bepideril, Cordarone, quinidine, and lidocaine cautiously. Monitoring may be required when used with Coumadin. Increases levels of fluticasone in Advair, Flonase, and Flovent); use only if the benefits outweigh the risks, and monitor for signs of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Effectiveness of birth control pills may be decreased; consider use of alternative or additional contraception. Oral contraception should contain no more than 30 mcg of ethinyl estradiol if taking Reyataz without Norvir and at least 30 mcg if taken with Norvir. Use caution when using itraconazole or ketoconazole. Vfend is not recommended. Monitor for Reyataz side effects when taking with Norvir and Cobicistat. Decreasing doses of rifabutin to 150 mg every other day or three times a week is recommended. Use caution with Tegretol, phenobarbital, and Dilantin. 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. Use with caution with bosen- tan, salmeterol, and immunosuppressants, and use lower dose of colchicine. Use with Norvir when taking buprenorphine. Monitor before sedation. Reyataz may decrease the effects of Malarone. Use of the hepatitis C drug Victrelis (boceprevir) along with a Norvir-boosted PI can potentially reduce the effectiveness of both drugs—combined use is not recommended.

More information
Norvir-boosted Reyataz is recommended by the U.S. HIV treatment guidelines for people starting HIV therapy for the first time. It’s set to be combined with the booster drug cobicistat (see cobicistat). A built-in cobicistat booster would both eliminate Norvir and reduce pill burden. Many people who started out with unboosted Reyataz continued to do as well as those on boosted Reyataz, but many folks are still concerned about data showing that unboosted use is associated with a higher risk of treatment failure. See the package insert for more complete information on potential side effects and interactions.

Doctor’s comments
The first of the “kindler, gentler PIs,” Reyataz was shown to be as effective as Kaletra for initial therapy, with less diarrhea and lipid elevations. It also has the most convenient dosing of any PI. Although I always prefer to boost Reyataz with Norvir, it is the only PI I would consider prescribing without boosting, because resistance to Reyataz doesn’t cause cross-resistance to other PIs. Because of an interaction with tenofovir, Reyataz must be boosted when taken with Viread or Truvada, and if taken with Sustiva or Atripla, an even higher dose of Reyataz should be used (400 mg plus 100 mg Norvir). Reyataz needs an acidic environment for absorption; it can’t be taken with most proton pump inhibitors, and strict dosing separation is required with other stomach acid reducers, such as H2 blockers and antacids. It’s probably better to just avoid Reyataz if you’re taking medications for reflux or ulcers. Reyataz also increases indirect bilirubin, which for most is a harmless lab abnormality, but for others, can result in yellowing of the eyes and/or skin. These side effects are harmless but unattractive, and most people who develop them elect to change drugs. —JOEL GALLANT, MD, MPH

Activist’s comments
If you don’t have to take acid reflux drugs and you really need to take a vacation from Norvir boosting, this may be the drug for you! Crowned as the first “once-a-day PI,” Reyataz should have been a blockbuster, but due to the list of complications with some drugs, it never gained a strong foothold in certain areas of the country. And with eerie side effects for some, like yellowing of the eyes, folks switch off of it quickly, never to return; but, it has great tolerability and no lipid or other lab problems. —JOEY Wynn
Potential side effects and toxicity
Most common include diarrhea, stomach discomfort, nausea, gas, weakness, and rash. People with phenylketonuria should be aware that the powder contains phenylalanine. See chart on page 71 for potential drug class side effects.

Potential drug interactions
PIs interact with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Viracept increases levels of Invirase and Crixivan, so dose adjustments may be needed. Do not take with alfuzosin, Revatio, oral Versed (midazolam), Cordarone (amiodarone), Halcion (triazolam), Rifadin (rifampin), Prilosec OTC (omeprazole), garlic supplements, or the herb St. John’s wort. Do not use Advicor, Altoprev, Livalo, Mecvar (lovastatin), Simcor, Vytorin, or Zoroc (simvastatin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor, Lescol, Lipitor, and Pravacol (pravastatin), but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects from these medications. Viracept may decrease methadone levels and methadone may need to be increased, but withdrawal rarely occurs. 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. Increases levels of fluticasone (found in Advair, Flonase, and Flovent); use only if the benefits outweigh the risks, and monitor for signs of Cushing’s syndrome (increased fat in the abdomen, fatty hump between the shoulders, rounded face, red/purple stretch marks on the skin, bone loss, possible high blood pressure, and sometimes diabetes). Effectiveness of birth control pills may be decreased; consider the use of alternative or additional methods of contraception. Also, increased levels of trazodone can occur and this combination should be used with caution. A lower dose of trazodone is recommended. Use with caution with bosentan, salmeterol, immunosuppressants (including transplant drugs), and colchicine (lower colchicine dose).

More information
Rarely used, Viracept is the only protease inhibitor that is never used with Norvir. Do not leave the pharmacy without anti-diarrhea meds such as Imodium, or Tums or other calcium products. Taking a 500 mg calcium supplement with doses hugely decreases diarrhea. Also try Solgar oat bran tablets, psyllium husk fiber bars, and pancreatic enzymes (all with meals). As an extra precaution, take a change of clothes with you every day for the first several weeks—stick it out, most often, symptoms improve after two or three weeks. The oral powder tastes horrible and requires a large amount for mixing into food. People using Viracept can crush adult tablets or dissolve tablets in a small amount of water. Mixing Viracept with acidic food or juice (e.g., orange/apple juice or apple sauce) is not recommended, due to resulting bitter taste. To get the full benefit of Viracept by increasing its level in the body, it must be taken with a meal. No longer a preferred PI in pregnancy, Viracept is still okay to use if the preferred and alternative PIs (Kaletra and Reyataz) are not an option. It has been used extensively in pregnancy in the past, and it is well tolerated during pregnancy. In 2007, Viracept manufactured in Europe was recalled from the market because of high levels of ethyl methane mesylate (EMS). Viracept manufactured in United States was found to have lower levels of EMS than the European product. However, the FDA recommended that pregnant women not be treated with Viracept and that pediatric patients not be started on Viracept. By early 2008, Viracept manufactured both in Europe and the U.S. was found to meet safety standards, and the FDA and European Medicines Agency lifted their warnings about safety. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
Viracept was once a popular alternative to more toxic or inconvenient PIs like Crixivan or Invirase/Norvir. However, there was a price to be paid for the greater convenience and relative tolerability (I say “relative” because it caused a lot of diarrhea). It was less effective than other PIs, a fact that became clear in a head-to-head comparison with Kaletra. This may have been due in part to variable absorption and drug levels. And while its initial claim to fame was that Viracept mutations didn’t cause resistance to other PIs, that wasn’t always the case, and people on Kaletra didn’t develop mutations anyway. Viracept, the only “unboostable” PI, gradually fell out of favor, and is no longer recommended or widely used.

—JOEL GALLANT, MD, MPH

Activist’s comments
One of the very first protease inhibitors, it has pretty much disappeared into the history books. Main side effects were diarrhea, and its only use I can think of now is for women trying to conceive, as it is one of the alternative drugs for prevention of mother-to-child transmission, especially in developing countries. I haven’t seen a person on it, or dealt with it in years. —JOEY WYNN
Potential side effects and toxicity

Very tolerable, but most common are diarrhea, nausea, headache, and fever. The side effect profile in children is comparable to adults. Less common are abdominal pain, vomiting, fatigue, weakness, dizziness, and lipodystrophy. 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 anemia, neutropenia, and gastritis. Increases in ALT, AST, and total bilirubin, all signs of liver toxicity, seen in around 8% of people taking Isentress, especially those co-infected with hepatitis B or C. Although rarely seen, side effects can include severe and potentially fatal skin and hypersensitivity (allergic) reactions and cerebellar ataxia (sudden, uncoordinated movement due to disease or injury of the brain). Seek medical attention and immediately stop taking Isentress and your other HIV medications if you develop a rash associated with any of the following symptoms, as it may be a sign of a more serious reaction such as Stevens-Johnson syndrome, toxic epidermal necrolysis or severe hypersensitivity: fever, general ill feeling, extreme tiredness, muscle or joint aches, blisters, oral lesions, swelling of the eyes, lips, mouth, or face, difficulty breathing, and/or signs and symptoms of liver problems (e.g., yellowing of the skin or whites of the eyes, dark or tea-colored urine, pale stools/bowel movements, nausea, vomiting, loss of appetite, or pain, aching, or sensitivity on the right side below the ribs). Chewable tablets contain phenylalanine, which can be harmful to patients with phenylketonuria. See chart on page 71 for potential drug class side effects.

Potential drug interactions

Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Reyataz and Reyataz/Norvir increase blood levels of Isentress, but no dose adjustment is recommended. Use caution with rifampin, which reduces plasma concentrations of Isentress; increase dose of Isentress to 800 mg twice a day. Remember to decrease the Isentress dose back to 400 mg twice a day when you finish taking rifampin. If rifabutin is used in place of rifampin, there is no need to increase the Isentress dose. There are no data to guide dosing of the new chewable tablets if combined with rifampin. Prilosec (omeprazole) can increase concentrations of Isentress, but no dose adjustment is recommended. There is no interaction with methadone.

More information

U.S. HIV guidelines list Isentress along with a Truvada backbone as a preferred regimen for first-time therapy. Isentress is the first drug in a class of HIV drugs called integrase inhibitors, with more on the way (see elvitegravir and dolutegravir). The data are in accord with the advocate view that advanced patients are having dramatic results and almost no side effects. The 96-week data in ART-naive and ART-experienced patients show that Isentress continues to be effective with almost no side effects. The guidelines note drawbacks: twice-a-day dosing and a lower barrier to drug resistance than seen with boosted PIs. Greater tolerability, which results in greater adherence however, may help overcome those issues. Also, it’s only one tablet per dose, and does not have to be taken with the dreaded Norvir, the way PIs are. The guidelines state that switching people from a boosted PI to Isentress should be done with caution, and avoided altogether in people who have HIV resistance to NRTI drugs unless they have fully active medications (to which their HIV is not resistant) to use. Moreover, the guidelines state that before prescribing Isentress, providers may want to order a resistance test that can measure INSTI resistance (standard tests cannot). See package insert for more complete information on potential side effects and interactions.

Activist’s comments

The ultimate game changer, Isentress made undetectable viral load a reality for so many people! My personal favorite drug of them all; small, no side effects (I’ve never heard anyone report a bad thing about it), and it gets along with almost all of the other drugs possible in a regimen. Merck programs for PAPs and copay cards are a breeze. The icing on the cake? Merck quickly negotiated price freezes for ADAPs and worked well with the community on getting PAPs up and running, especially in Florida. The downside? Twice-a-day dosing can be a barrier for some, but for the overwhelming majority, this is a godsend. Salvage therapy clients rejoiced at the introduction of Isentress and a few other drugs a few years back, and are enjoying a span of good clinical labs now. I’m one happy camper over this drug! Hopes that it could be a once-a-day pill proved unattainable; results showed once-daily dosing was not as effective as twice-daily. There are no challengers in its class (yet), so for now, it is unrivaled! —Joey Wynn
**dolutegravir**
BRAND NAME NOT YET ESTABLISHED

**dolutegravir, or DTG**
GENERIC NAME

**CLASS:** Integrase inhibitor (integrase strand transfer inhibitor or, INSTI)

**MANUFACTURER:** Viiv Healthcare | www.viivhealthcare.com, (877) 844-8872 and Shionogi | www.shionogi-inc.com, (800) 844-8872

**AWP:** TBD; investigational drug at press time.

**STANDARD DOSE:** One 50 mg tablet once a day chosen for Phase 3 research. Twice-daily dosing was shown to work better in people who have viral resistance to Isentress and the investigational elvitegravir in a short study, VIKING Cohort II, and a large Viiv Phase 3 trial will look at the twice-daily dose. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

**Potential side effects and toxicity**

Seen in clinical studies: nausea, diarrhea, headache, dizziness, fatigue, weakness, and upset stomach or indigestion. Lymphatic cancer occurred in one study participant, but there is no information yet about whether or not this was drug-related. Available data are limited due to investigational drug status.

**Potential drug interactions**

There is evidence that Aptivus/Norvir, Sustiva, and Intencil lower dolutegravir concentration. More drug interactions are anticipated, but data are limited right now due to investigational drug status. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not.

**More information**

Still in clinical study, but expected to be available this year through expanded access (free medication to those in great need). Dolutegravir is a second-generation INSTI, meaning that it can work in people whose virus has developed resistance to Isentress and the investigational elvitegravir, but it will likely need to be dosed twice daily in these individuals. Does not require use with a booster medication like elvitegravir (see elvitegravir page).

Development of a co-formulated single-tablet regimen with abacavir and lamivudine is in the works. It is being studied at a twice-daily dose with an optimized background regimen (the best regimen a medical provider can create for a study participant) in people with current or a history of treatment failure with an INSTI (basically, those for whom Isentress no longer works, but also those who experienced virologic failure on dolutegravir (2% of study participants) had no INSTI resistance mutations in their virus, a good sign and something you want to see in a new INSTI. This study had mostly young, white men as participants and these results may not be applicable to the general public. Another study indicates efficacy against virus that is resistant to Isentress and elvitegravir. Dolutegravir is being developed by Viiv Healthcare in collaboration with Shionogi. Providers may want to order a resistance test that can measure INSTI resistance (standard resistance tests cannot). See package insert, when available, for more complete information on potential side effects and interactions.

