POSITIVELY AWARE

THE HIV TREATMENT JOURNAL OF TEST POSITIVE AWARE NETWORK
MARCH+APRIL 2015

THE STATE OF **ANTIRETROVIRAL THERAPY**

PAYING FOR YOUR MEDS
WHERE TO GET HELP

NEW DRUGS
ON THE HORIZON

SPECIAL PULL-OUT CHART
THE 37 HIV MEDS

LIVE POSITIVE

FINDING YOUR BEST TREATMENT IS A CONVERSATION, NOT A CHOICE

THE 19TH ANNUAL HIV DRUG GUIDE

What is STRIBILD?

STRIBILD is a prescription medicine used to treat HIV-1 in adults who have never taken HIV-1 medicines before. It combines 4 medicines into 1 pill to be taken once a day with food. STRIBILD is a complete single-tablet regimen and should not be used with other HIV-1 medicines.

STRIBILD does not cure HIV-1 infection or AIDS. To control HIV-1 infection and decrease HIV-related illnesses you must keep taking STRIBILD. Ask your healthcare provider if you have questions about how to reduce the risk of passing HIV-1 to others. Always practice safer sex and use condoms to lower the chance of sexual contact with body fluids. Never reuse or share needles or other items that have body fluids on them.

IMPORTANT SAFETY INFORMATION

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

STRIBILD can cause serious side effects:

- **Build-up of an acid in your blood (lactic acidosis),** which is a serious medical emergency. Symptoms of lactic acidosis include feeling very weak or tired, unusual (not normal) muscle pain, trouble breathing, stomach pain with nausea or vomiting, feeling cold especially in your arms and legs, feeling dizzy or lightheaded, and/or a fast or irregular heartbeat.
- **Serious liver problems.** The liver may become large (hepatomegaly) and fatty (steatosis). Symptoms of liver problems include 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, and/or stomach pain.
- **You may be more likely to get lactic acidosis or serious liver problems** if you are female, very overweight (obese), or have been taking STRIBILD for a long time. In some cases, these serious conditions have led to death. Call your healthcare provider right away if you have any symptoms of these conditions.
- **Worsening of hepatitis B (HBV) infection.** If you also have HBV and stop taking STRIBILD, your hepatitis may suddenly get worse. Do not stop taking STRIBILD without first talking to your healthcare provider, as they will need to monitor your health. STRIBILD is not approved for the treatment of HBV.

Who should not take STRIBILD?

Do not take STRIBILD if you:

- **Take a medicine that contains:** alfuzosin, dihydroergotamine, ergotamine, methylergonovine, cisapride, lovastatin, simvastatin, pimozide, sildenafil when used for lung problems (Revatio®), triazolam, oral midazolam, rifampin or the herb St. John's wort.
- **For a list of brand names for these medicines,** please see the Brief Summary on the following pages.
- **Take any other medicines to treat HIV-1 infection,** or the medicine adefovir (Hepsera®).

What are the other possible side effects of STRIBILD?

Serious side effects of STRIBILD may also include:

- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do regular blood and urine tests to check your kidneys before and during treatment with STRIBILD. If you develop kidney problems, your healthcare provider may tell you to stop taking STRIBILD.
- **Bone problems,** including bone pain or bones getting soft or thin, which may lead to fractures. Your healthcare provider may do tests to check your bones.
- **Changes in body fat** can happen in people taking HIV-1 medicines.
- **Changes in your immune system.** Your immune system may get stronger and begin to fight infections. Tell your healthcare provider if you have any new symptoms after you start taking STRIBILD.

The most common side effects of STRIBILD include nausea and diarrhea. Tell your healthcare provider if you have any side effects that bother you or don't go away.

What should I tell my healthcare provider before taking STRIBILD?

- **All your health problems.** Be sure to tell your healthcare provider if you have or had any kidney, bone, or liver problems, including hepatitis virus infection.
- **All the medicines you take,** including prescription and nonprescription medicines, vitamins, and herbal supplements. STRIBILD may affect the way other medicines work, and other medicines may affect how STRIBILD works. Keep a list of all your medicines and show it to your healthcare provider and pharmacist. Do not start any new medicines while taking STRIBILD without first talking with your healthcare provider.
- **If you take hormone-based birth control** (pills, patches, rings, shots, etc).
- **If you take antacids.** Take antacids at least 2 hours before or after you take STRIBILD.
- **If you are pregnant** or plan to become pregnant. It is not known if STRIBILD can harm your unborn baby. Tell your healthcare provider if you become pregnant while taking STRIBILD.
- **If you are breastfeeding** (nursing) or plan to breast-feed. Do not breastfeed. HIV-1 can be passed to the baby in breast milk. Also, some medicines in STRIBILD can pass into breast milk, and it is not known if this can harm the baby.

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 Brief Summary of full Prescribing Information with **important warnings** on the following pages.

STRIBILD is a prescription medicine used as a complete single-tablet regimen to treat HIV-1 in adults who have never taken HIV-1 medicines before. STRIBILD does not cure HIV-1 or AIDS.

I started my personal revolution

Talk to your healthcare provider about starting treatment.

STRIBILD is a complete HIV-1 treatment in 1 pill, once a day.

Ask if it's right for you.

STRIBILD®

elvitegravir 150mg/ cobicistat 150mg/ emtricitabine 200mg/ tenofovir disoproxil fumarate 300mg tablets

GILEAD

Patient Information

STRIBILD® (STRY-bild)
(elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg) tablets

Brief summary of full Prescribing Information. For more information, please see the full Prescribing Information, including Patient Information.

What is STRIBILD?

- **STRIBILD is a prescription medicine used to treat HIV-1 in adults who have never taken HIV-1 medicines before.** STRIBILD is a complete regimen and should not be used with other HIV-1 medicines.
- **STRIBILD does not cure HIV-1 or AIDS.** You must stay on continuous HIV-1 therapy to control HIV-1 infection and decrease HIV-related illnesses.
- **Ask your healthcare provider about how to prevent passing HIV-1 to others.** Do not share or reuse needles, injection equipment, or personal items that can have blood or body fluids on them. Do not have sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

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

STRIBILD can cause serious side effects, including:

1. **Build-up of lactic acid in your blood (lactic acidosis).** Lactic acidosis can happen in some people who take STRIBILD 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:**
   - feel very weak or tired
   - have unusual (not normal) muscle pain
   - have trouble breathing
   - have stomach pain with nausea or 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 STRIBILD. 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). **Call your healthcare provider right away if you get 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 STRIBILD for a long time.
3. **Worsening of Hepatitis B infection.** If you have hepatitis B virus (HBV) infection and take STRIBILD, your HBV may get worse (flare-up) if you stop taking STRIBILD. A "flare-up" is when your HBV infection suddenly returns in a worse way than before.
   - Do not run out of STRIBILD. Refill your prescription or talk to your healthcare provider before your STRIBILD is all gone
   - Do not stop taking STRIBILD without first talking to your healthcare provider
   - If you stop taking STRIBILD, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking STRIBILD

Who should not take STRIBILD?

Do not take STRIBILD if you also take a medicine that contains:

- adefovir (Hepsera®)
- alfuzosin hydrochloride (Uroxatral®)
- cisapride (Propulsid®, Propulsid Quicksolv®)
- ergot-containing medicines, including: dihydroergotamine mesylate (D.H.E. 45®, Migranal®), ergotamine tartrate (Cafergot®, Migergot®, Ergostat®, Medihaler Ergotamine®, Wigraine®, Wigrettes®), and methylergonovine maleate (Ergotrate®, Methergine®)
- lovastatin (Advicor®, Altoprev®, Mevacor®)
- oral midazolam
- pimozide (Orap®)
- rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®)
- sildenafil (Revatio®), when used for treating lung problems
- simvastatin (Simcor®, Vytorin®, Zocor®)
- triazolam (Halcion®)
- the herb St. John's wort

Do not take STRIBILD if you also take any other HIV-1 medicines, including:

- Other medicines that contain tenofovir (Atripla®, Complera®, Viread®, Truvada®)
- Other medicines that contain emtricitabine, lamivudine, or ritonavir (Atripla®, Combivir®, Complera®, Emtriva®, Epivir® or Epivir-HBV®, Epzicom®, Kaletra®, Norvir®, Trizivir®, Truvada®)

STRIBILD is not for use in people who are less than 18 years old.

What are the possible side effects of STRIBILD?

STRIBILD may cause the following serious side effects:

- **See "What is the most important information I should know about STRIBILD?"**
- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do blood and urine tests to check your kidneys before you start and while you are taking STRIBILD. Your healthcare provider may tell you to stop taking STRIBILD if you develop new or worse kidney problems.
- **Bone problems** can happen in some people who take STRIBILD. Bone problems include bone pain, softening or thinning (which may lead to fractures). Your healthcare provider may need to do tests to check your bones.
- **Changes in body fat** can happen in people who take HIV-1 medicine. These changes may include increased amount of fat in the upper back and neck ("buffalo hump"), breast, and around the middle of your body (trunk). Loss of fat from the legs, arms and face may also happen. The exact cause and long-term health effects of these conditions are not known.
- **Changes in your immune system** (Immune Reconstitution Syndrome) can happen when you start taking HIV-1 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 right away if you start having any new symptoms after starting your HIV-1 medicine.

The most common side effects of STRIBILD include:

- Nausea
- Diarrhea

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 STRIBILD. For more information, ask your healthcare provider.
- Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

What should I tell my healthcare provider before taking STRIBILD?

Tell your healthcare provider about all your medical conditions, including:

- If you have or had any kidney, bone, or liver problems, including hepatitis B infection
- If you are pregnant or plan to become pregnant. It is not known if STRIBILD can harm your unborn baby. Tell your healthcare provider if you become pregnant while taking STRIBILD.
  - There is a pregnancy registry for women who take antiviral medicines during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk with your healthcare provider about how you can take part in this registry.
- If you are breastfeeding (nursing) or plan to breastfeed. Do not breastfeed if you take STRIBILD.
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
  - Two of the medicines in STRIBILD can pass to your baby in your breast milk. It is not known if the other medicines in STRIBILD can pass into your breast milk.
  - Talk with your healthcare provider about the best way to feed your baby.

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

- STRIBILD may affect the way other medicines work, and other medicines may affect how STRIBILD works.
- Be sure to tell your healthcare provider if you take any of the following medicines:
  - Hormone-based birth control (pills, patches, rings, shots, etc)
  - Antacid medicines that contain aluminum, magnesium hydroxide, or calcium carbonate. Take antacids at least 2 hours before or after you take STRIBILD
  - Medicines to treat depression, organ transplant rejection, or high blood pressure
  - amiodarone (Cordarone®, Pacerone®)
  - atorvastatin (Lipitor®, Caduet®)
  - bepridil hydrochloride (Vascor®, Bepadin®)
  - bosentan (Tracleer®)
  - buspirone
  - carbamazepine (Carbatrol®, Epitol®, Equetro®, Tegretol®)
  - clarithromycin (Biaxin®, Prevpac®)
  - clonazepam (Klonopin®)
  - clorazepate (Gen-xene®, Tranxene®)
  - colchicine (Colcrys®)
  - medicines that contain dexamethasone
  - diazepam (Valium®)
  - digoxin (Lanoxin®)
  - disopyramide (Norpace®)
  - estazolam
  - ethosuximide (Zarontin®)
  - flecainide (Tambocor®)
  - flurazepam
  - fluticasone (Flovent®, Flonase®, Flovent® Diskus®, Flovent® HFA, Veramyst®)
  - itraconazole (Sporanox®)
  - ketoconazole (Nizoral®)
  - lidocaine (Xylocaine®)
  - mexiletine
  - oxcarbazepine (Trileptal®)
  - perphenazine
  - phenobarbital (Luminal®)
  - phenytoin (Dilantin®, Phenytek®)
  - propafenone (Rythmol®)
  - quinidine (Neudexta®)
  - rifabutin (Mycobutin®)
  - rifapentine (Priftin®)
  - risperidone (Risperdal®, Risperdal Consta®)
  - salmeterol (Serevent®) or salmeterol when taken in combination with fluticasone (Advair Diskus®, Advair HFA®)
  - sildenafil (Viagra®), tadalafil (Cialis®) or vardenafil (Levitra®, Staxyn®), for the treatment of erectile dysfunction (ED). If you get dizzy or faint (low blood pressure), have vision changes or have an erection that last longer than 4 hours, call your healthcare provider or get medical help right away.
  - tadalafil (Adcirca®), for the treatment of pulmonary arterial hypertension
  - telithromycin (Ketek®)
  - thioridazine
  - voriconazole (Vfend®)
  - warfarin (Coumadin®, Jantoven®)
  - zolpidem (Ambien®, Edlular®, Intermezzo®, Zolpimist®)

Know the medicines you take. Keep a list of all your medicines and show it to your healthcare provider and pharmacist when you get a new medicine. Do not start any new medicines while you are taking STRIBILD without first talking with your healthcare provider.