**Doctor’s comments**

Dolutegravir is an investigational, once-daily integrase inhibitor that does not require boosting. Clinical trials suggest that the combination of dolutegravir plus two NRTIs is as effective as Atripla for initial therapy, with better tolerability. Resistance to dolutegravir has been uncommon so far, which may give it an advantage over Isentress and elvitegravir. Dolutegravir may have “second generation potential,” since it can still be active against virus that’s resistant to Isentress and elvitegravir, especially when it’s given at a higher dose. Still, it’s best to avoid extensive integrase inhibitor resistance by stopping integrase inhibitors that aren’t working, since some mutations cause more cross-resistance than others. —J

**Activist’s comments**

This new agent is a promising competitor to Isentress and another integrase inhibitor, elvitegravir. This second-generation drug doesn’t need a booster (can you say Hallelujah!) and has a less likely and different resistance profile than others in this class. After speaking to a few lucky folks already on this one, they all report feeling just fine. Isentress finally has some competition to be worried about! I heard there might be a combo involving Epzicom [emtricitabine and abacavir], but I’m not sure if that would catch hold in the treatment-experienced world, with all the baggage abacavir has had in the past. —Joey Wynn

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**For the latest information on dolutegravir, go to positivelyaware.com/dolutegravir**
Potential side effects and toxicity
Seen in clinical studies: diarrhea, upper respiratory tract infection, bronchitis, back pain, depression, sinusitis, joint pain, nausea, and urinary tract infection. The incidence of these side effects were the same as seen with Isentress in one clinical study (3% to 6%), with the exception of diarrhea, seen more often (12% vs. 7%). Laboratory abnormalities indicating potential liver damage (GGT, ALT, and AST) were lower with elvitegravir (3% vs. 6%, 2% vs. 5%, and 1% vs. 5%, respectively for elvitegravir and Isentress). Available data are limited due to investigational drug status. See chart on page 71 for potential drug class side effects.

Potential drug interactions
Elvitegravir is expected to interact with many other drugs. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Elvitegravir is metabolized primarily by the enzyme CYP450-3A (known as the P450 pathway) and any medications that affect this enzyme may affect the levels of elvitegravir. The smaller 85 mg dose must be used with Reyataz or Kaletra. Again, available data are limited due to investigational drug status.

Doctor’s comments
Elvitegravir is an investigational integrase inhibitor that is expected to be approved later this year, initially in a “Quad” single-tablet formulation that also includes tenofovir, emtricitabine, and the booster cobicistat. Boosting of elvitegravir is required to make it a once-daily drug. In recent clinical trials, the Quad appears to be as effective as Atripla or the combination of Truvada plus Reyataz/Norvir for initial therapy. Elvitegravir can also be used by treatment-experienced patients, but those who have developed resistance to Isentress are likely to have cross-resistance to elvitegravir.

Joel Gallant, MD, MPH

Activist’s comments
The jury is still out on this one. Elvitegravir will be convenient and another wonderful “easy to follow” drug cocktail when packaged in the “Quad” with three other drugs for a nice, new STR (single-tablet regimen). As an individual agent, however, it may not make much of a splash in the drug combo world. As a “me too” drug in the newest class, integrase inhibitors, this drug has the same genetic weaknesses as Isentress, so using it after failing Isentress is not an option.

Joey Wynn
**STANDARD DOSE:** One subcutaneous (under the skin, like insulin) injection of 90 mg (1 mL) twice daily (every 12 hours) into the upper arm, thigh, or abdomen. Each injection should be given in a different location from the previous one and at a site where there is no current injection site reaction from a previous dose. It is also approved for children 6 years or older. The dose for children is based on weight. Can be taken with or without food, with no dietary restrictions. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose.

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**Potential side effects and toxicity**

The most common are injection site reactions (ISRs), which occur in virtually all patients. The severity of reaction is variable, and for most is mild to moderate. Symptoms could include itching, swelling, redness, pain or tenderness, and 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 thighs). They will hurt with movement. Other side effects may include diarrhea, nausea, and fatigue, but these are more likely due to the other HIV medications taken along with Fuzeon. Hypersensitivity (allergic-like) reactions are possible. Results of a post-marketing observational study were added to Fuzeon’s drug label last year, showing a higher incidence of pneumonia in people taking Fuzeon. Risk factors for pneumonia included a low CD4+ T-cell count or high viral load when starting therapy, intravenous drug use, smoking, and a previous history of lung disease. 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. See chart on page 72 for potential drug class side effects.

**Potential drug interactions**

To date, none that are clinically significant have been found.

**More information**

With other powerful, newer drugs on the market, the twice-daily injectable Fuzeon is truly a medicine of last resort. Fuzeon is intended for treatment-experienced patients. Store kit at room temperature. Preparing and injecting Fuzeon can be complicated, so ask your health care provider to teach you how to do it. First, the drug needs to be dissolved with sterile water (provided in the kit), which may take up to 45 minutes. Never shake the vial with the Fuzeon; it will foam. Instead, roll it gently in your hands. To save time, you can prepare the two daily doses at the same time. You should store your second dose in the refrigerator, but it must be used within 24 hours of mixing it (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. Using insulin syringes to inject instead of the ones in the kit may help decrease the injection site reactions. Taking a shower before injecting helps warm and soften the skin and may also help reduce injection site reactions. Some patients use Arnica cream to decrease the inflammation. Follow proper hygiene instructions to avoid infection. ISR may worsen when injection is repeated in the same spot or given deeper than intended, for example, into the muscle. Always rotate injection sites frequently. Never inject into moles, scars, bruises, nodules, or the navel. Fuzeon can be taken at the same time as other HIV drugs. Fuzeon is the 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 (see Selzentry). See package insert for more complete information on potential side effects and interactions.

**Doctor’s comments**

Fuzeon inhibits fusion of the virus with the CD4 cell membrane, the final stage in the entry process. It was our first true “salvage drug,” a drug to be used in people with highly resistant virus. In fact, the original TORO trials not only led to the approval of Fuzeon, but ushered in the era of salvage therapy and set the standard for clinical trial design that would later lead to the approval of drugs like Prezista, Isentress, Selzentry, and Intelence. However, Fuzeon, never a big seller, is now rarely used. For most people, even those with the most highly resistant virus, there are easier, less expensive options that don’t require twice-daily subcutaneous injections that leave long-lasting painful bumps on the skin (injection site reactions, or ISRs). But I wouldn’t dismiss Fuzeon altogether. We may be in a “honeymoon period” with respect to salvage therapy, when almost everyone can keep their viral load undetectable with a combination of oral drugs. But the pipeline of drugs for treatment-experienced patients isn’t exactly gushing right now, and if we begin to see a lot of resistance to the newer drugs, especially Isentress, we may be forced to pull Fuzeon off the shelves again.

—JOEL GALLANT, MD, MPH
**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 that 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. Should not be used in people with severe kidney problems or end-stage kidney disease who are taking medications that can increase or decrease the levels of Selzentry (check with your 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. See chart on page 72 for potential drug class side effects.

**Potential drug interactions**

Selzentry interacts with many other drugs. See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, and supplements you are taking or thinking of taking, prescribed or not. Not recommended with rifampin or St. John’s wort. Dose adjustment needed for Biaxin, Dilantin (phenytoin), Tegretol (carbamazepine), phenobarbital, HIV NNRTIs and PIs, Mycobutin, Sporanox (itraconazole), Nizoral (ketoconazole), Vfend, oral contraceptives, and oral Versed (midazolam). See standard dose section for interactions with other anti-HIV medications.

**More information**

Selzentry is the only oral entry inhibitor available on the market. Originally approved for treatment-experienced patients infected only with CCR5-tropic virus (determined by the tropism assay), it has also been FDA approved for people starting HIV therapy for the first time. Complex dosing, the need for an expensive tropism test, and competition from newer drugs have dimmed some of the initial enthusiasm for this drug. The Trofile test needed, however, is now generally paid for by state public health departments, Medicare, and other private insurance coverage. ViiV may cover the payment if someone is ADAP-eligible and does not have insurance coverage for the Trofile test. Viral tropism refers to the types of HIV that a person can have: CCR5-tropic (R5) and/or CXCR4-tropic or (X4) virus. HIV attaches to the CD4 receptor on the surface of some T-cells (hence, CD4+ T-cells), and then it latches on to one or both of the two co-receptors on the surface of the cells, R5 or X4, thus gaining entry. As the name “CCR5 inhibitor” suggests, Selzentry inhibits (blocks) CCR5, shutting down this point of entry for the virus. X4 virus is usually associated with advanced HIV disease or extensive experience with taking HIV medications. Most people are infected with CCR5 virus, and then over time more CXCR4 and mixed viruses may accumulate. Results from various studies showed that blocking R5 with Selzentry does not cause virus to shift to X4 or show a negative effect on disease progression or CD4 count in so-called “dual tropic” people (their virus can use either R5 or X4). In 2007, the company reported that a switch to pre-existing X4—or dual-tropic virus—was transient and reversible when people went off Selzentry. A sub-analysis reported that Selzentry seems to have minimal impact on lipid levels. Selzentry has been studied in treatment-naive patients (first time on therapy) in the MERIT clinical trial. Although the initial analysis suggested that Selzentry was unable to match Sustiva’s viral loads of less than 50 copies (undetectable), a re-analysis of the data using the enhanced Trofile test (Trofile ES) showed the regimens to be comparable (59% for Selzentry vs. 63% for Sustiva) in undetectable viral loads at 96 weeks. The follow-up results of 96-week data led to its FDA approval for this population. See package insert for more complete information on potential side effects and interactions.

**Doctor’s comments**

Selzentry is an entry inhibitor that acts at an earlier stage of the entry process than Fuzeon: It blocks the binding of the virus to the CCR5 co-receptor on the CD4 cell surface. Some people have virus that can get into the cell using CXCR4, another co-receptor, and Selzentry won’t work against that kind of virus. As a result, it’s necessary to test the “tropism” of the virus before using Selzentry. Only those with purely “R5-tropic” virus should use the drug. The need for this test has been the main obstacle to widespread use of Selzentry, which is an effective, safe, and very well tolerated agent. The test currently in use in the United States, the Trofile assay, is expensive and time-consuming. Outside of the U.S., cheaper genotypic tests are being used. These may turn out to be good alternatives to Trofile, but we need more data on how well they measure tropism and predict success with Selzentry before they can be recommended. Selzentry has now been approved by the FDA for initial therapy, and people are more likely to have R5-tropic virus at early stages, before they’ve been treated. However, Selzentry is not yet being widely used for that purpose, and for initial therapy, it’s categorized as “acceptable” or “alternative” in the DHHS and IAS-USA guidelines, respectively. Selzentry is taken twice a day, but once-daily dosing is being studied.

—JOEL GALLANT, MD, MPH

**Activist’s comments**

One of my biggest disappointments, this new class of drugs, CCR5 antagonists, was a bust! Consider the fact that people have tropisms that can switch and add to that a tropism test that is more expensive than a month’s supply of the drug itself, and you get a number of barriers and reasons this drug never took off. The mode of activity—preventing fusion to occur in the first place—and relatively few side effects means more research is needed to see how we can use this new class with a better method of detecting who will benefit from it, other than the company making the super expensive trofile assay! —JOEY WYNN
STANDARD DOSE: One tablet (600 mg efavirenz / 200 mg emtricitabine / 300 mg tenofovir), once a day, preferably at bedtime, on an empty stomach or with a light, low-fat snack. Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Dose cannot be adjusted for people with kidney problems and Atripla should not be used in people with moderate or severe kidney or liver impairment.

Potential side effects and toxicity
See the individual drugs contained in Atripla—Sustiva, Emtriva, and Viread (efavirenz, emtricitabine, and tenofovir). Atripla is well tolerated in most, but not all, individuals. Use with caution in individuals with depression or other psychiatric issues. Diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. Kidney function should be assessed before initiating treatment and throughout therapy as determined by a provider. Women should not become pregnant on Atripla or for 12 weeks after discontinuation, and should not breast-feed while on it, because of the risk of birth defects. Dose cannot be adjusted for people with kidney problems. See chart on page 72 for potential drug class side effects.

Potential drug interactions
See the individual drugs contained in Atripla: Sustiva, Emtriva, and Viread. Do not take Atripla with Complera, Epivir, or Emtriva. Use with caution in individuals with depression or other psychiatric issues. Diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. Kidney function should be assessed before initiating treatment and throughout therapy as determined by a provider. Women should not become pregnant on Atripla or for 12 weeks after discontinuation, and should not breast-feed while on it, because of the risk of birth defects. Dose cannot be adjusted for people with kidney problems. See chart on page 72 for potential drug class side effects.

More information
Atripla was the first complete HIV treatment regimen in one pill, taken once daily, but now has head-to-head competition from Complera, approved in 2011, and there are more single-tablet regimens on the way (see the Quad, page 56). Atripla is on the list of preferred regimens for treatment-naïve patients in the DHHS HIV treatment guidelines. Atripla is one of the most commonly prescribed medications for those taking HIV medicine for the first time due to the ease of taking one pill, once a day. Another benefit: the single tablet cuts the number of insurance co-pays. Complera’s approval, however, makes Atripla’s side effect profile harder to overlook. Efavirenz should not be taken during pregnancy. According to one meta-analysis, if women get pregnant while on Sustiva (efavirenz) or Atripla, however, the risk of birth defects is minimal. The efavirenz in Atripla can cause a false positive for marijuana on certain drug tests. A more specific confirmatory test can be done. Atripla should not be used in patients under 18 years of age. Most treatment-experienced people (those who’ve already been on HIV therapy) may not be able to use Atripla due to having developed drug resistance (when their medications may no longer work against the virus), and Complera is not an option for people resistant to Atripla. Drug resistance most commonly occurs when people don’t take their HIV medicine as prescribed, but some 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. Be careful when stopping Atripla, so that you avoid the rapid development of HIV resistance to it—check with your doctor or pharmacist first. Use of tenofovir must be monitored in people with underlying kidney problems. In this combination product, the tenofovir dose cannot be adjusted. Therefore, Atripla should not be used in people with severe kidney problems. Tenofovir and emtricitabine are also both used to treat hepatitis B. If you are co-infected with hepatitis B, when you stop Atripla your hepatitis B may be reactivated. If your HIV develops resistance to tenofovir and/or emtricitabine, it does not mean that your hepatitis B is also resistant to them. Gilead and BMS are forever to be commended for collaborating to bring Atripla to market. See package insert for more complete information on potential side effects and interactions.

Doctor’s comments
Atripla was the first single-tablet, once-daily regimen. It’s a preferred regimen in all treatment guidelines based on its outstanding efficacy, safety, tolerability, and convenience. The main disadvantages include the potential for kidney toxicity with tenofovir (see Viread) and the early side effects of efavirenz (see Sustiva). Atripla is not a good choice for people who aren’t fully committed to staying on therapy without interruption. The long half-lives of the three drugs mean that an occasional missed dose or two won’t matter, but interrupting therapy altogether can cause drug resistance, especially to efavirenz.

—JOEL GALLANT, MD, MPH

Activist’s comments
The gold standard for realistic regimens we can take indefinitely, Atripla still has the benefits of simplicity: a once-daily pill with everything you need in it. The downside is the compound has the same drawbacks as Sustiva (efavirenz), which is one of its three ingredients, the other two being the Emtriva (emtricitabine) and Viread (tenofovir) found in Truvada. It can cause vivid dreams, nightmares, depression, out of range lipids, or bone density problems (for some people, not all). It has the easiest by far co-pay programs, as well as patient assistance programs (PAPs). This breakthrough product showed us that pharmaceutical companies can get along and work together (Gilead and Bristol-Myers Squibb). Still by far one of the most prescribed regimens in the ADAP world, we were very glad to see the companies work out a deal for price freezes and easy access patient assistance programs; helping to save Florida’s ADAP from getting deeper into fiscal debt.

—JOEY WYNN
Potential side effects and toxicity
See the individual drugs contained in Complera—Edurant and Truvada (rilpivirine / emtricitabine / tenofovir). Moderate to severe side effects are uncommon (2% or fewer of patients): insomnia, headache, nausea, dizziness, rash, abnormal dreams, and depressive disorders (depression, negative thoughts, suicidal thoughts or actions). See chart on page 72 for potential drug class side effects.

Potential drug interactions
Do not take this drug with Atripla, Combivir, Emtriva, Epivir, Epivir-HBV, Epzicom, Endurant, Trizivir, Truvada, or Viread, since Complera contains these medications or their equivalents. Antacids can be taken two hours before or four hours after a Complera dose. H2 receptor antagonists, such as Pepcid, Tagamet, and Zantac, can be taken 12 hours before or four hours after a Complera dose. Proton pump inhibitors, such as Nexium, Prevacid, and Prilosec can’t be taken with Complera. Do not take Complera with the anti-hepatitis B drug Hepsera; the anti-seizure medications carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the anti-TB drugs rifabutin, and rifapentine; or the herb St. John’s wort (other herbs have not been studied with Complera, but caution is advised if planning to take any herbs). Do not take with more than one dose of the injectable steroid dexamethasone. Clinically monitor drug levels of the antifungals Diflucan, Sporanox, Nizoral, Noraxil, and Vfend; no dose adjustments are needed. Use azithromycin when possible instead of the antibiotics Biaxin, erythromycin, and troleandomycin (Tao). These agents will increase rilpivirine levels, which can increase the risk for side effects. Methadone levels may be reduced and the dose of methadone may need to be adjusted to prevent withdrawal.

More information
Complera was approved by the FDA in 2011. It had been nicknamed “B-tripla” because it is a direct competitor to the first once-daily, single tablet, complete HIV regimen on the market, Atripla. There was a higher rate of virologic failure (inability to suppress viral load) in people with more than 100,000 viral load copies per mL compared to Atripla, and virologic failure was associated with a greater risk of drug resistance to the non-nuke class of medications than seen with Atripla. On the other hand, Complera was more tolerable than Atripla and did not have its cholesterol elevations. Rash was seen in 4.2% of the Complera group vs. 15.1% of the Atripla group. Head-to-head study is underway (complex dosing and multiple pills were used in previous research instead of the actual STR pills of Complera and Atripla). For proper absorption, it must be taken with a meal of at least 400 calories, including some fat. Nutritional drinks, even high-calorie protein shakes or products like Ensure, are not enough and do not constitute a meal. Taken with a protein shake, rilpivirine levels were still half of what they are with a meal. Meal examples include two slices of whole wheat toast with peanut butter, fresh fruit, and orange juice; a roast beef sandwich on a hard roll with mayo and cheese; or two cups of spaghetti with marinara sauce and a slice of bread. Concerns about switching from Atripla to Complera were eased when decreases in Complera levels were only seen in the first week of a 12-week study, and participants maintained their undetectable viral loads (less than 50 copies per mL). High doses (at least three pills) can lead to a risk of prolonged QT interval, which is a heart condition. While Sustiva (efavirenz) is associated with a risk of birth defects, Complera is Pregnancy Category B (found safe in animal studies). No trials in humans have been conducted, and Complera should be used in pregnancy only if the potential benefit justifies the potential risk. (Most HIV medications are Pregnancy Category B.) Rilpivirine, emtricitabine, and tenofovir all have long half-lives (time it takes a drug in the body to be reduced by half), making them a great combination. Complera pills are smaller in size than Atripla. Check for hepatitis B before starting therapy (see Truvada). Kudos to Janssen Therapeutics, developer of Edurant, and Gilead for collaborating on Complera. When Bristol-Myers Squibb and Gilead worked together to combine their drugs Sustiva and Truvada into Atripla, it was an unheard of collaboration among makers of HIV drugs. How soon we forget. Today such collaborations are expected and Gilead has more of them in the works. See package insert for more complete information on potential side effects and drug interactions.

Doctor’s comments
Complera is the second single-tablet regimen. The advantages and disadvantages of Complera vs. Atripla are discussed elsewhere (see Edurant). A head-to-head comparison of the two regimens is in progress, since the original Edurant studies didn’t use the single-tablet regimen. Well-tolerated Complera is a good choice for people who have trouble with Atripla, Sustiva, or boosted PIs, but be careful about switching directly from Atripla to Complera if your viral load isn’t undetectable yet. Sustiva lowers Edurant levels, and we don’t know whether early switches are safe.

Activist’s comments
Complera is one pill/once-a-day triple combo pack of Edurant (rilpivirine) with the powerhouse Truvada (emtricitabine/tenofovir). It offers the convenience of a single-tablet regimen (STR) without the downside of the other once-a-day agent Atripla. This drug has been an easy way to slide into taking daily medications for those just starting. As mentioned earlier, many experienced patients are moving to it because their side effects from Atripla persist after even four weeks. Since their viral loads are undetectable, doctors are switching them and experiencing pretty good results. —JOEL GALLANT, MD, MPH

FOR THE LATEST INFORMATION ON COMPLERA, GO TO positivelyaware.com/complera
Potential side effects and toxicity

See the individual drugs contained in the Quad: elvitegravir, Emtriva, Viread, and cobicistat. Seen in clinical study: Fatigue, diarrhea, headache, nausea, abdominal distention, rash, elevated lipid levels (cholesterol and triglycerides), increased serum creatinine, and decreased estimated glomerular filtration rate (e-GFR)—the last two are signs of possible kidney malfunction (see cobicistat page for more, and reassuring, information). Available data are limited due to investigational drug status. See chart on page 72 for potential drug class side effects.

Potential drug interactions

Do not take this drug with Atripla, cobicistat, Combivir, Complera, elvitegravir, Emtriva, Epivir, Epivir-HBV, Epzicom, Trizivir, Truvada, or Viread, since these medications are already in this fixed dose pill or it has equivalent medications. Because the Quad has cobicistat in it and cobicistat is a potent CYP3A4 inhibitor, there are expected to be numerous drug interactions. A complete list will be available in the package insert once the Quad is FDA approved. Again, available data are limited due to its investigational drug status.

More information

Still in experimental study, Gilead’s New Drug Application for the Quad was accepted by the FDA on December 23, 2011 and it has set a target review date of August 27, 2012. If approved, the Quad would be the third (see Atripla and Complera) once-daily, single-tablet HIV regimen and the only one containing an integrase inhibitor (INSTI). Integrase inhibitors interfere with HIV replication by blocking the ability of the virus to integrate into the genetic material of human cells. Isentress is the only INSTI currently on the market. In 2011, 48-week data showed the Quad was non-inferior (no better, no worse), as shown by achieving undetectable viral load of less than 50 copies per mL, to Atripla (Study 102, 88% for the Quad vs. 84% for Atripla) and to Norvir-boosted Reyataz/Norvir for initial therapy. Interestingly, the Quad will be approved before its novel component drugs, elvitegravir and cobicistat. It’s important to monitor kidney function when taking the Quad. As we know, the tenofovir component can sometimes cause kidney toxicity, and cobicistat, while not toxic to kidneys, does decrease creatinine secretion. This causes a small rise in the serum creatinine, which can give the appearance of kidney toxicity.

—JOEL GALLANT, MD, MPH

Activist’s comments

Okay, I’m all for single-tablet regimens (STRs), they help most folks stay on track and avoid missing doses. We were all hoping this was going to be The One. Now we hear the booster is no better than the existing one, and there are some unsettling side effects from the other drugs. I guess it’s not going to be the blockbuster we were hoping to have (sigh). I’m sure it will do wonders for some, but if you have kidney problems, this one may be a pass for you. —JOEY WYNN
cobicistat, (formerly GS-9350), or COBI

**Potential side effects and toxicity**

Seen in clinical studies: diarrhea, nausea, lipid elevations (increases in cholesterol and triglycerides), creatine kinase, hematuria (red blood cells in the urine—unlike Norvir may look reddish), increased serum creatinine, and decreased estimated glomerular filtration rate (e-GFR)—the last two are signs of possible kidney malfunction. The increase in serum creatinine is seen within days of initiating cobicistat, but it is reversible and kidney function returns to normal within a few days after stopping cobicistat. The decreased e-GFR appears to not impact health. Available data are limited due to investigational drug status.

**Potential drug interactions**

Cobicistat is a potent CYP3A4 inhibitor and is likely to increase blood levels of any medications that use this enzyme system to be metabolized. The drug interaction profile will likely not be as extensive as Norvir’s because cobicistat only affects CYP3A4, unlike Norvir, which affects other CYP enzymes resulting in more drug interactions. Again, available data are limited due to investigational drug status.