Keep STRIBILD and all medicines out of reach of children.

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

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POSITIVELY AWARE

JOURNALISM. INTEGRITY. HOPE.

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"This is the best HIV drug guide yet!"

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"Here it is—the most requested issue of the year!"

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"This is PA's biggest issue of the year—in every way. We're keenly aware how much people rely on it."

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Dr. Melanie Thompson is Principal Investigator of the AIDS Research Consortium of Atlanta where she has conducted over 400 studies of HIV, STDs, and viral hepatitis. She is a member and former chair of the National Institutes of Health's Office of AIDS Research Therapeutics Research Working Group. She also sits on the Board of Directors of the HIV Medicine Association (HIVMA) and the Steering Committee of the Ryan White Medical Providers Coalition. She chaired the Antiretroviral Guidelines Panel of the International Antiviral (formerly AIDS) Society-USA (IAS-USA) from 2009-2013, and an international panel on Guidelines for Improving Entry Into and Retention in Care, and Antiretroviral Adherence for Persons with HIV in 2010–2012. She is a member of the Part A Ryan White planning council. Most importantly, she is a medical provider for people with, and at risk for, HIV and viral hepatitis.

THE PHARMACIST
RENATA SMITH, PHARMD

Renata Smith, Pharm.D., AAHIVP, is Assistant Clinical Professor at the University of Illinois at Chicago (UIC) and the HIV Pharmacy PGY2 Director. She works in the Infectious Diseases clinic at UIC and also in several of the HIV Outreach clinics located in underserved areas of Chicago. The University of Illinois at Chicago provides care to individuals who are uninsured, underinsured, homeless, substance abusers, minorities, or formerly incarcerated from the areas of Chicago with the highest rates of HIV and STIs. Dr. Smith helps train pharmacy residents and pharmacy students in the areas of HIV and outpatient infectious diseases.

THE ACTIVIST
TIM HORN

Tim is the HIV Project Director at the Treatment Action Group (TAG), a global HIV, hepatitis C, and tuberculosis research and policy advocacy group based in New York. He is the former editor of AIDSmeds.com and has also worked for the Foundation for AIDS Research (amfAR), the AIDS Treatment Data Network, and the PWA Health Group. Tim is also a member of the AIDS Treatment Activists Coalition and the Fair Pricing Coalition and serves on several regional, federal, and global advisory boards and planning groups. He is also proud to be a co-author of the "Guidelines for Improving Entry Into and Retention in Care and Antiretroviral Adherence for Persons with HIV," led by Dr. Thompson and published in *Annals of Internal Medicine* in 2012. He has been living with HIV since the early 1990s.

THE ASSOCIATE EDITOR
ENID VÁZQUEZ

POSITIVELY AWARE Associate Editor Enid Vázquez earned her journalism degree from the University of Wisconsin-Madison. Her first journalism job was reporting for the *Hartford Courant*, the first newspaper founded in the United States. Enid looks forward each year to updating the drug guide alongside a pharmacist who's an expert in HIV care. She's grateful to Renata Smith, PharmD, for volunteering to work on the guide again this year—and to the pharmacists who helped to review and edit the individual drug pages. Enid welcomes comments from readers—those living with HIV as well as providers, case managers, and caregivers—on how to improve the HIV Drug Guide.

SPECIAL THANKS TO
Thomas D. Chiampas, Pharm.D., BCPS, AAHIVP; Whitney Dickson, PharmD, BCPS; and Farnaz Foolad

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POSITIVELY AWARE

TAKE FIVE: THE 18 PARTICIPANTS MINGLE IN BETWEEN TAKES AT PA'S COVER PHOTO SHOOT.

DEPARTMENTS

FEATURES

ONLY ON POSITIVELYAWARE.COM

ON THE COVER AND ON THIS PAGE
PHOTOGRAPHY: CHRIS KNIGHT. PHOTO ASSISTANT: WYLL MARTINEZ. LOCATION: SIDETRACK VIDEO BAR, CHICAGO

LIVE POSITIVE: THE POSITIVELY AWARE 2015 HIV DRUG GUIDE

LET'S CONNECT

All communications (letters, email, online posts, etc.) are treated as letters to the editor unless otherwise instructed. We reserve the right to edit for length, style, or clarity. Let us know if you prefer we not use your name and city. **Write to:** POSITIVELY AWARE, 5050 N. Broadway St., Suite 300, Chicago, IL 60640-3016 or **Tweet:** @PosAware.

CORRECTIONS: MARIA DAVIS

In the interview, "Maria Davis Speaks Out" (November+December 2014), we reported that Ms. Davis has three children. She has only two. In addition, *I Design* is two words, not one. POSITIVELY AWARE apologizes for the errors. Go to projectidesign.com.

KICKING *ASS*

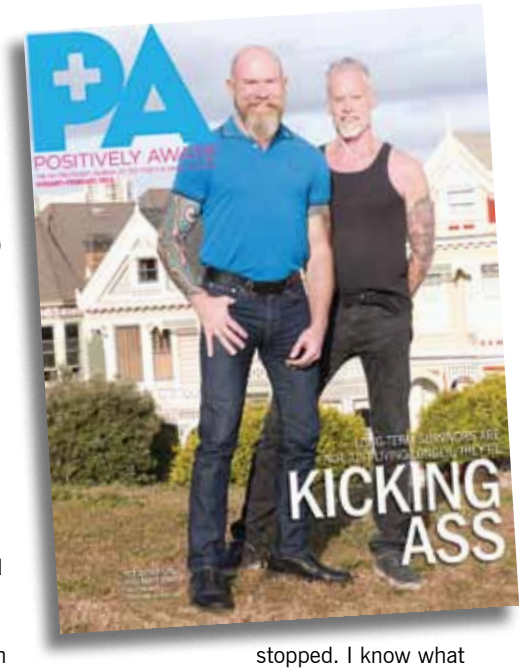
Jeff [Berry], I wanted to applaud you and thank you for the recent issue on aging with HIV and long-term survivors. You wrote a great editorial introduction. It is an excellent issue. Thank you.

REV. VILIUS RUDRA DUNDZILA, PH.D., D.MIN.
CHICAGO

I just wanted to comment on the January+February 2015 issue, "Kicking ASS." I really enjoyed reading the editor's note, "I'm a survivor." I related to it very much, since I am also in this group of aging with HIV/AIDS, a long-term survivor going on 30 years. Together with the poll responses, I felt not so alone anymore. I really appreciate that there is conversation about this topic now and I hope more will be done. I too have lost so many friends, acquaintances, and coworkers, and have had my own rollercoaster of obstacles related to having HIV/AIDS. I came through this trying to do the best I can with my life, but I still feel that there is a community that I'm left out of or don't feel a part of. Before I came to Chicago in 1999 I lived in Indiana, where I was diagnosed at the age of 19. I was one of the first people in Northwest Indiana to come out about their status publicly and felt the wrath of the stigma from the community around me. There were few resources and the silence about HIV was absolutely horrible. I was part of change in that neck of the woods. Since I moved to Chicago I have continued to be involved in various ways and through my work.

I'm pushing 50 now and currently I am not working. I feel isolated and lonely. I'd like to see more programs for people like us that lived through this and are surviving, but are also getting older, and I'd like to be part of letting other people know that they are not alone.

GREG SANCHEZ III
CHICAGO



I myself am not a long-term survivor, as I've been positive now for just over two years, but it is my plan to be a long-term survivor of this illness. Unfortunately, we as HIV-positive people face fear and stigma, especially when it comes from within the gay community, as was mentioned in the article ["Kicking ASS"]. We have spent many years battling forces from without on issues such as same sex marriage, equality, and just being recognized and validated for who we are as gay individuals.

We know discrimination well. Many are still afraid to come out of the closet due to fear. Yet, within the gay community where HIV is most prevalent, it's saddening that there is still such a great divide between positive and negative, "dirty and clean," to the point where I often find myself asking the question, "How can a house divided against itself stand?" I am often appalled at the lack of education within the gay community itself regarding HIV, the very community in which I am proud to be part of and live.

I do believe through education and awareness of the disease that things are indeed getting better, yet there is so much more work to be done. Or, perhaps, we choose to live in ignorance, and in the end, we do more harm than good. Unfortunately, it is this lack of education, this ignorance, that drives this stigma and fear that we face. I have several friends who are HIV-positive and have sworn me to secrecy concerning their status, and that's okay. I respect their desire, as it's a very personal and huge decision. I was once like that myself. God forbid anyone should know. I know living with the fear that surrounded that decision took me down a very dark road. I know what it's like to lose potential lovers. I know what it's like to reveal your status and have the phone go silent, the conversation stopped. I know what it's like to lose a man I was deeply in love with because we didn't have the conversation from the beginning. I know what it's like to lose friends and loved ones to this disease, and wonder if that was going to happen to me. I know what it's like to have an HIV-positive friend choose to take his life, simply because he could see no other way. All because of fear.

I chose to come out this past World AIDS Day and it's been one of the best decisions I've made. The love and support that has been shown to me by my family and friends has been simply amazing, to say the least. Yet, what I find truly sad, it's been my straight friends that have shown the most support. Very few of my gay friends, from my past or present, have reached out to me in the following months. I look forward to the day when HIV and labels have become a thing of the past.

HERSCHEL BOWEN
ST. PETERSBURG, FL

LONG-TERM SURVIVORS

I wrote in my book *Victory Deferred*, way back in 1999, that gay men who have lost entire circles of our friends in our younger years have a great deal in common with older people who are losing their own friends "naturally" in old age: the loneliness, depression, feeling that no one is left who really knows us ("The Cost of Long-Term Survival," January+Feburary 2015). I myself have found real connection

with older people, regardless of sexual orientation.

My physical and mental health at 56 is about as good as I think it can be, thanks to good medical care, adherence to my medication, a healthy diet, exercise, a positive attitude, and the joy I find in life through such activities as cooking and gardening.

But I will say honestly: I am worried about aging with HIV. Add financial worry to it, and it can be a serious stressor. Getting old is hard enough; getting old *and* having HIV? Fasten your seatbelt!

JOHN-MANUEL ANDRIOTE
NORWICH, CT
VIA THEBODY.COM

READERS POLL
THIS ISSUE'S QUESTION:

Does news of HIV medical developments make you feel more fearful or more hopeful?

VOTE AT POSITIVELYAWARE.COM.