**More information**

Still in experimental studies, cobicistat is not an HIV medication, but a drug used to boost blood levels of other medications. As such, it is being developed as an alternative to Norvir, an HIV medication used for this same purpose. Specifically, cobicistat and Norvir boost blood levels of HIV protease inhibitors, allowing for fewer pills and (usually) once-daily dosing. Norvir can be difficult to tolerate, has a long list of drug interactions, and its manufacturer angered the HIV community by raising its price 400% one year to make up for its widely used smaller booster dose (initially, it was used in higher doses to fight HIV, like other PIs). Cobicistat is in three advanced Phase 3 trials and Gilead hopes to file the NDA (new drug application) to the FDA during the second quarter of 2012. As an alternative to Norvir, COBI’s development has created a lot of excitement. Unfortunately, it has the increased cholesterol and triglycerides of Norvir, along with some of the stomach upsets. There are also concerns about a possible negative impact on the kidneys, although further findings have been reassuring. The 10% increase in creatinine levels that was seen in the first two weeks of study did not continue to increase out to 48 weeks, and was reversible upon stopping cobicistat. Gilead is also creating a single-tablet regimen with COBI in it (see the Quad page). Such is COBI’s promise that two other HIV drug manufacturers have signed agreements with Gilead to create co-formulations of their drugs with COBI in it. These include Prezista from Janssen Therapeutics and Reyataz from Bristol-Myers Squibb (BMS). While the agreement with BMS is for a boosted Reyataz pill, the agreement with Janssen is for a boosted Prezista pill, as well as a complete HIV regimen in one tablet that includes Prezista (darunavir), cobicistat, emtricitabine, and Gilead’s GS-7340, an investigational pro-drug (inactive substance that metabolizes into active form in the body) of its popular Viread (tenofovir). Reyataz boosted by COBI has been studied compared to Norvir-boosted Reyataz. Gilead will submit the results from its 114 study (atazanavir/emtricitabine/tenofovir/cobicistat vs. atazanavir/emtricitabine/tenofovir/ritonavir) at a scientific conference this year. The 48-week data from this study showed that 85% of patients taking the cobicistat formulation achieved undetectable viral load of less than 50 copies/mL, compared to 87% of patients taking the Norvir one. At 48 weeks, there was similar efficacy, safety, and tolerability. See package insert when available for more complete information on potential side effects and interactions.

**Doctor’s comments**

Cobicistat is expected to be the first approved non-Norvir boosting agent, to be combined with PIs and elvitegravir. Its main advantage over Norvir is likely to be co-formulation: while Norvir is currently co-formulated only with lopinavir in the form of Kaletra, cobicistat may eventually be co-formulated with elvitegravir (including a single-tablet “Quad” regimen that will also contain tenofovir and emtricitabine), atazanavir, and darunavir. A second “quad” tablet containing darunavir, cobicistat, emtricitabine, and an investigational tenofovir pro-drug is also being developed, which, if successful, will be the first single-tablet PI-based regimen.

—JOEL GALLANT, MD, MPH

Activist’s comments

Talk about hopes and expectations being too high! Many of us were hoping this would rid us of the typical boosters that cause diarrhea—the worst side effect there is, especially if you’re out and about and an accident happens! Unfortunately, this new booster has many of the same side effects as the existing Norvir booster. One glimmer of hope (or a silver lining if you will) will be in co-formulations. Having everything in one pill helps reduce pill burden, and reduce co-pays and deductibles for those having to pay. At least we’re getting more options out there, and that is always better. —JOEY WYNN
INDICATION
COMPLERA® (emtricitabine 200 mg/rilpivirine 25 mg/tenofovir disoproxil fumarate 300 mg) is a prescription HIV medicine that contains 3 medicines, EMTRIVA® (emtricitabine), EDURANT™ (rilpivirine), and VIREAD® (tenofovir disoproxil fumarate) combined in one pill. COMPLERA is used as a complete single-tablet regimen to treat HIV-1 infection in adults (age 18 and older) who have never taken HIV medicines before.

COMPLERA does not cure HIV and has not been shown to prevent passing HIV to others. It is important to always practice safer sex, use latex or polyurethane condoms to lower the chance of sexual contact with any body fluids, and to never re-use or share needles. Do not stop taking COMPLERA unless directed by your healthcare provider. See your healthcare provider regularly.

IMPORTANT SAFETY INFORMATION
Contact your healthcare provider right away if you get the following side effects or conditions while taking COMPLERA:

• 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), your liver disease may suddenly get worse if you stop taking COMPLERA. Do not stop taking COMPLERA without first talking to your healthcare provider. Your healthcare provider will monitor your condition

COMPLERA may affect the way other medicines work, and other medicines may affect how COMPLERA works, and may cause serious side effects.

Do not take COMPLERA if you are taking the following medicines:
• other HIV medicines (COMPLERA provides a complete treatment for HIV infection.)
• the anti-seizure medicines carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol-XR®, Teril®, Epitol®), oxcarbazepine (Trileptal®), phenobarbital (Luminal®), phenytoin (Dilantin®, Dilantin-125®, Phenytek®)
• the anti-tuberculosis medicines rifabutin (Mycobutin), rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®) and rifapentine (Priftin®)
• a proton pump inhibitor medicine for certain stomach or intestinal problems, including esomeprazole (Nexium®, Vimov®), lansoprazole (Prevacid®), omeprazole (Prilosec®), pantoprazole sodium (Protonix®), rabeprazole (AcipHex®)
• more than 1 dose of the steroid medicine dexamethasone or dexamethasone sodium phosphate
• St. John’s wort (Hypericum perforatum)
• other medicines that contain tenofovir (VIREAD®, TRUVADA®, ATRIPLA®)
• other medicines that contain emtricitabine or lamivudine (EMTRIVA®, Combivir®, Epivir® or Epivir-HBV®, Epzicom®, Trizivir®)
• rilpivirine (Edurant®)
• adefovir (HEPSERA®)

In addition, also tell your healthcare provider if you take:
• an antacid medicine that contains aluminum, magnesium hydroxide, or calcium carbonate. Take antacids at least 2 hours before or at least 4 hours after you take COMPLERA
• a histamine-2 blocker medicine, including famotidine (Pepcid®), cimetidine (Tagamet®), nizatidine (Axid®), or ranitidine hydrochloride (Zantac®). Take these medicines at least 12 hours before or at least 4 hours after you take COMPLERA
• the antibiotic medicines clarithromycin (Biaxin®), erythromycin (E-Mycin®, Eryc®, Ery-Tab®), PCE® Pedialoz®, llosone®), and troleandomycin (TAO®)
• an antifungal medicine by mouth, including fluconazole (Diflucan®), itraconazole (Sporanox®), ketoconazole (Nizoral®), posaconazole (Noxafil®), voriconazole (Vfend®)
• methadone (Dolophine®)

This list of medicines is not complete. Discuss with your healthcare provider all prescription and nonprescription medicines, vitamins, or herbal supplements you are taking or plan to take.

Do not stop taking COMPLERA unless directed by your healthcare provider.

Please see Patient Information for COMPLERA on the following pages.

Patient model. Pill shown is not actual size.
Complera is a prescription medicine used as a complete single-tablet regimen to treat HIV-1 in adults who have never taken HIV medicines before. Complera does not cure HIV or AIDS or help prevent passing HIV to others.

**COMPLERA.** A complete HIV treatment in only 1 pill a day.

Ask your healthcare provider if it's the one for you.

Before taking Complera, tell your healthcare provider if you:

- have liver problems, including hepatitis B or C virus infection
- have kidney problems
- have ever had a mental health problem
- have bone problems
- are pregnant or plan to become pregnant. It is not known if Complera can harm your unborn child
- are breastfeeding. Women with HIV should not breast-feed because they can pass HIV through their milk to the baby

Contact your healthcare provider right away if you experience any of the following serious or common side effects:

**Serious side effects associated with Complera:**

- New or worse kidney problems can happen in some people who take Complera. If you have had kidney problems in the past or take other medicines that can cause kidney problems, your healthcare provider may need to do blood tests to check your kidneys during your treatment with Complera.
- Depression or mood changes can happen in some people who take Complera. Tell your healthcare provider right away if you have any of the following symptoms: feeling sad or hopeless, feeling anxious or restless, or if you have thoughts of hurting yourself (suicide) or have tried to hurt yourself.
- Bone problems can happen in some people who take Complera. Bone problems include bone pain, softening or thinning (which may lead to fractures). Your healthcare provider may need to do additional tests to check your bones.
- Changes in body fat can happen in people taking HIV medicine. 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.
- Changes in your immune system (Immune Reconstitution Syndrome) can happen when you start taking HIV medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider if you start having new symptoms after starting your HIV medicine.

Common side effects associated with Complera:

- Trouble sleeping (insomnia), abnormal dreams, headache, dizziness, diarrhea, nausea, rash, tiredness, and depression

Other side effects associated with Complera:

- Vomiting, stomach pain or discomfort, skin discoloration (small spots or freckles), and pain

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of Complera. For more information, ask your healthcare provider or pharmacist. Call your healthcare provider for medical advice about side effects.

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.

Take Complera exactly as your healthcare provider tells you to take it

- Always take Complera with a meal. Taking Complera with a meal is important to help get the right amount of medicine in your body. A protein drink does not replace a meal.
- Stay under the care of your healthcare provider during treatment with Complera and see your healthcare provider regularly.

Please see Patient Information for Complera on the following pages.

Complera®

emtricitabine 200mg/rilpivirine 25mg/
tenofovir disoproxil fumarate 300mg tablets

Learn more at www.COMPLERA.com
Lactic acidosis can be hard to identify early, because the symptoms could seem like talking to your healthcare provider about your medical condition or treatment. Read this Patient Information before you start taking COMPLERA 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.

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

COMPLERA can cause serious side effects, including:

1. Build-up of an acid in your blood (lactic acidosis). Lactic acidosis can happen in some people who take COMPLERA or similar (nucleoside analogs) medicines. Lactic acidosis is a serious medical emergency that can lead to death.

Lactic acidosis can be hard to identify early, because the symptoms could seem like symptoms of other health problems. Call your healthcare provider right away if you get any of the following symptoms which could be signs of lactic acidosis:

- feeling very weak or tired
- have unusual (not normal) muscle pain
- have trouble breathing
- have stomach pain with
  - nausea (feel sick to your stomach)
  - vomiting
- feel cold, especially in your arms and legs
- feel dizzy or lightheaded
- have a fast or irregular heartbeat

2. Severe liver problems. Severe liver problems can happen in people who take COMPLERA or similar medicines. In some cases these liver problems can lead to death. Your liver may become large (hepatomegaly) and you may develop fat in your liver (steatosis) when you take COMPLERA.

Call your healthcare provider right away if you have any of the following symptoms of liver problems:

- your skin or the white part of your eyes turns yellow (jaundice),
- dark "tea-colored" urine
- light-colored bowel movements (stools)
- loss of appetite for several days or longer
- nausea
- stomach pain

You may be more likely to get lactic acidosis or severe liver problems if you are female, very overweight (obese), or have been taking COMPLERA or a similar medicine containing nucleoside analogs for a long time.

3. Worsening of Hepatitis B infection. If you also have hepatitis B virus (HBV) infection and you stop taking COMPLERA, your HBV infection may become worse (flare-up). A "flare-up" is when your HBV infection suddenly returns in a worse way than before. COMPLERA is not approved for the treatment of HBV, so you must discuss your HBV therapy with your healthcare provider.

- Do not let your COMPLERA run out. Refill your prescription or talk to your healthcare provider before you stop COMPLERA.
- Do not stop taking COMPLERA without first talking to your healthcare provider.
- If you stop taking COMPLERA, your healthcare provider will need to check your health often and do regular blood tests to check your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking COMPLERA.

What is COMPLERA?

COMPLERA is a prescription HIV (Human Immunodeficiency Virus) medicine that:
- is used to treat HIV-1 in adults who have never taken HIV medicines before. HIV is the virus that causes AIDS (Acquired Immunodeficiency Syndrome).
- contains 3 medicines, (rilpivirine, emtricitabine, tenofovir disoproxil fumarate) combined in one tablet. EMTRIVA and VIREAD are HIV-1 (human immunodeficiency virus) nucleoside analog reverse transcriptase inhibitors (NRTIs) and EDURANT is an HIV-1 non-nucleoside analog reverse transcriptase inhibitor (NNRTI).

It is not known if COMPLERA is safe and effective in children under the age of 18 years.

COMPLERA may help:
- Reduce the amount of HIV in your blood. This is called your "viral load".
- Increase the number of white blood cells called CD4+ (T) cells that help fight off other infections.

Reducing the amount of HIV and increasing the CD4+ (T) cell count may improve your immune system. This may reduce your risk of death or infections that can happen when your immune system is weak (opportunistic infections).

COMPLERA does not cure HIV infections or AIDS.
- Always practice safer sex.
- Use latex or polyurethane condoms 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 healthcare provider if you have any questions about how to prevent passing HIV to other people.

Who should not take COMPLERA?

- Do not take COMPLERA if you have liver problems.
- Do not take COMPLERA if you have bone problems.
- Do not take COMPLERA if you are pregnant or plan to become pregnant.

What should I tell my healthcare provider before taking COMPLERA?

Before you take COMPLERA, tell your healthcare provider if you:
- have liver problems, including hepatitis B or C virus infection
- have kidney problems
- have ever had a mental health problem
- have bone problems
- are pregnant or plan to become pregnant. It is not known if COMPLERA can harm your unborn child

Pregnancy Registry. There is a pregnancy registry for women who take antiviral medicines during pregnancy. Its purpose is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry.

- are breast-feeding or plan to breast-feed. The Centers for Disease Control and Prevention recommends that mothers with HIV not breastfeed because they can pass the HIV through their milk to the baby.

Tell your healthcare provider about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements.

COMPLERA may affect the way other medicines work, and other medicines may affect how COMPLERA works, and may cause serious side effects. If you take certain medicines with COMPLERA, the amount of COMPLERA in your body may be too low and it may not work to help control your HIV infection. The HIV virus in your body may become resistant to COMPLERA or other HIV medicines that are like it.