I'm 62 and was infected about 30 years ago. I was living in San Francisco and experienced the pandemic from the start. What a nightmare! Almost all my gay male friends died and I thought I would too. Then came all the new drugs and somehow here I am. My partner died two years ago of AIDS. After grieving for a year-and-a-half, I'm feeling much better. My positive attitude has returned and I still enjoy living; however, to be honest, I'm tired. I do not wish to have another relationship. After years of taking care of other people I want some time to myself now. I think I share issues affecting many single older men, gay or straight, positive or not. I wonder if I'll wake up the next day. What if I become ill? There's no one to take care of me now. I, like everyone, want to be independent until the end. I live only on my social security and worry about living on a fixed income while everything else goes up in price. Thank god I don't seem to need much. I miss my friends and family. Now it's my turn to grow older and I'm not sure what I'm supposed to do. My health, of course, is always an issue and I wonder what living with HIV for so long has done to me. How will it manifest itself? I recently heard inflammation causes cancer. HIV causes inflammation. I've had my share of side effects, hospitals, and ER visits. I'm not really afraid of the future but I know how things change when it hits home. I was prepared to die in 1995. I think about how much time I've had and my buddies didn't. I'm grateful to have each day and try to make the best of them. But if I do become sick I don't think I'm going to kick and scream and do anything to survive another year, or month or day.

It's okay. I'm happy now. I just have to keep my sense of humor, especially when I look in the mirror. Thanks for letting me express myself. What a long, strange journey it's been.

NAME WITHHELD
NEW YORK STATE
VIA THEBODY.COM

As a 72-year-old long-term survivor (possibly infected in 1982), I have had my share of health problems, including diabetes, double-bypass operation, and non-Hodgkin's [lymphoma], plus a number of minor ailments that influence my day, such as neuropathy. This is not easy, I can assure you. However, it is very important to note how you are dealing with these physical setbacks. One must re-appraise life every time something annoying happens and one must try to stay positive in one's outlook on life. Of course this becomes more difficult as one gets older, but even in a difficult situation there is some good to enjoy if only you grab these possibilities with both hands instead of letting yourself be overwhelmed by the negative aspects of an aging, unappetizing body full of physical defects. In a way this is not so very different from the aging process of supposed "healthy" people. Aging is no fun, but there is always something that one can enjoy!

NAME WITHHELD
THE NETHERLANDS
VIA THEBODY.COM

Being HIV-positive isn't easy at times, but I find POSITIVELY AWARE a great comfort. I learn about a lot of new and interesting treatments for prevention and hopefully, one day, a cure, but you also discuss other illnesses that are co-infections with HIV as well as the ones we face as we get older. Please keep up the great work.

NATHAN MCBRIDE
SAN QUENTIN

I've been positive for 18 years, and I've been on medication for 10 of them. I've remained undetectable and my CD4 has varied from 800 to 1,222. I had a brother and a sister die from this disease and I know firsthand what it can do. What's worse is the way family will treat you. I don't want another person to have their mom feed them from separate personal plates, drinking glasses, and eating utensils. It makes you feel alienated and unloved. Even though you know they care, you also know they're scared. Fear can be dangerous to us, especially here in the prison system, when your status has been leaked. You're hated before you're known. I've never faced this virus. Never thought it would be me.

NAME WITHHELD
KERSHAW, SC

STRENGTH IN NUMBERS

A PHOTO SHOOT TURNS INTO A POSITIVE SOCIAL GATHERING

THE MESSAGE BEHIND THE COVER photo of this year's HIV Drug Guide is to portray the many faces of HIV. Eighteen people living with the virus answered our call. They ranged in age from 21 to 62, from long-term survivors who have been positive more than 20 years to someone who were only recently diagnosed. They shared their thoughts about being HIV-positive.

"As a long-time survivor of living with HIV, the word *strength* comes to mind," said Christina Joly, 41, who has been HIV-positive 26 years. "Not only my own strength, but the strength of our community. The strength of friends, family, partners, and even strangers, who stand by our side in good times and bad."

"HIV is but one small part of me; it doesn't define me," said Rob Garofalo, 49, HIV-positive since 2010. "It has, however, made me a stronger and kinder person. It hasn't always been easy, but it won't stop me."

Jerry Tamar Forrest, 28, viewed HIV as a challenge for personal growth. "I use my status to empower myself," Forrest said. "It's an enforced opportunity to emerge and evolve into something greater. Evolution is my solution."

"Being HIV-positive gave me a positive outlook on life," said Frank Karels, 57, HIV-positive 10 years. "It has made me appreciate life more."

"This summer I will celebrate 20 years of living positive," said Mary L. Miller. "I look forward to the future."

Johnny Conner, 57, has been HIV-positive 20 years. "Everything you do right today helps you stay healthy for tomorrow," he said.

Staying healthy has become possible, even easier, with development of the medications available today. "It's a chronic manageable disease, that's what I tell people," said Rob Campbell, 41, HIV-positive 10 years. "Just like someone's diabetes or another person's heart issue, or any other illness managed by medications. It's only an issue if someone makes it an issue. But with education and conversation it doesn't have to be."

Many of those who took part in the photo shoot expressed a desire to give back to community and to reach out to those in need. Scott C. Weidler, 55, has been HIV-positive 12 years. "I've been very lucky—fully insured, good doctor, early diagnosis, supportive friends," he said. "As one of the lucky ones, I feel a sense of responsibility to care for others and to offer advocacy for all."

"In this season of my life, it is necessary to give back, help my fellow HIV-positive veterans with their struggles," said Roy Ferguson, 63, HIV-positive more than 18 years, and coordinator of a self-help/education group for HIV-positive veterans at a Veterans Administration hospital. "I go to the Illinois State House and Senate three times a year to lobby for needed social services, and to change criminal transmission laws about HIV to reflect scientific knowledge rather than fear."

During the photo shoot, 26-year-old AJ Miranda had looked as if he wanted to say something. Afterward, he talked about how he had been given a copy of POSITIVELY AWARE when he tested positive in March 2014.

"I can't lie and say this hasn't been a difficult experience, with so many different emotions," Miranda said. "But honestly, it's better to know your status and to face it. That way you can take care of yourself and lead a healthy life."

Taking part in the cover shoot was his way of encouraging other young people to get tested and take control of their lives.

"I feel like I've come full circle," Miranda said. —**RICK GUASCO**

READ MORE REMARKS FROM THE COVER PHOTO SUBJECTS AT POSITIVELYAWARE.COM/PHOTOSHOOT.

EDITOR'S NOTE
JEFF BERRY

A BANNER YEAR

2015 is starting out to be an exciting year in HIV treatment. Two new drugs were just approved in February, with more in development, including new classes of drugs and novel, long-acting injectable formulations. While not nearly as exciting as the 1996 Vancouver conference, when the dawn of protease inhibitors caused a dramatic and profound shift in the HIV/AIDS landscape, it's encouraging to see that research and development is still being conducted to identify newer and better treatments for those who need them.

It's hard to stay excited when we've developed therapies that work so well and are so tolerable that, frankly, some companies have moved on to other areas of research, such as hepatitis C, where development has been proceeding at a rapid pace—and a cure is attainable! But even in light of all that, an estimated 1.5 million people worldwide still die each year from HIV/AIDS. We need to remain focused and committed to ensuring improved access to these drugs and to basic health care, and demand that drugs are reasonably and affordably priced.

But excited and hopeful we remain, and when you read on you'll understand why. There are now 37 drugs listed in POSITIVELY AWARE's 19th Annual HIV Drug Guide, with another 11 that are either in Phase 2 or 3 of development, covered in a pipeline review article by Tim Horn, our activist for this issue. Melanie Thompson provided the physician commentary for the drugs in this year's guide. Dr. Thompson also made a few suggestions on how we might want to think about ordering and structuring the drugs in a way that calls attention to those that are recommended, while placing less emphasis on the ones that are rarely or no longer used (see "Getting the Most Out of Your Drug Guide" on page 18). So we took her up on that!

The fact that the very drugs that we were excited about in 1996 are no longer used, and are even considered toxic, is an achievement in itself. But the goal remains the same, to get the virus to undetectable, and to stay there by taking your meds every day, as prescribed. If you're HIV-negative there are new methods to help you stay that way. So we are including in our online version of this year's drug guide a page devoted entirely to PrEP, or pre-exposure prophylaxis. We also provide information on how to help pay for PrEP, HIV meds, and other drugs commonly used in HIV in our co-pay and patient assistance chart beginning on page 74.

I learn something every year as we go through the production process for this guide. This year it was side effects of a treatment that a friend is on and has been experiencing, unaware that it could be due to his medication. So I challenge you to learn something new about HIV treatment, whether you're a provider, a long-term survivor, or someone who is newly diagnosed and considering starting therapy. There is something for everyone in this guide. Some people go straight to the doctor and activist comments for each drug, and that's all they want to see. Others may only choose to read about the drugs that they are on, or are considering switching to. And there are probably a few who read it from cover to cover—twice!

This is intended as a resource, a tool—use it in the way that suits you best. There is no perfect way, just your way. Make it your guide to successful treatment, so that you can spend the rest of your time getting to those things in your life that *truly* matter, resting easy knowing that you took the time to empower yourself with the information you need to take care of your body, and your health.

Thanks to so many amazing people who helped us with this year's guide, including Tim Horn, Melanie Thompson, Joel Gallant, Renata Smith and her team at UIC, Drew Halbur and his team at Walgreens, Jason Lancaster, Chris Knight, John Peller—and most importantly Enid Vázquez and Rick Guasco. I couldn't do what I do without Enid and Rick; they are the backbone of this publication, and they both make it a joy to come to work each day. Thanks, Vaca and Peanut!

This is the eleventh HIV Drug Guide on which I have served as editor, and I'm blessed to be able to work at an incredible organization that does such great work, to love the people I work with, and to still be able to enjoy what I do and look forward to coming to work each day. Thank you, Universe.

Be good to yourself, and each other.

The fact that the very drugs we were excited about in 1996 are no longer used, and are even considered toxic, is an achievement in itself.

FOLLOW JEFF
@PAEDITOR

PHOTO: CHRIS KNIGHT

CHART YOUR COURSE: THE HIV DRUG CHART

FIND IT IN PRINT AND ONLINE

THE 2015 POSITIVELY AWARE HIV Drug Chart, sponsored by Walgreens, is also available as a stand-alone chart printed on heavy card-stock paper. The charts are free, but supplies are limited and orders will be filled on a first-come, first-served basis (maximum of 25 copies per order, please). Email distribution@tpan.com or write/fax your request to POSITIVELY AWARE, Attn.: 2015 HIV Drug Chart, 5050 N. Broadway St., Suite 300, Chicago, IL 60640; fax (773) 989-9494.

Custom URLs make it easier to go directly to the page you want to read in the online Drug Guide. Positivelyaware.com/drugchart takes you to the online version of the HIV Drug Chart.

Positivelyaware.com/copay takes you to the co-pay and patient assistance charts starting on page 82.

Also, **each drug name has its own custom URL**. For example, positivelyaware.com/stribild for Stribild, or positivelyaware.com/isentress for Isentress. Go to positivelyaware.com/drugguide for the Drug Guide homepage.

Conveniently page through the **digital edition** of the 2015 HIV Drug Guide on your computer, tablet, or mobile device, seeing it just as you would in print. Go to positivelyaware.com and click on the link, or read the digital edition at issuu.com/positivelyaware.

Positivelyaware.com also offers **additional content not found in the print edition**, including Truvada for PrEP (postitivelyaware.com/truvadaforprep).

For additional copies of the Drug Guide, email your request to distribution@tpan.com or write/fax your request to the address/phone listed above.

ANTIRETROVIRAL THERAPY IN

ONE DOCTOR'S PERSPECTIVE ON THE STATE OF HIV TREATMENT

BY **JOEL GALLANT, MD, MPH**

Antiretroviral therapy (ART) options continue to expand and improve, making antiretroviral therapy (ART) easier, better tolerated, and more convenient. In this article, I'll discuss my own opinions on options for initial therapy, and what's in the pipeline.

INITIAL THERAPY

There's a wealth of potential options for first-line therapy, but only a few combinations that we're now starting with on a regular basis. Integrase inhibitors are *hot* these days, because in trial after trial, they're either as good or better than older regimens, with clear tolerability advantages. Speaking for myself, there are just a handful of **"go-to" regimens for patients starting ART without baseline resistance**, listed here in no particular order.

- **Stribild**
- **Triumeq**
- **Tivicay plus Truvada**
- **Boosted Prezista plus either Truvada or Epzicom**

Of course, I have patients on many other first-line regimens. There's no reason to switch therapy in someone doing well on Atripla, Complera, Viramune, or Isentress, for example. But I generally stick with one of the choices mentioned above if I'm starting ART for the first time. Here's why.

Atripla is an effective medication that has served us well for many years, but the early and *usually* temporary neuropsychiatric side effects (vivid dreams, dizziness, mood and cognitive changes) have always been a nuisance—one that we don't have to put up with anymore using other combinations. Some people have lingering side effects: dizziness, depression, difficulty focusing or concentrating, or sleep changes that persist long after the more intense early side effects have resolved. These changes may be subtle, and it's often impossible to know whether they're caused by Atripla without making a switch. I leave people on Atripla if they're doing well without side effects, but I don't use it any longer in people starting ART.

Viramune becomes a fine drug after the first month or two, but it has potentially serious and even life-threatening toxicities during the first few weeks, especially in people with high CD4 counts. Now that we're starting ART at high CD4 counts, Viramune isn't a great choice for most people to start with. But there's no need to switch therapy in people doing well on Viramune—even people with high CD4 counts—unless they prefer a single-tablet regimen.

Isentress is a great drug: it's effective, well tolerated, and has few drug interactions. Its only downsides are that it's taken twice a day and isn't available as part of a single-tablet regimen, unlike the other two integrase inhibitors. If you don't mind twice-daily dosing or are already taking other twice-a-day medications, there's no reason to switch, but for those who would prefer something more convenient, Stribild and Triumeq offer easier alternatives.

Complera is a well tolerated single-tablet regimen. I have many patients taking it, and have often used it as a regimen to switch to in people who wanted something simpler or easier to tolerate. It's still a good choice for initial therapy in people with baseline viral loads below 100,000, provided they're not taking drugs that lower stomach acid and can consistently take it with a full meal. However, those limitations don't apply to integrase inhibitor-based regimens, making them more attractive options for many people.

So how do I choose among my favorite regimens?

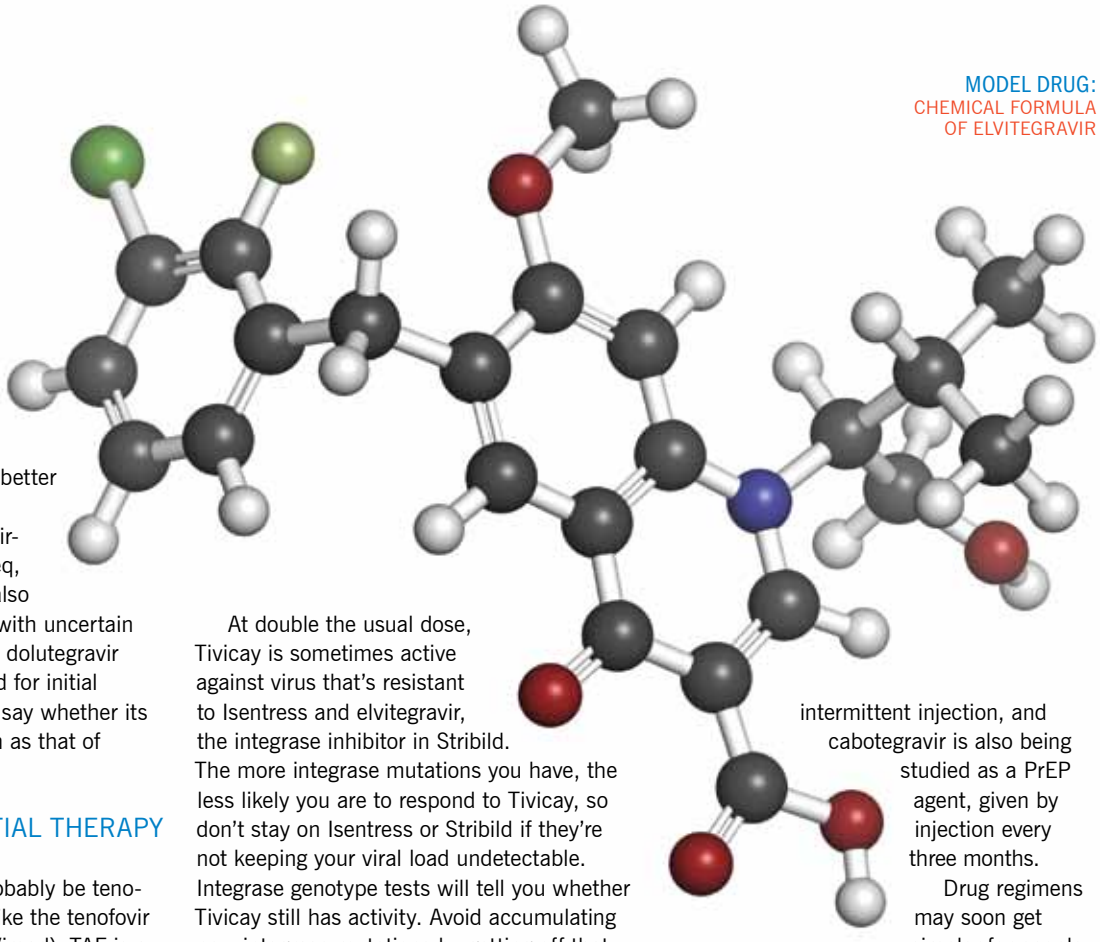
Stribild is a great choice for people who want an easy, single-tablet regimen, even with high viral loads or low CD4 counts. It contains an integrase inhibitor (elvitegravir) along with a pharmacologic "booster" (cobicistat). I avoid it in people with kidney disease or those who need drugs that can't be taken with cobicistat, which is similar to Norvir in terms of drug interactions.

Triumeq is another very effective single-tablet regimen. Like Stribild, it includes an integrase inhibitor (dolutegravir). Unlike Stribild, it does not need a booster, which means fewer concerns about drug interactions. Triumeq also contains a different nucleoside "backbone": abacavir/lamivudine rather than tenofovir/emtricitabine. Abacavir has no kidney toxicity, but there is still a lingering debate about whether it increases the risk of heart attack. Current guidelines recommend avoiding abacavir (including Triumeq) if you have high risk for heart disease. Pre-screening for abacavir hypersensitivity with an HLA B*5701 test is necessary before starting Triumeq.

Tivicay plus Truvada: This is a good two-pill option for people who want to take the dolutegravir (Tivicay) included in Triumeq without the abacavir/lamivudine (Epzicom) backbone. This would usually be due to high cardiac risk or a positive HLA B*5701 test indicating abacavir hypersensitivity.

Boosted Prezista plus either Truvada or Epzicom: I generally choose a boosted protease inhibitor (PI) when adherence is uncertain: in people with substance abuse or mental health issues, people who miss lots of clinic appointments, people with no prior experience taking long-term medications, or the very young. That's because it's almost impossible to develop PI resistance on a boosted PI, no matter how badly you screw up. There's always the option of switching to a single-tablet regimen later, once it's clear that non-adherence won't be a problem. Fortunately, PI-based regimens aren't as complicated as they used to be. Up to now, we've been boosting Prezista with a separate tablet of Norvir, but you are now able to take a two-pill-per-day regimen using Prezcobix (a new Prezista/cobicistat combination pill) plus either Truvada or Epzicom. A

2015



MODEL DRUG:
CHEMICAL FORMULA
OF ELVITEGRAVIR

single-tablet Prezista-based regimen is also in the works. EvoTaz (Reyataz/cobicistat) is also now available, but of the available PIs, I generally prefer Prezista because it's a little better tolerated than Reyataz.

I should add that dolutegravir-containing regimens (Triumeq, or Tivicay + Truvada) may also be good choices for people with uncertain adherence. We haven't seen dolutegravir resistance yet when it's used for initial therapy, but it's too early to say whether its "resistance barrier" is as high as that of a boosted PI.

WHAT'S NEW FOR INITIAL THERAPY

The next big thing will probably be tenofovir alafenamide ("TAF"). Like the tenofovir DF that we use now (TDF, Viread), TAF is a "pro-drug," meaning it doesn't get turned into active tenofovir until after it's absorbed. TAF achieves higher tenofovir levels within cells than TDF, but blood levels are lower. This translates into reduced toxicity (kidney and bone), with greater activity against resistant virus. There will be new versions of Truvada, Stribild, and Complera using TAF instead of TDF, as well as entirely new combinations, such as a single-tablet PI regimen (darunavir/cobicistat/emtricitabine/TAF). In fact, TAF could completely replace TDF for all purposes, although that will ultimately depend on pricing and the whims of insurance companies.

TREATMENT-EXPERIENCED PATIENTS

Because there are now so few people with HIV that's "untreatable" with the available drugs, drug companies have less interest in developing drugs for what we used to call "salvage therapy." Most drugs in development are intended for first-line use, which is where the money is. That being said, there is some good news for people with extensive drug resistance.

At double the usual dose, Tivicay is sometimes active against virus that's resistant to Isentress and elvitegravir, the integrase inhibitor in Stribild. The more integrase mutations you have, the less likely you are to respond to Tivicay, so don't stay on Isentress or Stribild if they're not keeping your viral load undetectable. Integrase genotype tests will tell you whether Tivicay still has activity. Avoid accumulating new integrase mutations by getting off that class of drugs until you can combine Tivicay with at least one other active drug.

Because it achieves higher tenofovir levels within cells, TAF, discussed above, is more active than TDF against NRTI-resistant virus, including some TDF-resistant virus.

Doravirine, an investigational non-nucleoside reverse transcriptase inhibitor (NNRTI), has activity against common mutations that cause resistance to the existing NNRTIs (Viramune, Sustiva, and perhaps even Intelence).

Finally, there are new drugs in development with entirely new mechanisms of action, interfering with the very first stage of viral entry. BMS-663068 blocks the attachment of the virus to the CD4 receptor, and ibalizumab is a monoclonal antibody that binds to the CD4 receptor. These attachment inhibitors have promise for people who have run out of other options.

Other NRTIs, integrase inhibitors, and protease inhibitors are also being developed, including long-acting drugs that could be given by intermittent injections. For example, the combination of the integrase inhibitor cabotegravir and a long-acting version of rilpivirine (Edurant) could be given by intermittent injection, and cabotegravir is also being studied as a PrEP agent, given by injection every three months.

Drug regimens may soon get simpler for people with extensive resistance. For example, it may not be long before someone with 3-class resistance to NRTIs, NNRTIs, and PIs could take a regimen consisting of a single tablet of the TAF-version of Stribild plus a single tablet of Prezista. That two tablet "salvage" regimen would be a remarkable improvement over the more complex regimens that many treatment-experienced patients are taking now.

JOEL GALLANT is Medical Director of Specialty Services at Southwest CARE Center in Santa Fe, New Mexico, adjunct professor of medicine at the Johns Hopkins School of Medicine, and clinical professor of medicine at the University of New Mexico. He treats patients and conducts clinical trials on the treatment of HIV infection. He is Immediate Past-Chair of the HIV Medicine Association and is on the Board of Directors of the IAS-USA. He is a member of the IAS-USA Antiretroviral Guidelines panel and the IDSA/HIVMA HIV Primary Care Guidelines panel. He authored *100 Questions and Answers about HIV and AIDS* and has an interactive question and answer blog at hivforum.tumblr.com.