Do not take COMPLERA if you also take these medicines:

- COMPLERA provides a complete treatment for HIV infection. Do not take other HIV medicines with COMPLERA.
  - the anti-seizure medicines carbamazepine (CARBATROL®), EQUETRO®, TEGERTOL®, TEGERTOL-XR®, TERIL®, EPITOL®), oxcarbaemepine (TRILEPTAL®), phenobarbital (LUMINAL®), phenytoin (DILANTIN®, DILANTIN-125®, PHENYTEX®)
  - the anti-tuberculosis medicines rifabutin (MYCOBUTIN®), rifampin (RIFATER®, RIFAMATE®, RIMACTANE®, RIFADIN®) and rifapentine (PRIFITIN®)
  - a proton pump inhibitor medicine for certain stomach or intestinal problems, including esomeprazole (NEXIUM®, VIMOVO®), lansopazole (PREVACID®), omeprazole (PRILoseC®), pantoprazole sodium (PROTONIX®), rabeprazole (ACIPHEX®)
  - more than 1 dose of the steroid medicine dexamethasone or dexamethasone sodium phosphate
  - St. John’s wort (Hypericum perforatum)

If you are taking COMPLERA, you should not take:

- other medicines that contain tenofovir (VIREAD®, TRUVADA®, ATRIPLA®)
- other medicines that contain emtricitabine or lamivudine (EMTRIVA®, COMBIVIR®, EPIVIR® or EPIVIR-HBV®, EPZICOM®, TRIZIVIR®)
- rilpivirine (EDURANT™)
- adefovir (HEPSERA®)
Also tell your healthcare provider if you take:
• an antacid medicine that contains aluminum, magnesium hydroxide, or calcium carbonate. Take antacids at least 2 hours before or at least 4 hours after you take COMPLERA.
• a histamine-2 blocker medicine, including famotidine (PEPCID®), cimetidine (TAGAMET®), nizatidine (AXID®), or ranitidine hydrochloride (ZANTAC®). Take these medicines at least 12 hours before or at least 4 hours after you take COMPLERA.
• the antibiotic medicines clarithromycin (BIAXIN®), erythromycin (E-MYCIN®), ERY-TAB®, PCE®, PEDIAZOLE®, ILOSONE®, and troleandomycin (TAO®)
• an antifungal medicine by mouth, including fluconazole (DIFLUCAN®), itraconazole (SPORANOX®), ketoconazole (NIZORAL®), posaconazole (NOXAFIL®), voriconazole (VFEND®)
• methadone (DOLOPHINE®)

Ask your healthcare provider or pharmacist if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine. Your healthcare provider and pharmacist can tell you if you can take these medicines with COMPLERA. Do not start any new medicines while you are taking COMPLERA without first talking with your healthcare provider or pharmacist. You can ask your healthcare provider or pharmacist for a list of medicines that can interact with COMPLERA.

How should I take COMPLERA?
• Stay under the care of your healthcare provider during treatment with COMPLERA.
• Take COMPLERA exactly as your healthcare provider tells you to take it.
• Always take COMPLERA with a meal. Taking COMPLERA with a meal is important to help get the right amount of medicine in your body. A protein drink does not replace a meal.
• Do not change your dose or stop taking COMPLERA without first talking with your healthcare provider. See your healthcare provider regularly while taking COMPLERA.
• If you miss a dose of COMPLERA within 12 hours of the time you usually take it, take your dose of COMPLERA with a meal as soon as possible. Then, take your next dose of COMPLERA at the regularly scheduled time. If you miss a dose of COMPLERA by more than 12 hours of the time you usually take it, wait and then take the next dose of COMPLERA at the regularly scheduled time.
• Do not take more than your prescribed dose to make up for a missed dose.
• When your COMPLERA supply starts to run low, get more from your healthcare provider or pharmacy. It is very important not to run out of COMPLERA. The amount of virus in your blood may increase if the medicine is stopped for even a short time.
• If you take too much COMPLERA, contact your local poison control center or go to the nearest hospital emergency room right away.

What are the possible side effects of COMPLERA?
COMPLERA may cause the following serious side effects, including:
• See “What is the most important information I should know about COMPLERA?”
• New or worse kidney problems can happen in some people who take COMPLERA.
If you have had kidney problems in the past or take other medicines that can cause kidney problems, your healthcare provider may need to do blood tests to check your kidneys during your treatment with COMPLERA.
• Depression or mood changes. Tell your healthcare provider right away if you have any of the following symptoms:
  - feeling sad or hopeless
  - feeling anxious or restless
  - have thoughts of hurting yourself (suicide) or have tried to hurt yourself
• Bone problems can happen in some people who take COMPLERA. Bone problems include bone pain, softening or thinning (which may lead to fractures). Your healthcare provider may need to do additional tests to check your bones.
• Changes in body fat can happen in people taking HIV medicine. 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.
• Changes in your immune system (Immune Reconstitution Syndrome) can happen when you start taking HIV medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider if you start having new symptoms after starting your HIV medicine.

The most common side effects of COMPLERA include:
• trouble sleeping (insomnia)
• abnormal dreams
• headache
• dizziness
• diarrhea
• nausea
• rash
• tiredness
• depression

Additional common side effects include:
• vomiting
• stomach pain or discomfort
• skin discoloration (small spots or freckles)
• pain

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of COMPLERA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 (1-800-332-1088).

How do I store COMPLERA?
• Store COMPLERA at room temperature 77 °F (25 °C).
• Keep COMPLERA in its original container and keep the container tightly closed.
• Do not use COMPLERA if the seal over the bottle opening is broken or missing.

Keep COMPLERA and all other medicines out of reach of children.

General information about COMPLERA:
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use COMPLERA for a condition for which it was not prescribed. Do not give COMPLERA to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about COMPLERA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about COMPLERA that is written for health professionals. For more information, call (1-800-445-3235) or go to www.COMPLERA.com.

What are the ingredients of COMPLERA?
Active ingredients: emtricitabine, rilpivirine hydrochloride, and tenofovir disoproxil fumarate
Inactive ingredients: pregelatinized starch, lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, povidone, polysorbate 20. The tablet film coating contains polyethylene glycol, hypromellose, lactose monohydrate, triacetin, titanium dioxide, iron oxide red, FD&C Blue #2 aluminum lake, FD&C Yellow #6 aluminum lake.

This Patient Information has been approved by the U.S. Food and Drug Administration
Manufactured and distributed by:
Gilead Sciences, Inc.
Foster City, CA 94404

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Drug interactions

Are you a good interaction, or a bad interaction?

A guide to HIV drug interactions

UPDATED BY RENATA SMITH, PHARM.D. AND ENID VÁZQUEZ

Read the drug’s page in the Drug Guide, or refer to the package insert for a comprehensive list of potential drug interactions. **NOTE:** If “Do not take with” appears before a list of drugs, it’s because they contain the drug you’re looking up or equivalent drug(s). This is different from an “interaction.” Some drugs may only need a dose adjustment, while others may either decrease effectiveness, or worse, lead to a potentially fatal reaction. Be sure you tell your providers about all the drugs, herbs, or supplements you’re taking or planning to take, prescribed or not.

Discuss any symptoms, however minor, with your health care providers, including your pharmacist, since small reactions may become serious. A database is available at www.hiv-druginteractions.org that allows you to look up interactions and has downloadable PDFs of charts listing interactions between antiretrovirals and other drugs.

GET THE LATEST INFORMATION ON HIV DRUGS AT POSITIVELYAWARE.COM.

Nucleoside reverse transcriptase inhibitors (NRTIs)

<table>
<thead>
<tr>
<th>Potential drug class interactions</th>
<th>None.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMBIVIR</strong>&lt;sup&gt; &lt;/sup&gt;(lamivudine / zidovudine)</td>
<td>See Epivir and Retrovir. Do not take with Atripla, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Retrovir, Trizivir, or Truvada. Interacts with Zerit.</td>
</tr>
<tr>
<td><strong>EMTRIVA</strong>&lt;sup&gt; &lt;/sup&gt;(emtricitabine, or FTC)</td>
<td>Do not take with Atripla, Combivir, Complera, Epivir, Epivir-HBV, Epzicom, Trizivir, or Truvada. No other significant drug interactions.</td>
</tr>
<tr>
<td><strong>EPIVIR</strong>&lt;sup&gt; &lt;/sup&gt;(lamivudine, or 3TC)</td>
<td>Do not take with Atripla, Combivir, Complera, Emtriva, Epivir-HBV, Epzicom, Trizivir, or Truvada. No other significant drug interactions.</td>
</tr>
<tr>
<td><strong>EPZICOM</strong>&lt;sup&gt; &lt;/sup&gt;(abacavir / lamivudine)</td>
<td>See Epivir and ZiaGen. Do not take with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Trizivir, or ZiaGen.</td>
</tr>
<tr>
<td><strong>RETOVIR</strong>&lt;sup&gt; &lt;/sup&gt;(zidovudine, AZT, or ZDV)</td>
<td>Do not take with Combivir or Trizivir. Amphotericin B, Aptivus, Benemid, Biaxin, dapsone, Depakote, doxorubicin, fluocytosine, ganciclovir, hydroxyurea, interferon-alpha, Kaletra, methadone, pentamidine, phenytoin (Dilantin and others), ribavirin, rifampin, sulfadiazine, Valcyte, and Zerit.</td>
</tr>
<tr>
<td><strong>TRIZIVIR</strong>&lt;sup&gt; &lt;/sup&gt;(abacavir / lamivudine / zidovudine)</td>
<td>See Epivir, Retrovir, and ZiaGen. Do not take with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Retrovir, Truvada, or ZiaGen. Interacts with Zerit.</td>
</tr>
<tr>
<td><strong>TRUVADA</strong>&lt;sup&gt; &lt;/sup&gt;(emtricitabine / tenofovir)</td>
<td>See Emtriva and Viread. Do not take with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Retrovir, Truvada, or ZiaGen. Interacts with Zerit.</td>
</tr>
<tr>
<td><strong>VIDEX EC and VIDEIX</strong>&lt;sup&gt; &lt;/sup&gt;(didanosine, or ddi)</td>
<td>Alcohol, allopurinol, Aptivus, Atripla, cimetidine, Complera, dapsone, ganciclovir, HIV protease inhibitors, hydroxyurea, itraconazole, ketoconazole, Kaletra, methadone, pentamidine, Rescriptor, Retrovir, Reyataz, ribavirin, valganciclovir, Viread, and Zerit.</td>
</tr>
<tr>
<td><strong>VIREAD</strong>&lt;sup&gt; &lt;/sup&gt;(tenofovir, or TDF)</td>
<td>Do not take with Atripla, Complera, or Truvada. Interacts with Hepsera, Incivek, Kaletra, Norvir, Reyataz, and Viread or Viread-EC.</td>
</tr>
<tr>
<td><strong>ZERIT</strong>&lt;sup&gt; &lt;/sup&gt;(stavudine, or d4T)</td>
<td>Amphotericin B, Combivir, dapsone, foscarnet, ganciclovir, pentamidine, Retrovir, Trizivir, Valcyte, and Viread or Viread-EC.</td>
</tr>
<tr>
<td><strong>ZIAEN</strong>&lt;sup&gt; &lt;/sup&gt;(abacavir, or ABC)</td>
<td>Do not take with Epzicom or Trizivir. Interacts with alcohol, Aptivus, and Kaletra.</td>
</tr>
</tbody>
</table>
### Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