GETTING THE MOST OUT OF YOUR

Understanding HIV treatment doesn't need to be difficult, and the POSITIVELY AWARE Annual HIV Drug Guide is here to help! Below are tips to help give you the knowledge you need to work with your providers to make empowered, informed choices about your treatment. Medications that are included in the HIV Drug Guide are only those drugs in the U.S. that are either FDA approved, expected to be approved this year, or are available through an expanded access program (EAP).

There are several changes to this year's HIV Drug Guide that will improve your experience and the way that you use this guide.

THE ORDER IN WHICH DRUGS ARE LISTED

When we started this guide 19 years ago, we listed drugs in the order they were approved. There have been several variations since then in how drugs have been listed in the guide as new treatments and new classes of drugs became available. Today, with so many good options out there, we wanted to try to highlight those drugs that are the best options and list them first, followed by other drugs in the same drug class that are less frequently used or prescribed. To quickly find your drug, see an alphabetical listing of all the drugs along with their corresponding drug page number on page 24.

DRUG CLASSES

THERE ARE CURRENTLY FIVE CLASSES OF HIV DRUGS (SEE ILLUSTRATION AT RIGHT):

- **NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs OR NUKES)**
- **NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs OR NON-NUKES)**
- **PROTEASE INHIBITORS (PIs)**
- **INTEGRASE STRAND TRANSFER INHIBITORS (INSTIs OR INTEGRASE INHIBITORS)**
- **ENTRY INHIBITORS (EIs)**

WHILE NOT A CLASS, **SINGLE-TABLET REGIMENS (STRs)** ARE GROUPED TOGETHER TOO. THERE ARE ALSO SEVERAL NON-HIV DRUGS THAT ARE USED COMMONLY BY PEOPLE WITH HIV WHICH ARE INCLUDED IN THIS GUIDE.

RECOMMENDATIONS FOR USE

The Department of Health and Human Services (DHHS) and the International AIDS Society-USA (IAS-USA) both publish recommendations for the use of HIV antiretroviral drugs. These recommendations focus on drug regimens more than single agents, but are essential tools that help providers and individuals choose a regimen that's best suited for them. This year we include information on some of these recommendations at the top of each drug page, as well as the pull-out drug chart. DHHS and IAS-USA guidelines are very similar in their recommendations, so for consistency we reference the DHHS guidelines. For the full list of recommendations go to aidsinfo.nih.gov or ias-usa.org/guidelines.

NO LONGER RECOMMENDED FOR USE

HIV drugs that are no longer recommended for use are published online only at positivelyaware.com; however, they are still included in the HIV Drug Chart. This includes six of some of the oldest HIV drugs that either have intolerable side effects or for which there are better options now available.

DRUG CLASSES AND CO-FORMULATIONS

A **fixed-dose combination** (FDC) combines two or more drugs in one tablet, such as Epzicom (lamivudine/abacavir). A **single-tablet regimen** (STR) contains drugs from different classes and is a complete regimen in one pill, such as Triumeq (dolutegravir/lamivudine/abacavir). Atripla, Complera, Stribild, and Triumeq are the four single-tablet regimens that are now available.

When a drug is a **co-formulation** (combination) of different drugs, the generic names will be separated by slashes—for example, Stribild is the co-formulation of elvitegravir/cobicistat/emtricitabine/tenofovir.

Remember that anti-HIV drugs should always be taken in combination using two or more drug classes (for example, a boosted protease inhibitor plus two non-nukes). While not a drug class, **single-tablet regimens (STRs)** are in their own category. STRs are widely used for first-time treatment and for their convenience, but they are not for everybody. For those who are treatment-experienced or have multi-drug resistance, they may not be able to use these STRs and will still have to combine two to three or more single agents from different drug classes, the old-fashioned way.

There are also several non-HIV drugs that are used commonly by people with HIV which are included in this guide. In addition, there is a Truvada for PrEP (pre-exposure prophylaxis, for prevention) page that is online only.

DRUG NAMES

When a drug is in development and before it's approved, it's first given a **"generic" name** (such as dolutegravir), which health care providers may identify it with even after approval. Once it is approved, it's given its **brand name** (Tivicay is the brand name of dolutegravir), which most consumers know it by. At medical conferences and presentations you will often see three-character abbreviations used (DTG in the case of dolutegravir). A good rule of thumb is, **brand names are always capitalized and generic names are always lower case**. Within each drug's page, you will see the drug referred to by any or all of its names, including in a few cases the "street" or common name it's known by (such as Reyataz [atazanavir or ATV]). All of each drug's names appear at the top of its page and also on the pullout drug chart, so if you're confused, look them up there!

Viread (tenofovir) is a drug of special circumstances. It is the only "nuke" that is a nucleotide reverse transcriptase inhibitor, as opposed to nucleoside; however, both types of nukes have a similar mechanism of action. Viread is also in three out of the four single-tablet regimens (STRs) currently available, as well as being one of the two drugs in Truvada, the only drug FDA approved for

DRUG GUIDE

HOW HIV MEDS WORK

TREATING HIV REQUIRES A MULTI-PRONGED APPROACH. DIFFERENT CLASSES OF HIV DRUGS FIGHT THE VIRUS ON DIFFERENT FRONTS

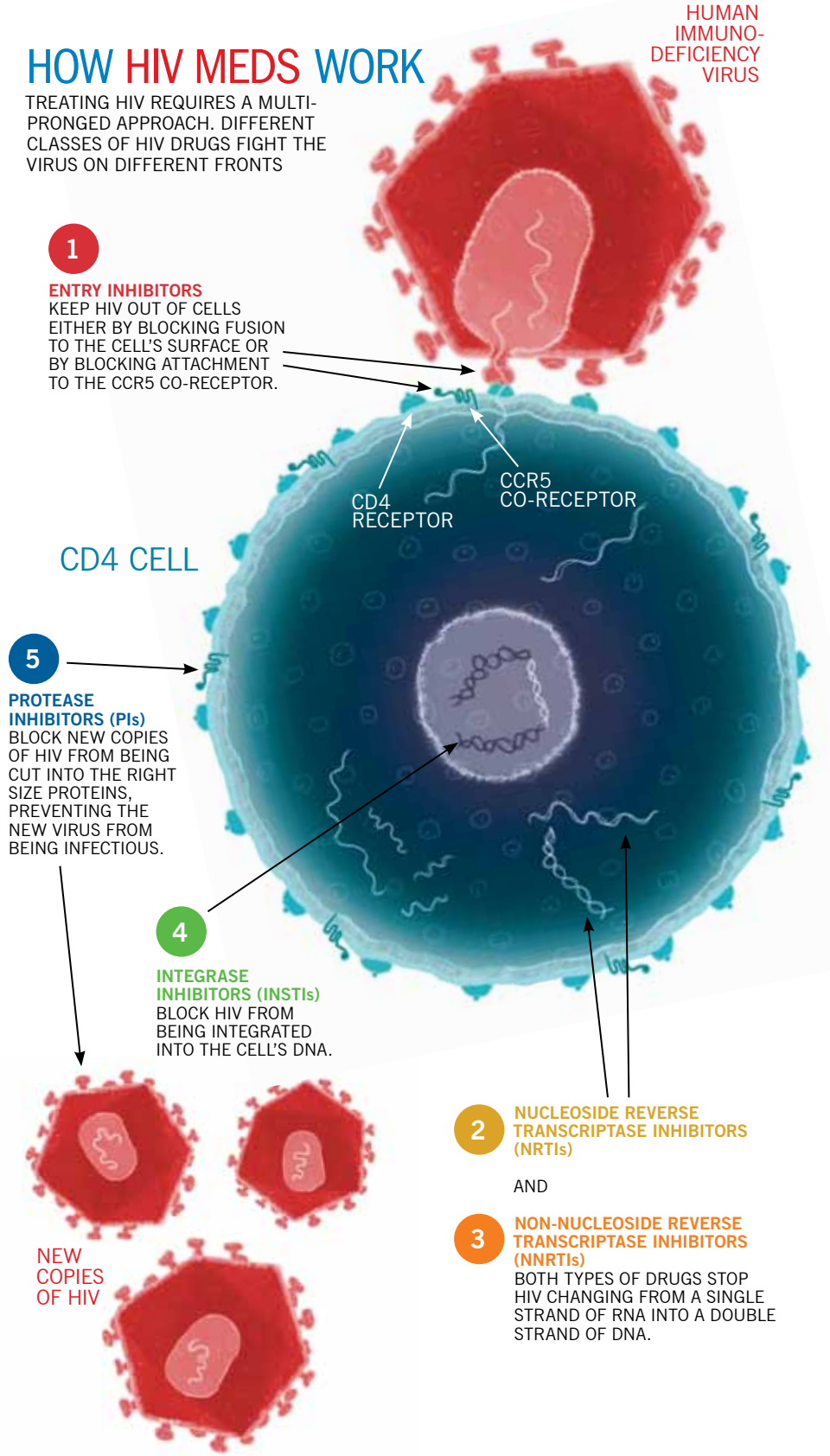


ILLUSTRATION: ABBEY DENLINGER

PrEP. You'll also notice that Viread is referred to by its generic name, tenofovir DF (disoproxil fumarate), but also just by "tenofovir"—another version, tenofovir alafenamide (TAF), is on its way. For now, whenever you see "tenofovir" without the DF, assume that it's the DF version.

DRUG PRICE AND ACCESS

The **Average Wholesale Price** (AWP) is a way to compare costs of drugs. It is not necessarily what you would pay if you had to pay the full retail price.

HIV drugs are not cheap and with all the continuing changes in drug coverage due to the Affordable Care Act (ACA), figuring out how to pay for them can be a challenge. Luckily, there are programs that can help cover all or part of the costs and help facilitate access. Of course many of us take drugs for conditions other than HIV, so in our drug co-pay and patient assistance program chart we include information on drugs used to treat hepatitis B and C, as well as several other non-HIV drugs that are often used by people with HIV. See page 74.

NAVIGATING YOUR TREATMENT

There is a wealth of information available about HIV and the drugs used to treat it. Knowing where to look and understanding some of the basics will help you sort through it all, giving you peace of mind and the knowledge you need to live a better, healthier life with HIV.

ONLINE EXTRAS

ADDITIONAL INFORMATION, such as a Truvada for PrEP drug page, will be available exclusively online at positivelyaware.com.

You can easily read up on each drug online by entering the drug name after our URL. For example, you'll find the Drug Guide's page for Prezista by typing positivelyaware.com/prezista.

ISENTRESS®
raltegravir film-coated tablets 400 mg

HIV Positive Model

In a clinical study lasting more than 4 years (240 weeks), patients being treated with HIV medication for the first time demonstrated that ISENTRESS® (raltegravir) plus *Truvada*®:

- May reduce viral load to undetectable (less than 50 copies/mL)
- May significantly increase CD4 cell counts
- ISENTRESS may not have these effects on all patients
- Patients had a low rate of these moderate-to-severe common side effects (that interfered with or kept patients from performing daily activities): trouble sleeping (4%), headache (4%), nausea (3%), dizziness (2%), and tiredness (2%).

INDICATION

ISENTRESS is a prescription HIV-1 medicine used with other antiretroviral medicines to treat human immunodeficiency virus (HIV-1) infection in people 4 weeks of age and older. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

It is not known if ISENTRESS is safe and effective in babies under 4 weeks of age.

The use of other medicines active against HIV-1 in combination with ISENTRESS may increase your ability to fight HIV.

ISENTRESS does not cure HIV-1 infection or AIDS.

You must stay on continuous HIV therapy to control HIV-1 infection and decrease HIV-related illnesses.

IMPORTANT RISK INFORMATION

- Some people who take ISENTRESS develop serious skin reactions and allergic reactions that can be severe, and may be life-threatening or lead to death. If you develop a rash with any of the following symptoms, stop using ISENTRESS and call your doctor right away: fever, generally ill feeling, extreme tiredness, muscle or joint aches, blisters or sores in mouth, blisters or peeling of skin, redness or swelling of the eyes, swelling of the mouth or face, problems breathing.
- Sometimes allergic reactions can affect body organs, such as your liver. Call your doctor right away if you have any of the following signs or symptoms of liver problems: yellowing of your skin or whites of your eyes, dark or tea-colored urine, pale-colored stools (bowel movements), nausea or vomiting, loss of appetite, pain, aching or tenderness on the right side of your stomach area.
- Changes in your immune system (Immune Reconstitution Syndrome) can happen when you start taking HIV-1 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 doctor right away if you start having new symptoms after starting your HIV-1 medicine.
- People taking ISENTRESS may still develop infections or other conditions associated with HIV infections.
- The most common side effects of ISENTRESS include: trouble sleeping, headache, dizziness, nausea, and tiredness. Less common side effects include: depression, hepatitis, genital herpes, herpes zoster including shingles, kidney failure, kidney stones, indigestion or stomach area pain, vomiting, suicidal thoughts and actions, and weakness.
- Tell your doctor before you take ISENTRESS if you have a history of a muscle disorder called rhabdomyolysis or myopathy or increased levels of creatine kinase in your blood.
- ISENTRESS Chewable Tablets contain phenylalanine as part of the artificial sweetener, aspartame. The artificial sweetener may be harmful to people with phenylketonuria.
- Tell your doctor right away if you get unexplained muscle pain, tenderness, or weakness while taking ISENTRESS. This may be signs of a rare serious muscle problem that can lead to kidney problems.
- These are not all the possible side effects of ISENTRESS. For more information, ask your doctor or pharmacists. Tell your doctor if you have any side effect that bothers you or that does not go away.
- Tell your doctor about all your medical conditions, including if you have any allergies, are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed. ISENTRESS is not recommended for use during pregnancy. Women with HIV should not breastfeed because their babies could be infected with HIV through their breast milk.
- Tell your doctor about all the medicines you take, including: prescription medicines like rifampin (a medicine commonly used to treat tuberculosis), over-the-counter medicines, vitamins, and herbal supplements. Especially tell your doctor if you take any of these medicines: rifampin (Rifadin, Rifamate, Rifater, Rimactane), an antacid medicine that contains aluminum or magnesium, a cholesterol lowering medicine (statin), a medicine that contains fenofibrate (Antara, Lipofen, Tricor, Trilipix), gemfibrozil (Lopid), a medicine that contains zidovudine (Combivir, Retrovir, Trizivir).

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

Please read the Patient Information on the adjacent page for more detailed information.

Need help paying for ISENTRESS? Call 1-866-350-9232

Talk to your healthcare professional about ISENTRESS and visit isentress.com.

MERCK

Patient Information
ISENTRESS® (eye sen tris) (raltegravir) film-coated tablets

ISENTRESS raltegravir film-coated tablets 400 mg

Read this Patient Information before you start taking ISENTRESS and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is ISENTRESS?
ISENTRESS is a prescription HIV medicine used with other antiretroviral medicines to treat Human Immunodeficiency Virus (HIV-1) infection in people 4 weeks of age and older. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

It is not known if ISENTRESS is safe and effective in babies under 4 weeks of age.

When used with other HIV medicines to treat HIV-1 infection, ISENTRESS may help:
- reduce the amount of HIV in your blood. This is called " viral load".
- increase the number of white blood cells called CD4+ (T) cells in your blood, which help fight off other infections.
- reduce the amount of HIV-1 and increase the CD4+ (T) cells in your blood, which may help improve your immune system. This may reduce your risk of death or getting infections that can happen when your immune system is weak (opportunistic infections).

ISENTRESS does not cure HIV-1 infection or AIDS.

You must stay on continuous HIV therapy to control HIV-1 infection and decrease HIV-related illnesses.

Avoid doing things that can spread HIV-1 infection to others:
- Do not share needles or re-use needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.
- Do not have any kind of sex without protection. Always practice safe 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.

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

What should I tell my doctor before taking ISENTRESS?
Before taking ISENTRESS, tell your doctor if you:
- have liver problems
- have a history of a muscle disorder called rhabdomyolysis or myopathy
- have increased levels of creatine kinase in your blood
- have phenylketonuria (PKU). ISENTRESS chewable tablets contain phenylalanine as part of the artificial sweetener, aspartame. The artificial sweetener may be harmful to people with PKU.
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if ISENTRESS can harm your unborn baby.
  Pregnancy Registry: There is a pregnancy registry for women who take antiviral medicines during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your doctor about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. **Do not breastfeed if you take ISENTRESS.**
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
  - It is not known if ISENTRESS passes into your breast milk.
  - Talk with your doctor about the best way to feed your baby.

Tell your doctor about all the medicines you take, including: prescription and over-the-counter medicines, vitamins, and herbal supplements. ISENTRESS and certain other medicines may affect each other causing serious side effects. ISENTRESS may affect the way other medicines work and other medicines may affect how ISENTRESS works.

Especially tell your doctor if you take any of these medicines:
- rifampin (Rifadin, Rifamate, Rifater, Rimactane)
- an antacid medicine that contains aluminum or magnesium
- a cholesterol lowering medicine (statin)
- a medicine that contains fenofibrate (Antara, Lipofen, Tricor, Trilipix)
- gemfibrozil (Lopid)
- a medicine that contains zidovudine (Combivir, Retrovir, Trizivir)

Ask your doctor 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 them to show your doctor and pharmacist when you get a new medicine. Do not start any new medicines while you are taking ISENTRESS without first talking with your doctor.

How should I take ISENTRESS?
- Take ISENTRESS exactly as prescribed by your doctor.
- **Do not** change your dose of ISENTRESS or stop your treatment without talking with your doctor first.
- Stay under the care of your doctor while taking ISENTRESS.
- ISENTRESS film-coated tablets must be swallowed whole.
- ISENTRESS chewable tablets may be chewed or swallowed whole.
- ISENTRESS for oral suspension should be given to your child within 30 minutes of mixing. **See the detailed Instructions for Use that comes with ISENTRESS for oral suspension**, for information about the correct way to mix and give a dose of ISENTRESS for oral suspension. If you have questions about how to mix or give ISENTRESS for oral suspension, talk to your doctor or pharmacist.
- **Do not switch between the film-coated tablet, the chewable tablet, or the oral suspension without talking with your doctor first.**
- **Do not** run out of ISENTRESS. Get a refill of your ISENTRESS from your doctor or pharmacy before you run out.
- If you miss a dose, take it as soon as you remember. If you do not remember until it is time for your next dose, skip the missed dose and go back to your regular schedule. Do not double your next dose or take more ISENTRESS than prescribed.
- If you take too much ISENTRESS, call your doctor or go to the nearest hospital emergency room right away.

What are the possible side effects of ISENTRESS?

ISENTRESS can cause serious side effects including:
- **Serious skin reactions and allergic reactions.** Some people who take ISENTRESS develop serious skin reactions and allergic reactions that can be severe, and may be life-threatening or lead to death. If you develop a rash with any of the following symptoms, stop using ISENTRESS and contact your doctor right away:
  - fever
  - generally ill feeling
  - extreme tiredness
  - muscle or joint aches
  - blisters or sores in mouth
  - blisters or peeling of the skin
  - redness or swelling of the eyes
  - swelling of the mouth or face
  - problems breathing

  Sometimes allergic reactions can affect body organs, such as your liver. Call your doctor right away if you have any of the following signs or symptoms of liver problems:
  - yellowing of the skin or whites of your eyes
  - dark or tea colored urine
  - pale colored stools (bowel movements)
  - nausea or vomiting
  - loss of appetite
  - pain, aching, or tenderness on the right side of your stomach area
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 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 doctor right away if you start having new symptoms after starting your HIV-1 medicine.

The most common side effects of ISENTRESS include:
- trouble sleeping
- headache
- dizziness
- nausea
- tiredness

Less common side effects include:
- depression
- hepatitis
- genital herpes
- herpes zoster including shingles
- kidney failure
- kidney stones
- indigestion or stomach area pain
- vomiting
- suicidal thoughts and actions
- weakness

Tell your doctor right away if you get unexplained muscle pain, tenderness, or weakness while taking ISENTRESS. These may be signs of a rare serious muscle problem that can lead to kidney problems.

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

These are not all the possible side effects of ISENTRESS. For more information, ask your doctor or pharmacist.

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

How should I store ISENTRESS?

Film-Coated Tablets:
- Store ISENTRESS Film-Coated Tablets at room temperature between 68°F to 77°F (20°C to 25°C).

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

General information about ISENTRESS

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

You can ask your doctor or pharmacist for information about ISENTRESS that is written for health professionals.

For more information go to www.ISENTRESS.com or call 1-800-622-4477.

What are the ingredients in ISENTRESS?

ISENTRESS film-coated tablets:

Active ingredient: raltegravir
Inactive ingredients: calcium phosphate dibasic anhydrous, hypromellose 2208, lactose monohydrate, magnesium stearate, microcrystalline cellulose, poloxamer 407 (contains 0.01% butylated hydroxytoluene as antioxidant), sodium stearyl fumarate.
The film coating contains: black iron oxide, polyethylene glycol 3350, polyvinyl alcohol, red iron oxide, talc and titanium dioxide.

This Patient Information has been approved by the U.S. Food and Drug Administration.

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Whitehouse Station, NJ 08889, USA

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FROM THE PA ARCHIVES

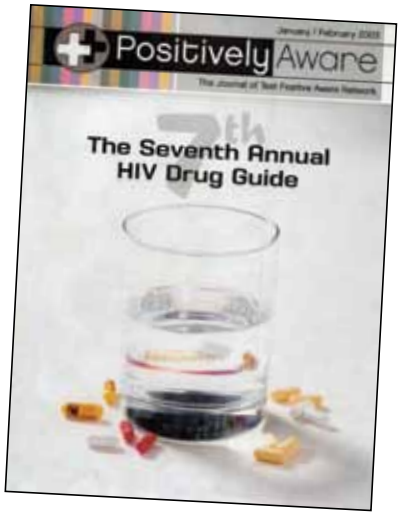
FROM JANUARY/FEBRUARY 2003:

Depending whether you see the glass as half-full or half-empty, 2002 was either a promising or a disappointing year for antiretroviral therapy, wrote then-PA editor Charles E. Clifton in the seventh annual HIV Drug Guide in the January/February 2003 issue.

The guide featured 19 drugs in three basic drug classes. Today, there are 37 drugs in five classes, but the lines between classes are increasingly being blurred with the development of new types of treatments that combine drugs that fight HIV along multiple fronts.

Among the experimental drugs that looked promising were T-20, FTC, 908, and atazanavir—known today respectively as Fuzeon, Emtriva, Lexiva, and Reyataz.