<table>
<thead>
<tr>
<th>Potential drug class interactions</th>
<th>Anti-convulsants, HIV protease inhibitors, methadone.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EDURANT</strong> (rilpivirine, or RPV)</td>
<td>Do not take with Complera, Intencel, Rescriptor, Sustiva, or Viramune. Antacids, Biaxin, dexamethasone, erythromycin, fluconazole, H2RAs (such as Pepcid, Tagamet, and Zantac), Hepsera, itraconazole, ketoconazole, medications with a known risk of Torsade de Pointes or QT prolongation, methadone, Noxafil, oscarbazepine, phenobarbital, phenytoin (Dilantin and others), proton pump inhibitors (Nexium, Prevacid, and Prilosec OTC), rifabutin, rifampin, rifapentine, St. John’s wort, Tegetrol, troleandomycin (Tao), and Vfend.</td>
</tr>
<tr>
<td><strong>INTELENCE</strong> (etravirine, or ETR)</td>
<td>Do not take with other NNRTIs. The only PIs it can be taken with are Kaletra, Invirase/ Norvir, and Prezista/Norvir. Biaxin, Cialis, Coumadin, diazepam, dolutegravir, fluconazole, Levitra, Mycobutin, phenobarbital, phenytoin (Dilantin and others), Pivax, rifampin, Selzentry, St. John’s wort, Tegetrol, Viagra, and voriconazole.</td>
</tr>
<tr>
<td><strong>RESCRIPTOR</strong> (delavirdine, or DLV)</td>
<td>Do not take with other NNRTIs. Amlodipine, certain amphetamines and antiarrhythmic drugs, Biaxin, birth control pills, Cialis, cisispride, Coumadin, dapsone, felodipine, fluticasone (Advair, Flonase, Flovent), immunosuppressants, Levitra, lovastatin, methadone, midazolam, Mycobutin, nifedipine, Norvir, phenobarbital, phenytoin (Dilantin and others), pimozide, Propulsid, quinidine, rifampin, simvastatin, St. John’s wort, Tegetrol, trazodone, triazolam, Viagra, Viracept, Vytinol, and Xanax.</td>
</tr>
<tr>
<td><strong>SUSTIVA</strong> (efavirenz, or EFV)</td>
<td>Do not take with Atripla or other NNRTIs. Biaxin, birth control pills, buproporphine, bupropion, Coumadin, Crixivan, diltiazem, dolutegravir, Gingko biloba, immunosuppressants, Invirase, itraconazole, Kaletra, Levita, Lipitor, Malarone, methadone, midazolam, Mycobutin, Norvir, Noxafil, phenobarbital, phenytoin (Dilantin and others), pimozide, pravastatin, Reyataz, rifampin, sertraline, simvastatin, St. John’s wort, Tegetrol, triazolam, Vfend, Vtcrelis, and Zoloft.</td>
</tr>
<tr>
<td><strong>VIRAMUNE XR</strong> and <strong>VIRAMUNE</strong> (nevirapine, or NVP)</td>
<td>Do not take with other NNRTIs. Biaxin, birth control pills, calcium channel blockers (Adalat, Norvasc, Procardia, etc.), cisapride, clonazepam, Cordarone, Coumadin, Crixivan, disopyramide, ethosuxomide, flucanozole, immunosuppressants, Invirase, Kaletra, ketoconazole, Lexiva, lidocaine, methadone, midazolam, Mycobutin, Norvir, phenobarbital, phenytoin (Dilantin, etc.), pimonazole, pravastatin, Reyataz, rifampin, sertraline, simvastatin, St. John’s wort, Tegetrol, triazolam, Vfend, Vtcrelis, and Zoloft.</td>
</tr>
</tbody>
</table>

### Protease inhibitors (PIs)

<table>
<thead>
<tr>
<th>Potential drug class interactions</th>
<th>Birth control pills, cardiac medications, cholesterol medications, dexamethasone, erectile dysfunction drugs, fluticasone, immunosuppressants, sedatives, St. John’s wort, and tuberculosis drugs.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>APTVUS</strong> (tipranavir, or TPV)</td>
<td>Advicor, alfuzosin, Altoprev, Antabuse, antacids, birth control pills, bosentan, buprenorphine, bupropion, calcium channel blockers (Adalat, Norvasc, Procardia, and others), Cialis, colchicine, Coumadin, Crestor, dolutegravir, Flagyl, fluconazole, flucasone (Advair, Flonase, Flovent), Fuzeon, other HIV protease inhibitors, immunosuppressants, itraconazole, ketoconazole, Lescol, Levitra, Lipitor, Livaro, lovastatin, methadone, midazolam (oral), Mycobutin, Paxil, phenobarbital, phenytoin (Dilantin, etc.), pimozide, pravastatin, Prilosec, quinidine, Retrovir, Revatio, rifabutin, rifampin, Rythmol, salmeterol, simvastatin, St. John’s wort, Suboxone, Tambocor, Tegetrol, trazodone, triazolam, valproic acid, Viagra, Vtcrelis, Videx and Videx EC, vitamin E, Vytinol, Ziajen, and Zoloft.</td>
</tr>
</tbody>
</table>

*positivelyaware.com/drugguide*
### Protease inhibitors (PIs)

#### CRIXIVAN (indinavir sulfate, or IDV)
- Advicor, alcohol, alfuzosin, Altoprev, Aptivus/Norvir, birth control pills, bosentan, calcium channel blockers (Adalat, Norvasc, Procardia, etc.), Cialis, coffee, colchicine, Cordarone, Coumadin, fluticasone (Advair, Flonase, Flovent), garlic supplements, grapefruit juice, itraconazole, immunosuppressants, Invirase, ketoconazole, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam, Mycobutin, phenobarbital, phenytoin (Dilantin and others), pimozide, pravastatin, Rescriptor, Revatio, Reyataz, rifampin, Rythmol, salmeterol, simvastatin, St. John’s wort, Sustiva, Tambocor, Tegretol, trazodone, triazolam, Viagra, Victrelis, Virmume, vitamin C, and Vytorin.

#### INVIRASE (saquinavir, or SQV) (must be taken with Norvir)
- Advicor, alfuzosin, Altoprev, Aptivus/Norvir, Biaxin, birth control pills, bosentan, Cialis, colchicine, Cordarone, Coumadin, Crestor, Crixivan, dapsone, dexamethasone, digoxin, fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, Kaletra, Lanoxin, Lescol, Levitra, Lipitor, lovastatin, methadone, midazolam (oral), Mycobutin, Nizoral, pimozide, pravastatin, proton pump inhibitors (such as Nexium, Prevacid, Prilosec OTC), quinidine, Rescriptor, Revatio, Reyataz, rifampin, Rythmol, salmeterol, simvastatin, St. John’s wort, Sporanox, Sustiva, Tambocor, trazodone, triazolam, Viagra, Victrelis, Viracept, Virmume, and Vytorin.

#### KALETRA (lopinavir / ritonavir, or LPV / r)
- Advicor, alfuzosin, Altoprev, anti-convulsants, Aptivus/Norvir, Biaxin, birth control pills, bosentan, bupropion, certain calcium channel blockers, Cialis, colchicine, Cordarone, Coumadin, digoxin, elvitegravir, Flagyl, fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, Incivek, itraconazole, Lescol, Levitra, Lexiva, Lipitor, Livalo, lovastatin, Mepron, methadone, midazolam (oral), Mycobutin, nifedipine, phenobarbital, phenytoin (Dilantin and others), pimozide, pravastatin, Retrovir, Revatio, rifabutin, rifampin, Rythmol, salmeterol, simvastatin, St. John’s wort, steroids (especially Decadron), Sustiva, Tegretol, trazodone, triazolam, Viagra, Victrelis, Videx and Videx EC, Virmume, Vytorin, and Ziaegen.

#### LEXIVA (fosamprenavir calcium, or FPV)
- Advicor, alfuzosin, Altoprev, Antabuse, Aptivus/Norvir, Biaxin, birth control pills, bosentan, calcium channel blockers, Cialis, colchicine, Coumadin (warfarin), Crestor, Flagyl, fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, Incivek, Kaletra, Lescol, Levitra, Lipitor, Livalo, lovastatin, Paxil, pimozide, pravastatin, Rescriptor, Revatio, Rythmol, methadone, midazolam (oral), Mycobutin, rifampin, salmeterol, simvastatin, St. John’s wort, steroids (especially Decadron), Sustiva, Tambocor, trazodone, triazolam, Viagra, Vicrelis, and Vytorin.

#### NORVIR (ritonavir, or RTV)
- Advicor, alcohol, alfuzosin, Altoprev, Antabuse, Biaxin, birth control pills, bosentan, Cialis, colchicine, Cordarone, Ecstasy, Flagyl, fluticasone (Advair, Flonase, Flovent), garlic supplements, GHB, immunosuppressants, Lescol, Levitra, Lipitor, Lovastatin, Paxil, pimozide, pravastatin, Rescriptor, Revatio, Rythmol, methadone, midazolam (oral), Mycobutin, nifedipine, phenobarbital, phenytoin (Dilantin and others), pimozide, pravastatin, Revatio, rifampin, Rythmol, salmeterol, simvastatin, St. John’s wort, Tambocor, Tegretol, tobacco, trazodone, triazolam, Vfend, Viagra, Victrelis, and Vytorin.

#### PREZISTA (darunavir, or DRV) (must be taken with Norvir)
- Advicor, alfuzosin, Altoprev, Aptivus/Norvir, Biaxin, birth control pills, bosentan, calcium channel blockers (Norvasc, Procardia, etc.), Cialis, cisapride, cobicistat, colchicine, Coumadin, Creator, desipramine, fluticasone (Advair, Flonase, and Flovent), immunosuppressants, Incivek, Intelence, Invirase, itraconazole, ketoconazole, Levitra, Lipitor, Livalo, lovastatin, methadone, Mevacor, midazolam (oral), nifedipine, Paxil, phenobarbital, phenytoin (Dilantin and others), pimozide, pravastatin, Revatio, rifabutin, rifampin, salmeterol, Simcor, simvastatin, St. John’s wort, Suboxone, Subutex, Tegretol, trazodone, triazolam, Vfend, Viagra, Victrelis, Vytorin, and Zoloft.
# Drug Interactions

## REYATAZ
(atazanavir sulfate, or ATV)
Advicor, alfuzosin, Altoprev, antacids (Rolaids, Tums, Mylanta, Pepcid, Zantac, etc.), Aptivus/Norvir, bepridil, birth control pills, bosentan, buprenorphine, calcium channel blockers (Adalat, Norvasc, Procardia, etc.), Campsposar, Cialis, cobicistat, colchicine, Coumadin, Cordarone, Crixivan, elvitegravir, fluticasone (Advair, Flonase, Flovent), garlic supplements, H2RAs (such as Pepcid, Tagamet, and Zantac), immunosuppressants, Invirase, Isentress, itraconazole, ketoconazole, Lescol, Levitra, lidocaine, Lipitor, Livalo, lovastatin, midazolam (oral), phenobarbital, phenytoin (Dilantin, etc.), pimozide, pravastatin, proton pump inhibitors (such as Nexium, Prevacid, Prilosec OTC), quinidine, Revatio, rifabutin, rifampin, salmeterol, simvastatin, St. John’s wort, Sustiva, Tegetrol, trazodone, triazolam, Vfend, Viagra, Vicrelis, Videx and Videx-EC, Viread, and Vytorin.

## VIRACEPT
(nelfinavir, or NFV)
Advicor, alfuzosin, Altoprev, Aptivus/Norvir, birth control pills, bosentan, Cialis, colchicine, Cordarone, Crixivan, fluticasone (Advair, Flonase, Flovent), garlic supplements, immunosuppressants, Invirase, Lescol, Levitra, Lipitor, Livalo, lovastatin, methadone, midazolam (oral), Mycobutin, phenobarbital, phenytoin (Dilantin and others), pravastatin, Prilosec OTC, Revatio, rifampin, salmeterol, simvastatin, St. John’s wort, Sustiva, Tegetrol, trazodone, triazolam, Vfend, Viagra, Vicrelis, Videx and Videx-EC, Viread, and Vytorin.

## Integrase inhibitors (INSTIs)

### ISENTRESS (raltegravir, or RAL)
Aptivus/Norvir, Prilosec, Reyataz, Reyataz/Norvir, and rifampin.

### DOLUTEGRAVIR (or DTG)
(investigational drug)
Aptivus/Norvir, Intence, and Sustiva. Available data is limited due to its investigational drug status at press time.

### ELVITEGRAVIR (or EVG)
(investigational drug)
Cobicistat, Kaletra, and Reyataz. Available data is limited due to its investigational drug status at press time.

## Entry inhibitors

### FUZEON (enfuvirtide, T-20, ENF)
None found to be clinically significant.

### SELZENTRY (maraviroc, or MVC)
Biaxin, Coumadin, Intence, Invirase, itraconazole, Kaletra, ketoconazole, midazolam (oral), Mycobutin, non-nucleosides, Norvir, oral contraceptives, phenobarbital, phenytoin (Dilantin and others), Reyataz, rifampin, St. John’s wort, Sustiva, Tegetrol, Vfend, and Viramune.

## Single-tablet regimens (STRs)

### TRIPLA
(efavirenz / emtricitabine / tenofovir)
See Sustiva and Truvada. Do not take with Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Sustiva, Trizivir, Truvada, or Viread.

### COMPLERA
(rilpivirine / emtricitabine / tenofovir)
See Edurant and Truvada. Do not take with Atripla, Combivir, Complera, Edurant, Emtriva, Epivir, Epivir-HBV, Epzicom, Sustiva, Trizivir, Truvada, or Viread.

### THE “QUAD”
(elvitegravir / cobicistat / emtricitabine / tenofovir) (investigational drug)
See elvitegravir, cobicistat, and Truvada. Do not take with Atripla, cobicistat, Combivir, Complera, elvitegravir, Emtriva, Epivir, Epivir-HBV, Epzicom, Trizivir, Truvada, or Viread. Available data is limited due to investigational drug status at press time.

## PK enhancer

### COBICISTAT (or COBI)
(investigational drug)
Likely to increase levels of certain medications. Elvitegravir, Prezista, and Reyataz. Available data is limited due to investigational drug status at press time.
PREZISTA IMPORTANT SAFETY INFORMATION AND INDICATION

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 your ability to fight HIV. Your healthcare professional will work with you to find the right combination of HIV medicines.

• It is important that you remain under the care of your healthcare professional during treatment with PREZISTA.

PREZISTA does not cure HIV infection or AIDS. You must stay on continuous HIV therapy to control infection and decrease HIV-related illnesses.

Please read Important Safety Information below, and talk to your healthcare professional to learn if PREZISTA is right for you.