In the news briefs section of the issue, Enid Vázquez reported on an expanded access program for atanazavir for those who were failing their regimen and had no other treatment options. —**RICK GUASCO**



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FIND YOUR HIV DRUG HERE

PAGE	BRAND NAME	GENERIC NAME	DRUG CLASS
35	Aptivus	tipranavir, or TPV	PI
27	Atripla	efavirenz / emtricitabine / tenofovir, or EFV / FTC / TDF	STR
52	Combivir	lamivudine / zidovudine, or 3TC / AZT	NRTI
28	Complera	rilpivirine / emtricitabine / tenofovir, or RPV / FTC / TDF	STR
ONLINE	Crixivan	indinavir, or IDV	PI
43	Edurant	rilpivirine, or RPV	NNRTI
48	Emtriva	emtricitabine, or FTC	NRTI
49	Epivir	lamivudine, or 3TC	NRTI
47	Epzicom	abacavir / lamivudine, or ABC / 3TC	NRTI
40	EvoTaz	atazanavir / cobicistat, or ATC / COBI	PI/PKE
55	Fuzeon	enfuvirtide, T-20, or ENF	EI
44	Intelence	etravirine, or ETR	NNRTI
37	Invirase	saquinavir, or SQV	PI
29	Isentress	raltegravir, or RAL	INSTI
34	Kaletra	lopinavir / ritonavir, or LPV / r	PI
36	Lexiva	fosamprenavir, or FPV	PI
38	Norvir	ritonavir, or RTV	PI
41	Prezcobix	darunavir / cobicistat, or DRV / COBI	PI/PKE
32	Prezista	darunavir, or DRV	PI
ONLINE	Rescriptor	delavirdine, or DLV	NNRTI
53	Retrovir	zidovudine, AZT, or ZDV	NRTI
33	Reyataz	atazanavir, or ATV	PI
54	Selzentry	maraviroc, or MVC	EI
25	Stribild	elvitegravir / cobicistat / emtricitabine / tenofovir, or EVG / COBI / FTC / TDF	STR
42	Sustiva	efavirenz, or EFV	NNRTI
30	Tivicay	dolutegravir, or DTG	INSTI
26	Triumeq	dolutegravir / abacavir / lamivudine, or DTG / ABC / 3TC	STR
ONLINE	Trizivir	abacavir / lamivudine / zidovudine, or ABC / 3TC / AZT	NRTI
46	Truvada	emtricitabine / tenofovir, or FTC / TDF	NtRTI/NRTI
ONLINE	Truvada for PrEP	emtricitabine / tenofovir, or FTC / TDF	NtRTI/NRTI
39	Tybost	cobicistat, or COBI	PKE
ONLINE	Videx EC	didanosine, or ddI	NRTI
ONLINE	Viracept	nelfinavir, or NFV	PI
45	Viramune XR	nevirapine, or NVP	NNRTI
50	Viread	tenofovir disoproxil fumarate (tenofovir), or TDF	NtRTI
31	Vitekta	elvitegravir, or EVG	INSTI
ONLINE	Zerit	stavudine, or d4T	NRTI
51	Ziagen	abacavir, or ABC	NRTI

NON-HIV DRUGS

56	Egrifta	tesamorelin for injection	FOR HIV-RELATED EXCESS BELLY FAT
56	Fulyzaq	crofelemer	FOR HIV/AIDS TREATMENT-ASSOCIATED DIARRHEA
57	Serostim	somatropin (rDNA origin) for injection	FOR HIV-RELATED WASTING

DRUG CLASSES ARE COLOR CODED IN THIS DRUG GUIDE:

NRTIs
NUCLEOSIDE / NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS ("NUKES")

NNRTIs
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS ("NON-NUKES")

PIs
PROTEASE INHIBITORS

INSTIs
INTEGRASE STRAND TRANSFER INHIBITORS (INTEGRASE INHIBITORS)

EIs
ENTRY INHIBITORS

STRs
SINGLE-TABLET REGIMENS

PKE
PHARMACOKINETIC ENHANCER (BOOSTER)

PI-PKE
PROTEASE INHIBITOR / PHARMACOKINETIC ENHANCER (BOOSTER)

NON-HIV
OTHER DRUGS

Stribild

DHHS RECOMMENDED FOR FIRST-LINE USE

elvitegravir / cobicistat / emtricitabine / tenofovir, or EVG / COBI / FTC / TDF

POTENTIAL SIDE EFFECTS AND TOXICITY

See the individual drugs contained in Stribild: Vitekta, Emtriva, Viread, and Tybost. Most common are nausea, diarrhea, and headache. Abnormal dreams and fatigue have also been seen. Others include changes in kidney function tests (see Tybost for more, and reassuring, information), increases in total cholesterol, bone problems, and elevated liver function tests.

POTENTIAL DRUG INTERACTIONS

See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. Do not take with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Hepsera, Isentress, Kaletra, Norvir, Tivicay, Triumeq, Trizivir, Truvada, Tybost, Viread, or Vitekta, since these medications are already in Stribild or it has equivalent medications. Do not take at the same time with antacids. Separate by at least 2 hours from antacids containing aluminum, magnesium hydroxide, or calcium carbonate. Stribild is safe to take with other medications used for heartburn and GERD such as Nexium, Pepcid, Prevacid, Prilosec, Tagamet, and Zantac. Elvitegravir can decrease blood levels of many medications. Cobicistat has many drug interactions similar to those seen with Norvir. Do not take Stribild with Advicor, alfuzosin, Altoprev, methylergonovine, Mevacor, oral midazolam, pimozide, Revatio, rifabutin, Rifadin, rifampin, Simcor, triazolam, Uroxatral, Vytorin, Zocor, or St. John's wort. Risks vs. benefits of using Stribild and voriconazole together should be assessed. Cholesterol-lowering drugs such as Crestor, Lipitor, and Pravachol should be used with caution and started at the lowest dose possible. Other cholesterol medication in this class (statins) should not be used. Monitor closely for increased side effects from these medications, such as muscle pain. Concentrations of antidepressants such as trazodone or Prozac may be increased by Stribild, and their doses may need to be reduced. Use with caution and therapeutic monitoring, if available, for antiarrhythmic drugs like digoxin. Stribild increases levels of fluticasone (found in Advair, Flonase, and Flovent) and should be monitored for signs of Cushing's syndrome (such as rounded face). Use caution with anti-convulsants such as carbamazepine, phenobarbital, and phenytoin; and calcium channel blockers. 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 using alternative contraception methods. Use with caution with bosentan, salmeterol, and immunosuppressants like Prograf, Gengraf, Neoral, and Sandimmune. Taking with Harvoni, Olysio, or Viekira Pak is not recommended.

MORE INFORMATION

Stribild is a DHHS-recommended regimen for HIV treatment-naïve people with CrCl (creatinine clearance) equal to or greater than 70 mL/min. Data through 144 weeks confirmed that Stribild remained non-inferior to Atripla and Norvir-boosted Reyataz with Truvada. Stribild has an FDA indication (use) for people switching from another HIV regimen if they have a viral load less than 50 on a stable therapy and no history of drug resistance to the medications in Stribild or treatment failure. The indication was granted based on two switch studies showing that Stribild was non-inferior in people with undetectable viral load changing their PI/Truvada or NNRTI/Truvada regimen.

See package insert for more complete information on potential side effects and interactions.

STANDARD DOSE

One tablet (150 mg elvitegravir / 150 mg cobicistat / 200 mg emtricitabine /300 mg tenofovir) once daily with 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. Dose cannot be adjusted for people with kidney problems, therefore it should not be started in individuals with estimated creatinine clearance (CrCl) less than 70 mL/minute and should be discontinued if CrCl decreases to less than 50 mL/minute.

MANUFACTURER

Gilead Sciences, Inc.
gilead.com
(800) GILEAD-5
(445–3235)

AWP

$2,948.70 / month

DOCTOR'S COMMENTS

The first co-formulation of an integrase inhibitor (and the first 4-drug combination), E/C/F/TDF was found to be non-inferior to the gold standard Atripla for initial therapy. It was approved before its individual components elvitegravir and cobicistat were approved, a regulatory first in the U.S. Elvitegravir is an integrase inhibitor that is similar to raltegravir in its resistance pattern, but uses cobicistat (COBI) boosting to make dosing once daily. Cobicistat has no anti-HIV activity and, unfortunately, its lipid effects and drug interactions are similar to those of ritonavir. In addition, COBI causes elevations in creatinine "on paper" that do not signify any actual change in kidney function (see Tybost). The other side effects of the drug are the typical kidney and bone effects of tenofovir. On the whole, Stribild is very well tolerated and convenient. Because it does not have the nervous system effects of Atripla, many are turning to Stribild as first line or as a switch from Atripla. Because its integrase resistance profile is the same as Isentress (raltegravir), it cannot be used after raltegravir resistance has occurred. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Stribild is the first once-daily single-tablet regimen containing four different compounds, a testament to ingenuity (Gilead certainly had the impetus—all four drugs involved belong to the company). Though it didn't become an overnight best seller, it is gaining traction as a strong option for people starting therapy for the first time and those wanting to switch off other regimens. Its efficacy is proven. The only drawbacks appear to be some relatively minor side effects and drug-drug interactions associated with cobicistat and the potential for kidney toxicity and bone loss associated with tenofovir. The good news is that a new version of Stribild, which swaps out the older version of tenofovir for TAF, may help minimize the risk of these latter problems. Let's just hope the change doesn't prompt Gilead to price the newer combination tablet higher than Stribild, which has an estimated wholesale cost of $82… per tablet.
—TIM HORN

Triumeq

DHHS RECOMMENDED FOR FIRST-LINE USE

dolutegravir / abacavir / lamivudine, or DTG / ABC / 3TC

STANDARD DOSE

One tablet (50 mg dolutegravir / 600 mg abacavir / 300 mg lamivudine) once a day, with or without food, for people with no evidence of INSTI resistance. An additional 50 mg dose of dolutegravir (brand name Tivicay) separated by 12 hours from Triumeq is required for people who have resistance to Isentress or elvitegravir (Vitekta, also found in Stribild), or are taking certain other medications (Aptivus/Norvir, Lexiva/Norivr, rifampin, or Sustiva).

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.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$2,648.84 / month

POTENTIAL SIDE EFFECTS AND TOXICITY

See the individual drugs contained in Triumeq: Tivicay, Ziagen, and Epivir. Most common side effects are insomnia, headache, and fatigue. A creatinine clearance of greater than 50 mL/min is required before taking Triumeq. A small increase in serum creatinine may be seen, but is only a benign laboratory finding and not a sign of kidney toxicity. Conflicting data suggest a small risk for heart problems when using Ziagen-containing regimens in people with high blood pressure, high cholesterol, diabetes, smoking, or a previous heart attack or stroke. The risk should be considered and action taken to reduce risk factors, if possible, before starting treatment. Monitor for signs of hypersensitivity reaction to Ziagen (may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, fatigue, muscle or joint aches, difficulty breathing, blisters, sores in the mouth, skin peeling, facial swelling, cough, or sore throat), especially in the first six weeks after starting therapy. All individuals prior to starting Triumeq should be given a blood test for HLA-B*5701 (a genetic marker) to identify patients at risk for this reaction. This test is covered by most insurance and also by LabCorp/ViiV (see co-pay chart, page 67). Symptoms of HSR usually worsen, very slowly, with each dose. If HSR occurs a patient should never be given an abacavir-containing medication again (re-challenged). Liver enzymes should be monitored in people with hepatitis B or C. Stop taking Triumeq if you experience signs of liver problems (yellowing of the skin or whites of the eyes, dark or tea-colored urine, pale-colored bowel movements, nausea or vomiting, loss of appetite, or tenderness on the right side below the ribs). Pregnancy Category C—potential fetal risk seen in animal data.