IMPORTANT SAFETY INFORMATION

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

• PREZISTA can interact with other medicines and cause serious side effects. See "Who should not take PREZISTA?"

• PREZISTA may cause liver problems. Some people taking PREZISTA, together with Norvir®, have developed liver problems which may be life-threatening. Your healthcare professional should do blood tests before and during your combination treatment with 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.

• Tell your healthcare professional if you have any of these signs and symptoms of liver problems: dark (tea-colored) urine, yellowing of your skin or whites of your eyes, pale-colored stools (bowel movements), nausea, vomiting, pain or tenderness on your right side below your ribs, or loss of appetite.

• PREZISTA may cause a severe or life-threatening skin reaction or rash. Sometimes these skin reactions and skin rashes can become severe and require treatment in a hospital. You should call your healthcare professional immediately if you develop a rash. However, stop taking PREZISTA and ritonavir combination treatment and call your healthcare professional immediately if you develop any skin changes with these symptoms: fever, tiredness, muscle or joint pain, blisters or skin lesions, mouth sores or ulcers, red or inflamed eyes, like "pink eye." Rash occurred more often in patients taking PREZISTA and raltegravir together than with either drug separately, but was generally mild.

Who should not take PREZISTA?

• Do not take PREZISTA if you are taking the following medicines: alfuzosin (Uroxatral®), dihydroergotamine (D.H.E.45®), Embolex®, Migranril®, ergonovine, ergotamine (Calergot® Ergonar®, methylergonovine, cisapride (Propulsid®), pimozone (Orap®), oral midazolam, triazolam (Halcion®), the herbal supplement St. John's Wort (Hypericum perforatum), lovastatin (Mevacor®), Atorvastatin (Pravachol®), simvastatin (Zocor®), Simcor®), Vytorin®, rifampin (Rifadin®, Rifater®, Rimactane®, sildenafil (Revatio®) when used to treat pulmonary arterial hypertension, indinavir (Crixivan®), lopinavir/ritonavir (Kaletra®), saquinavir (Invirase®), or telaprevir (Incivek™).

Before taking PREZISTA, tell your healthcare professional if you are taking sildenafil (Viagra®, Revatio®), vardenafil (Levitra®, Staxyn®), tadalafl (Cialis®, Adcirca®), atorvastatin (Lipitor®), rosuvastatin (Crestor®), or clophilene (Colcrys®, Col-Probenedex®). 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.

This is not a complete 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.

What should I tell my doctor before I take PREZISTA?

• Before taking PREZISTA, tell your healthcare professional if you have any medical conditions, including liver problems (including hepatitis B or C), allergy to sulfa medicines, diabetes, 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.

What are the possible side effects of PREZISTA?

• 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.

• Changes in your immune system can happen when you start taking HIV medicines. Your immune system may get stronger and begin to fight infections that have been hidden.

• The most common side effects related to taking PREZISTA include diarrhea, nausea, rash, headache, stomach pain, and vomiting. This is not a complete list of all possible side effects. If you experience these or other side effects, talk to your healthcare professional. Do not stop taking PREZISTA or any other medicines without first talking to your healthcare professional.

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 refer to the ritonavir (Norvir®) Product Information (PI and PPI) for additional information on precautionary measures.

Dosing Information:

For adults taking HIV meds for the first time and for many adults who have taken HIV meds in the past:

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. For some adults, who have taken HIV meds in the past:

PREZISTA 600 mg/Norvir® 100 mg must be taken twice daily at the same time every day with food. Your healthcare professional can determine which dose is right for you.

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.
For adults who have not taken HIV medications before and also for many adults who have taken HIV medications in the past

Once-Daily PREZISTA 800 mg (two 400-mg tablets) must be taken with Norvir® 100 mg and food at the same time every day, as part of combination HIV therapy.

Talk to your healthcare professional about your HIV treatment options and ask if Once-Daily PREZISTA is right for you.

Please read Important Safety Information and dosing information on adjacent page.

www.PREZISTA.com
Increasing the CD4 (T) cell count may improve your immune system. This may help fight off other infections. Reducing the amount of HIV and preventing the spread of HIV can also reduce your risk of death or infections that can happen when your immune system is weak. Patients must stay on continuous HIV therapy to control infection and decrease HIV-related illnesses.

Always practice safer sex by using a latex or polyurethane condom 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 healthcare provider if you have any questions on how to prevent passing HIV to other people.

PREZISTA is a prescription anti-HIV medicine used with ritonavir and another HIV medicine to decrease the amount of HIV in your blood (called "viral load"). PREZISTA may also help to increase the number of white blood cells called CD4 (T) cells which help fight off other infections. Reducing the amount of HIV and increasing the CD4 (T) cell count may improve your immune system. This may reduce your risk of death or infections that can happen when your immune system is weak (opportunistic infections).

PREZISTA does not cure HIV infection or AIDS. People taking PREZISTA may still develop infections or other conditions associated with HIV infection. Some of these conditions are pneumonia, herpes virus infections, and Mycobacterium avium complex (MAC) infections. Patients must stay on continuous HIV therapy to control infection and decrease HIV-related illnesses.

Always practice safer sex by using a latex or polyurethane condom 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 healthcare provider if you have any questions on how to prevent passing HIV to other people.

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

- **PREZISTA can interact with other medicines and cause serious side effects.** It is important to know the medicines that should not be taken with PREZISTA. See the section “Who should not take PREZISTA?”

- **PREZISTA may cause liver problems.** Some people taking PREZISTA in combination with NORVIR® (ritonavir) have developed liver problems which may be life-threatening. Your healthcare provider should check your blood tests more often because you have an increased chance of developing liver problems.

Tell your healthcare provider if you have any of the below signs and symptoms of liver problems:
- Dark (tea colored) urine
- Yellowing of your skin or whites of your eyes
- Pale colored stools (bowel movements)
- Nausea
- Vomiting
- Pain or tenderness on your right side below your ribs
- Loss of appetite

PREZISTA may cause severe or life-threatening skin reactions or rash. Sometimes these skin reactions and skin rashes can become severe and require treatment in a hospital. You should call your healthcare provider immediately if you develop a rash. However, stop taking PREZISTA and ritonavir combination treatment and call your healthcare provider immediately if you develop any skin changes with symptoms below:
- Fever
- Tiredness
- Muscle or joint pain
- Blisters or skin lesions
- Mouth sores or ulcers
- Red or inflamed eyes, like “pink eye” (conjunctivitis)

Rash occurred more often in patients taking PREZISTA and raltegravir together than with either drug separately, but was generally mild.

See “What are the possible side effects of PREZISTA?” for more information about side effects.

What is PREZISTA?

PREZISTA is a prescription anti-HIV medicine used with ritonavir and other anti-HIV medicines to treat adults and children 6 years of age and older with human immunodeficiency virus (HIV-1) infection. PREZISTA is a type of anti-HIV medicine called a protease inhibitor. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

When used with other HIV medicines, PREZISTA may help to reduce the amount of HIV in your blood (called “viral load”). PREZISTA may also help to increase the number of white blood cells called CD4 (T) cell which help fight off other infections. Reducing the amount of HIV and increasing the CD4 (T) cell count may improve your immune system. This may reduce your risk of death or infections that can happen when your immune system is weak (opportunistic infections).

PREZISTA does not cure HIV infection or AIDS. People taking PREZISTA may still develop infections or other conditions associated with HIV infection. Some of these conditions are pneumonia, herpes virus infections, and Mycobacterium avium complex (MAC) infections. Patients must stay on continuous HIV therapy to control infection and decrease HIV-related illnesses.

Always practice safer sex by using a latex or polyurethane condom 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 healthcare provider if you have any questions on how to prevent passing HIV to other people.

Who should not take PREZISTA?

Do not take PREZISTA with any of the following medicines:
- alfuzosin (Uroxatral®)
- dihydroergotamine (D.H.E. 45®, Embolex®, Migranal®), ergonovine, ergotamine (Cafergot®, Ergomar®) methylergometine
- cisapride
- pimozone (Orap®)
- oral midazolam, triazolam (Halcion®)
- the herbal supplement St. John’s Wort (Hypericum perforatum)
- the cholesterol lowering medicines lovastatin (Mevacor®, Altovue®, Advicor®) or simvastatin (Zocor®, Simcor®, Vytorin®)
- rifampin (Rifadin®, Rifater®, Rifamate®, Rimactane®)
- sildenafil (Revatio®) only when used for the treatment of pulmonary arterial hypertension.

Serious problems can happen if you or your child take any of these medicines with PREZISTA.

What should I tell my doctor before I take PREZISTA?

PREZISTA may not be right for you. Before taking PREZISTA, tell your healthcare provider if you:
- have liver problems, including hepatitis B or hepatitis C
- are allergic to sulfa medicines
- have high blood sugar (diabetes)
- have hemophilia
- are pregnant or planning to become pregnant. It is not known if PREZISTA will harm your unborn baby.

**Pregnancy Registry:** You and your healthcare provider will need to decide if taking PREZISTA is right for you. If you take PREZISTA while you are pregnant, talk to your healthcare provider about how you can be included in the Antiretroviral Pregnancy Registry. The purpose of the registry is follow the health of you and your baby.
- are breastfeeding or plan to breastfeed. 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 healthcare provider about the best way to feed your baby. The Centers for Disease Control and Prevention (CDC) recommends that HIV-infected mothers not breastfeed to avoid the risk of passing HIV infection to your baby.

Tell your healthcare provider about all the medicines you take including prescription and nonprescription medicines, vitamins, and herbal supplements. Using PREZISTA and certain other medicines may affect each other causing serious side effects. PREZISTA may affect the way other medicines work and other medicines may affect how PREZISTA works.

Especially tell your healthcare provider if you take:
- medicine to treat HIV
- 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.
- medicine for your heart such as bepridil, lidocaine (Xylocaine Viscous®), quinidine (Nuedexta®), amiodarone (Pacerone®, Cardarone®), digoxin (Lanoxin®), flecainide (Tambocor®), propafenone (Rythmol®)
- warfarin (Coumadin®, Jantoven®)
- medicine for seizures such as carbamazepine (Carbatrol®, Equetro®, Teegretol®, Epitol®), phenobarbital, phenytoin (Dilantin®, Phenytek®)
- medicine for depression such as trazadone and desipramine (Norpramin®)
- clarithromycin (Prevpac®, Biaxin®)
- medicine for fungal infections such as ketoconazole (Nizoral®), itraconazole (Sporanox®, Onmel®), voriconazole (VFend®)
- colchicine (Colcrys®, Col-Probenecid®)
- rifabutin (Mycobutin®)
- medicine used to treat blood pressure, a heart attack, heart failure, or to lower pressure in the eye such as metoprolol (Lopressor®, Toprol-XL®), timolol (Cosopt®, Betimol®, Timoptic®, Isaltiol®, Combigan®)
- midazolam administered by injection
Headache, and nausea, and fatigue. Oh, my!

A look at the possible side effects that can result from HIV medications

Updated by Renata Smith, PharmD and Enid Vázquez

Read the drug’s page in the Drug Guide for details, or refer to the manufacturer’s package insert for a 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 symptoms, however minor, with your health care providers, including your pharmacist, since small reactions may become serious. There may also be management techniques for side effects. Table begins on next page.
## Side effects

### Nucleoside reverse transcriptase inhibitors (NRTIs)

<table>
<thead>
<tr>
<th>Potential drug class side effects</th>
<th>Rare but potentially serious toxicity with all NRTIs: enlarged, fatty liver (hepatomegaly with steatosis) and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis may cause persistent fatigue, abdominal pain or distension, nausea/vomiting, difficulty breathing or shortness of breath, and enlarged liver.</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMBIVIR (lamivudine / zidovudine)</td>
<td>See Epivir and Retrovir.</td>
</tr>
<tr>
<td>EMTRIVA (emtricitabine, or FTC)</td>
<td>A very tolerable drug, but side effects may include headache, diarrhea, nausea, and rash. Darkening of the skin on the palms and the soles of the feet has also been reported.</td>
</tr>
<tr>
<td>EPIVIR (lamivudine, or 3TC)</td>
<td>A very tolerable drug, but side effects may include headache, nausea, vomiting, diarrhea, fever, fatigue, hair loss, insomnia, malaise, nasal symptoms, and cough.</td>
</tr>
<tr>
<td>EPZICOM (abacavir / lamivudine)</td>
<td>See Epivir and Ziden.</td>
</tr>
<tr>
<td>RETROVIR (zidovudine, AZT, or ZDV)</td>
<td>Headaches, fever, chills, muscle soreness and/or damage, fatigue, nausea, lipodystrophy, fingernail discoloration, anemia (low red blood cell count), and neutropenia (low white blood cell count).</td>
</tr>
<tr>
<td>TRIZIVIR (abacavir / lamivudine / zidovudine)</td>
<td>See Epivir, Retrovir, and Ziden.</td>
</tr>
<tr>
<td>VIDEX EC and VIDEX (didanosine, or ddl)</td>
<td>Peripheral neuropathy, upset stomach, diarrhea, headache, pancreatitis (inflammation of the pancreas), eye changes and optic neuritis, increased uric acid levels, insomnia, and body fat redistribution.</td>
</tr>
<tr>
<td>VIREAD (tenofovir DF, or TDF)</td>
<td>Overall fairly well tolerated; however, side effects may include nausea, diarrhea, vomiting, flatulence (gas), bone changes, kidney toxicities, decreased bone mineral density, and low blood phosphate.</td>
</tr>
<tr>
<td>ZERIT (stavudine, or d4T)</td>
<td>Headache, diarrhea, nausea, rash, peripheral neuropathy, lipoatrophy (including facial wasting), mitochondrial toxicities (a variety of symptoms caused by cell damage), and elevated cholesterol levels.</td>
</tr>
<tr>
<td>ZIAGEN (abacavir, or ABC)</td>
<td>Hypersensitivity reaction, nausea, vomiting, diarrhea, fatigue, headache, fever, rash, and loss of appetite.</td>
</tr>
</tbody>
</table>

### Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

<table>
<thead>
<tr>
<th>Potential drug class side effects</th>
<th>Rash. Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDURANT (rilpivirine, or RPV)</td>
<td>Insomnia, headache, rash, and depressive disorders.</td>
</tr>
<tr>
<td>INTELENCE (etravirine, or ETR)</td>
<td>Rash, diarrhea, nausea, nasopharyngitis (symptoms like a common cold), headache, hypersensitivity, and increased liver enzyme levels.</td>
</tr>
<tr>
<td>RESCRIPTOR (delavirdine, or DLV)</td>
<td>Increased liver enzyme levels and itchy skin or rash.</td>
</tr>
<tr>
<td>SUSTIVA (efavirenz, or EFV)</td>
<td>Central nervous system (CNS) and psychiatric symptoms. Rash, nausea, vomiting, diarrhea, fever, insomnia, and increases in triglycerides, bad cholesterol (LDL), good cholesterol (HDL), and liver enzyme levels. False positive tests for marijuana. Birth defects.</td>
</tr>
<tr>
<td>VIRAMUNE XR and VIRAMUNE (nevirapine, or NVP)</td>
<td>Headache, nausea, vomiting, fever, rash, Stevens-Johnson syndrome, increased liver enzyme levels, liver damage, and drug-induced hepatitis.</td>
</tr>
</tbody>
</table>
### Protease inhibitors (PIs)

#### Potential drug class side effects

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

#### APTIVUS
(tipranavir, or TPV)
(must be taken with Norvir)
- 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; use with caution in patients with allergies to sulfa drugs. Also see Norvir.

#### CRIXIVAN
(indinavir sulfate, or IDV)
- Headache, fatigue or weakness, malaise, nausea, diarrhea, stomach pain, 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.

#### INGINASE
(saquinavir, or SQV)
(must be taken with Norvir)
- Diarrhea, abdominal discomfort, vomiting, and nausea. Also see Norvir.

#### KALETRA
(lopinavir / ritonavir, or LPV / r)
- Rash, diarrhea, nausea, vomiting, stomach pain, headache, muscle weakness, increased cholesterol and triglycerides, and increased liver enzyme levels. Also see Norvir.

#### LEXIVA
(fosamprenavir calcium, or FPV)
Nausea, rash, diarrhea, headache, vomiting, fatigue, and abdominal pain. Lexiva has a sulfa component; use with caution in patients with allergies to sulfa drugs.

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

#### PREZISTA
(daranavir, or DRV)
(must be taken with Norvir)
- Rash, diarrhea, nausea, headache, abdominal pain, and increased liver enzyme levels. Prezista has a sulfa component; use with caution in patients with allergies to sulfa drugs. Also see Norvir.

#### REYATAZ
(atazanavir sulfate, or ATV)
- Dizziness, lightheadedness, rash, kidney stones, and elevated liver enzyme levels, including elevated levels of unconjugated bilirubin.

#### VIRACEPT
(nelfinavir, or NFV)
- Diarrhea, stomach discomfort, nausea, gas, weakness, and rash.

### Integrase inhibitors (INSTIs)

#### Potential drug class side effects

- Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.

#### ISENTRESS
(raltegravir, or RAL)
- A very tolerable drug, but side effects may include diarrhea, nausea, vomiting, headache, fever, abdominal pain, fatigue, weakness, dizziness, lipodystrophy, increased levels of liver enzymes and creatine kinase, allergic reaction, and cerebellar ataxia.

#### DOLUTEGRAVIR
(or DTG)
(investigational drug)
- Seen in clinical study: nausea, diarrhea, headache, dizziness, fatigue, weakness, and upset stomach or indigestion. Available data is limited due to investigational status at press time.

#### ELVITEGRAVIR
(or EVG)
(investigational drug)
- Seen in clinical study: diarrhea, upper respiratory tract infection, bronchitis, back pain, depression, sinusitis, joint pain, nausea, and urinary tract infection. Available data is limited due to investigational status at press time.
### Entry inhibitors

<table>
<thead>
<tr>
<th>Potential drug class side effects</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune Reconstitution Inflammatory Syndrome (IRIS) may occur as the immune system regains strength; signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is initiated. Report symptoms of illness, such as shingles and TB, to a health care provider.</td>
<td></td>
</tr>
</tbody>
</table>

| FUZEON (enfuvirtide, T-20, ENF) | Injection site reactions (ISRs), pneumonia, diarrhea, nausea, and fatigue. Hypersensitivity reactions are possible. |

| SELZENTRY (maraviroc, or MVC) | Cough, fever, cold, rash, muscle and joint pain, stomach pain, dizziness, liver toxicity, allergic reaction, low blood pressure, and possible increased risk of infections and cancer. |

### Single-tablet regimens (STRs)


| COMPLERA (rilpivirine / emtricitabine / tenofovir) | See Edurant and Truvada (Emtriva and Viread). Complera dose cannot be adjusted for people with kidney problems. Insomnia, headache, nausea, dizziness, rash, abnormal dreams, and depressive disorders. |


### PK enhancer

| COBICISTAT (or COBI) (investigational drug) | Seen in clinical study: diarrhea, nausea, lipid elevations (increases in cholesterol and triglycerides), creatine kinase, red blood cells in urine, increased serum creatinine, and decreased estimated glomerular filtration rate (e-GFR). Available data is limited due to investigational status at press time. |
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¹ For eligible privately insured patients. Not valid for residents of Massachusetts. Restrictions apply. Please see full Terms and Conditions on isentress.com.
PAYING FOR YOUR MEDS

It doesn’t have to break the bank

BY JEFF BERRY

LET’S FACE IT, HIV MEDICATIONS ARE EXPENSIVE, EVEN FOR those with health insurance. Fortunately, financial assistance is available to help cover some, if not all, of the costs associated with treating HIV. The last thing anyone needs to worry about is not being able to pay for their medications, so hopefully this article will help you to navigate the system and keep your medicine chest full, while keeping your stress level to a minimum.

CO-PAY AND PATIENT ASSISTANCE PROGRAMS
Most pharmaceutical companies provide some level of assistance to individuals who are unable to afford their HIV medications, through the use of a patient assistance program, or PAP. These PAPs are typically for patients without insurance and who don’t qualify for Medicare, Medicaid, or ADAP. Qualifications and criteria vary by program and are based on a percentage of Federal Poverty Level (FPL), for example 300%. 100% of FPL is currently $10,890 for a single individual, so 300% would be $32,670. Some companies are now covering up to 500% FPL and even higher, so check the details of each program.

Patients or providers should contact the manufacturer directly to see if they are eligible (see chart, page 76).

Many companies also have co-pay assistance programs which are designed for those who have drug coverage through privately held insurance. These programs may cover all or part of the drug co-pay up to a specified amount, and for a predetermined period of time (for example, up to one year). Certain restrictions and eligibility requirements apply (for example, recipients of ADAP, Medicare, and Medicaid are not eligible), and may vary from program to program. Individuals usually get the co-pay card directly from their provider, the manufacturer’s website, or by calling a toll-free number. Once enrolled, they bring the co-pay card to the pharmacy when filling their prescription and the pharmacy is reimbursed for the amount covered.

The Fair Pricing Coalition (FPC) regularly meets with drug companies on pricing issues and in an effort to help control costs and improve access to these life-saving medications. The existing HIV and hepatitis drug co-pay programs are the direct result of ongoing discussions between the FPC and representatives of the pharmaceutical industry. After concerns were voiced by both the FPC and members of the community over rising costs and people not being able to get their medications, many companies increased coverage for their co-pay programs, raised the qualifying level of income for some PAPs and eased restrictions, thereby making the programs even more accessible to people who in the past may not have qualified.

MEDICARE AND MEDICAID
 Medicare is a federally-funded program focusing primarily on the older population. It is a social insurance program for people age 65 or older, people under age 65 with certain disabilities, including HIV/AIDS, and people of all ages with end stage renal disease. Medicare Part A covers hospital bills, Medicare Part B covers basic medical and preventive services, and Medicare Part D covers prescription drugs. Medicare operates similar to a single-payer health care system, the key difference being that its coverage only extends to 80% of any given medical cost; the remaining 20% must be paid by other means, such as privately-held supplemental insurance, or by the patient.

Medicaid is a program that is not entirely funded at the federal level—states provide up to half of the funding, and counties also contribute funds in some states. Eligibility is determined largely by limited income and financial resources. Medicaid covers a wider range of health care services than Medicare, and it is CONTINUED ON PAGE 76>>
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To order, go to www.adaywithhiv.com/book

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>> CONTINUED FROM PAGE 74

Currently the largest single payer for prescription drugs.

**ADAP AND WELVISTA**

Around one-third of all people receiving HIV treatment in the U.S. get their medications through AIDS Drug Assistance Programs (ADAPs), which are a set of federal- and state-funded programs in each state that provide medications to low-income patients. Welvista is a non-profit organization funded by the Heinz Family Philanthropies and through grants from many of the major pharmaceutical companies. Currently, seven companies that market HIV drugs are participating in the program, which is designed to facilitate access to HIV meds for those on ADAP waiting lists by streamlining paperwork and using a single mail-order pharmacy, rather than having to access multiple patient assistance programs. You will need to be certified by your state ADAP and on a waiting list to participate in this program. Welvista is a stand-alone non-profit company that dispenses medicines for other disease states, not just HIV. Visit www.welvista.com.

This past year several pharmaceutical companies continued to expand coverage for their co-pay and patient assistance programs, and provided additional cost rebates to AIDS Drug Assistance Programs (ADAPs) around the country. However, budget cuts continue to hit ADAPs hard, and many states have continued to slash formularies, cap enrollment, and institute waiting lists, among other harsh measures.

**ADDITIONAL PROGRAMS**

People living with HIV/AIDS may need medications for other conditions such as high cholesterol or diabetes. To learn more about patient assistance or drug co-pay programs for these and other medications, talk to your provider, contact the manufacturer directly, or visit www.needymeds.org. TogetherRx is a prescription savings program for uninsured individuals sponsored by many of the nation’s leading pharmaceutical companies for uninsured individuals; call toll-free 800-966-0407, or enroll online at www.TogetherRxAccess.com.

SurvivorRxPlan offers help to get many medications not covered by ADAP, including alternative therapies and generics. Patients can use the program even if they receive medicines through another discount program. It is available to individuals with incomes of up to $36,425, and higher based on family size. Visit www.SurvivorRxPlan.com.

Additional co-pay and patient assistance programs are available for drugs used to treat hepatitis B and C, as well as medications or treatments used for other HIV-related conditions such as lipodystrophy. For example, Egrifta, used to treat lipohypertrophy, has a co-pay program and a PAP; and Sculptra, which is used to treat facial lipoatrophy, has a PAP which provides the facial filler for free or on a sliding scale. Contact the manufacturer, discuss with your provider, or visit www.fairpricingcoalition.org.

**STAY INFORMED AND UP TO DATE**

Keeping the lines of communication open between you and your health care provider, pharmacist, and case manager is essential when managing your health, so stay informed. In some cases your health care provider may not be aware of all the programs available, so use the adjacent chart to check specific details for all HIV drug programs. You can also visit www.positivelyaware.com for the most current information, as details of specific programs may change.

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**SPECIAL THANKS TO THE FAIR PRICING COALITION FOR SOME OF THE INFORMATION CONTAINED IN THIS ARTICLE. NOTE: THE AUTHOR IS A MEMBER OF THE FAIR PRICING COALITION.**

The chart at right gives a brief description of current HIV co-pay and patient assistance programs. If you need help, call the Project Inform Hotline at 800-822-7422, or call the number listed for each program. Also go to www.positivelyaware.com/copay.shtml as details of specific programs may change.

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**HIV CO-PAY & PATIENT ASSISTANCE**

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<tr>
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<tr>
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You can talk to us. We speak HIV.

When you need to talk, we’re here for you.

You can turn to Walgreens pharmacists for expert advice on everything from managing your medication therapy and side effects to navigating your insurance benefits.

✓ HIV/AIDS-trained pharmacists
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✓ Support services available at no additional cost

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