POTENTIAL DRUG INTERACTIONS

See the individual drugs contained in Triumeq: Tivicay, Ziagen, and Epivir. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. Do not take with the anti-arrhythmic dofetilide (Tikosyn), due to the potential for serious or life-threatening reaction. Do not take Triumeq with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Isentress, Stribild, Tivicay (unless required), Trizivir, Truvada, Viread, Vitekta, or Ziagen, since these medications are already in Triumeq or they have equivalent medications. Intelence decreases dolutegravir levels by 88%, so your HIV provider would also need to prescribe Kaletra, boosted Prezista, or boosted Reyataz. Triumeq should be taken two hours before or six hours after taking antacids (like Maalox), the ulcer medication Carafate, iron or calcium supplements, or buffered medications. These medications reduce the absorption of dolutegravir; however, Triumeq can be taken with iron or calcium-containing supplements if taken together with food. Non-antacid acid reflux/heartburn medications (like Prilosec) are okay to use. Avoid taking with some seizure medicines (carbamazepine, oxcarbazepine, phenobarbital, and phenytoin) and St. John's wort. Metformin levels are increased by dolutegravir and a dose reduction in metformin should be considered. Triumeq has no effect on Versed, methadone, or oral contraceptives.

MORE INFORMATION

Triumeq was FDA approved on August 22nd, 2014. See the individual drugs contained in Triumeq—Tivicay, Ziagen, and Epivir as well as Epzicom (Ziagen/Epivir)—for more information. Triumeq is one of the recommended initial regimens in U.S. HIV treatment guidelines. Based on the current data, Triumeq appears to be an exciting addition to the current antiretrovirals. It gives us another single-tablet complete regimen. It has fewer drug interactions than Stribild and is well tolerated. The SINGLE study (which used individual components of the STRs) showed that Triumeq was superior to Atripla in patients who are treatment-naïve (meaning that they have never been on HIV medications before). Differences in the better outcomes for Triumeq were mostly driven by a higher rate of discontinuation due to side effects in the Atripla group. Check for hepatitis B before starting therapy and if Triumeq is discontinued monitor hepatitis B (HBV) closely (see Epivir).

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

In the SINGLE trial, the combination of dolutegravir with co-formulated ABC/3TC (the three drugs that make up Triumeq) was the first regimen shown to be superior to Atripla (EFV/TDF/FTC) at 48 weeks, largely due to higher discontinuation in the Atripla arm. There were also fewer side effects (especially neuropsychological effects) in the dolutegravir arm. The recently approved STR was shown to be comparable to this regimen. The availability of another integrase STR affords the simplicity of one pill, once-daily dosing for patients without resistant virus and avoids the lipid complications of COBI. As abacavir (ABC) and lamivudine (sister drug to FTC) are already generic as individual drugs, pricing will remain an issue for this compound. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Formerly known as 572-Trii, Triumeq is the awaited single-tablet regimen containing dolutegravir, along with abacavir and lamivudine. It was approved in August 2014. It is certainly a more convenient way to take these three drugs, which have worked quite well together. In fact, its better safety profile translated into better effectiveness in one clinical trial versus reigning champion Atripla. Will Triumeq see a meteoric rise in use? It's not yet clear. Some providers and community advocates have lingering concerns about abacavir, including efficacy (at higher viral loads) and heart attack concerns when it was used in regimens that preceded the arrival of dolutegravir. It might take a bit of time for abacavir to fully regain trust and acceptability. —TIM HORN

Atripla

DHHS RECOMMENDED FOR FIRST-LINE USE

efavirenz / emtricitabine / tenofovir, or EFV / FTC / TDF

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 who are not under a psychiatrist's care. A 2014 study reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-stressed the fact that efavirenz has an association with suicidality, and should be used with caution in patients with a severe or uncontrolled depression and/or a history of suicidality. Other side effects may include diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. These common side effects may go away after a few weeks. Kidney function should be assessed before initiating treatment and throughout therapy as determined by a provider. Women should not become pregnant on efavirenz (in Atripla) or for 12 weeks after discontinuation, because of the slight risk of a serious birth defect (greatest in the first trimester). However, because the birth defect risk is limited to the first 13 weeks of pregnancy and pregnancy is rarely recognized before six weeks, the recommendation is that women in their first trimester continue taking Sustiva as long as their viral load remains undetectable; however, efavirenz should only be used if the potential benefit outweighs the potential risk (as when other treatment options are not available). Dose cannot be adjusted for people with kidney problems. The efavirenz in Atripla can cause a false positive for marijuana on certain drug tests. A more specific confirmatory test can be done.

POTENTIAL DRUG INTERACTIONS

See the individual drugs contained in Atripla: Sustiva, Emtriva, and Viread. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions which are not listed here. Do not take Atripla with Combivir, Complera, Edurant, Emtriva, Epivir, Epivir-HBV, Epzicom, Hepsera, Intelence, Rescriptor, Stribild, Sustiva, Triumeq, Trizivir, Truvada, Viramune, or Viread, since these medications are already in Atripla or they have equivalent medications. Atripla should not be taken with ergot derivatives, midazolam (Versed), pimozide, triazolam, Vascor, voriconazole (Vfend), or St. John's wort. No dose adjustment of Atripla needed with Sovaldi. If Atripla is taken with Harvoni, tenofovir (Viread) levels should be monitored due to potential increased tenofovir levels and risk of tenofovir toxicity. Atripla should not be taken with Olysio or Viekira Pak. Use with caution with Harvoni.

MORE INFORMATION

Atripla was the first complete HIV treatment regimen in one pill, taken once daily. It is one of the recommended regimens for treatment-naïve patients in the Department of Health and Human Services (DHHS) HIV treatment guidelines. One benefit of a single-tablet regimen (STR) is a decrease in the number of insurance co-pays. 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). 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 (or all) 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 provider or pharmacist first. Use of tenofovir (in Atripla) must be monitored in people with underlying kidney problems. In this co-formulation, the Viread and Emtriva dose cannot be adjusted. Therefore, Atripla should not be used in people with severe kidney problems. Check for hepatitis B before starting therapy (see Emtriva). Gilead and BMS are forever to be commended for working together to bring Atripla to market, the first collaboration of its kind.

See package insert for more complete information on potential side effects and interactions.

STANDARD DOSE

One tablet (600 mg efavirenz / 200 mg emtricitabine / 300 mg tenofovir), once daily, preferably at bedtime, on an empty stomach or with a light, low-fat snack. However, to minimize potential side effects it is often recommended to take Atripla on an empty stomach at bedtime. For patients 12 years and older weighing at least 88 pounds.

Take a 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. Do not split or crush the tablet. 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.

MANUFACTURERS

Bristol-Myers Squibb
bms.com
atripla.com
(800) 321–1335

Gilead Sciences, Inc.
(800) GILEAD-5
(445–3235)

AWP

$2,551.99 / month

DOCTOR'S COMMENTS

Atripla was the first single-tablet regimen to incorporate drugs of different classes and even different manufacturers. It revolutionized HIV therapy with an appealing "one pill, once a day" message and has been the most widely used initial HIV therapy since its introduction in 2006. The main tolerability issues with Atripla are the central nervous system side effects of efavirenz, while the long-term toxicities are those of tenofovir (effect on kidney and bones). Today, Atripla is recommended worldwide for initial therapy, but newer drugs are being used more and more frequently, including E/C/F/TDF (Stribild) and combinations of nukes with darunavir/ritonavir, atazanavir/ritonavir, or dolutegravir. Although efavirenz is inching toward generic status, it is not clear that the generic version will be co-formulated with TDF/FTC in order to decrease costs (although there is talk of a generic efavirenz/3TC formulation that could be taken with a third drug). Nor is a TAF version currently in trials, indicating that this combination may have been abandoned by Gilead in favor of the TAF version of Complera.
—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

At the time of its approval in 2006, Atripla was nothing short of a marvel. Memories of taking fistfuls of pills two or more times a day were fresh on everyone's minds and it seemed astonishing that a one-pill, once-daily regimen was really capable of its demonstrated efficacy. For years, it was the simplified drug regimen to beat. Newer regimens ultimately matched its potency, but with better tolerability—notably fewer (and much less severe) central nervous system side effects. In fact, Atripla is much less likely to be prescribed for first-time treatment takers these days, given the availability of highly effective and tolerable combinations involving newer drugs. —TIM HORN

Complera

DHHS RECOMMENDED, BUT ONLY IF HIV RNA < 100,000 C/ML AND CD4 > 200 CELLS/MM³

rilpivirine / emtricitabine / tenofovir, or RPV / FTC / TDF

STANDARD DOSE

One tablet (25 mg rilpivirine / 200 mg emtricitabine / 300 mg tenofovir) once daily, with a standard meal with some fat, such as a slice of pizza; two slices of whole wheat toast with peanut butter and fresh fruit; a roast beef sandwich on a hard roll with mayo; pasta and meat sauce with salad; or tortilla with chicken, rice, and beans. Nutritional drinks, even high-calorie protein shakes or products like Ensure, should not be used in place of a meal. Taken with a protein shake, rilpivirine levels were still half of what they are with a meal.

Take a 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. The doses in this single-tablet regimen cannot be adjusted for people with kidney function of less than 50 mL/min—therefore, it should be used with caution in individuals with kidney problems.

MANUFACTURERS

Gilead Sciences, Inc.
gilead.com
complera.com
(800) GILEAD-5
(445–3235)

Janssen Therapeutics
(800) JANSSEN
(526-7736)

AWP

$2,463.37 / month

POTENTIAL SIDE EFFECTS AND TOXICITY

See the individual drugs contained in Complera—Edurant and Truvada. Moderate to severe side effects are uncommon: insomnia, headache, and depressive disorders (depression, negative thoughts, suicidal thoughts or actions) were each seen in 2% of study participants. A slight decrease in renal function and a slight increase in liver enzymes was also seen.

POTENTIAL DRUG INTERACTIONS

Do not take this drug with Atripla, Combivir, Edurant, Emtriva, Epivir, Epivir-HBV, Epzicom, Hepsera, Intelence, Rescriptor, Stribild, Sustiva, Triumeq, Trizivir, Truvada, Viramune, or Viread, since Complera contains these medications or has equivalent medication. Tell your provider or pharmacist about all medications, herbal products, and supplements you are taking or thinking of taking, prescribed or not, as there are many other drug interactions which are not listed here. Proton pump inhibitors (PPIs, stomach acid drugs like Nexium, Prevacid, Prilosec, etc.) can't be taken with Complera. Antacids can be taken two hours before or four hours after a Complera dose. Acid reducing drugs like Pepcid, Tagamet, and Zantac can be taken 12 hours before or four hours after a Complera dose. Do not take Complera with carbamazepine (Tegretol), oxcarbazepine, phenobarbital, or phenytoin (Dilantin); rifampin, or Priftin; or the herb St. John's wort (other herbs have not been studied with Complera, but use caution if planning to take any herbs). Rifabutin must be taken with an extra Edurant tablet in addition to Complera. Do not take with more than one dose of the injectable steroid dexamethasone (sometimes given in the ER or hospital). Use caution if used with Diflucan, Sporanox, Nizoral, Noxafil, and Vfend. Use azithromycin when possible instead of the antibiotics clarithromycin (Biaxin), erythromycin, or Ketek, because these drugs increase rilpivirine levels, which can increase the risk for side effects. Reduced methadone levels can be seen and while dose adjustments are not necessary, it is recommended to monitor for withdrawal. Early data shows that Complera may be taken with Harvoni, Olysio, and Sovaldi. Cannot be taken with Viekira Pak.

MORE INFORMATION

Complera can be difficult to take because of its food requirement and drug interactions, and excellent adherence is critical. Moreover, the risk of virologic failure (not achieving undetectable viral load) and developing resistance and a greater number of drug resistance mutations is greater with Complera than with Atripla in people starting with viral loads greater than 100,000 copies or with a CD4 count less than 200. Those with a viral load of 500,000 or more in the STaR study had a greater risk of virologic failure. See Edurant for more information. Accordingly, Complera is FDA approved for people starting therapy for the first time who have viral loads of 100,000 or less and for treatment-experienced patients with undetectable viral loads (less than 50) who are switching from another regimen and have never had HIV treatment failure before. In the STaR study, Complera was more tolerable than Atripla, with only 2% (2 out of 100) of study participants stopping Complera due to side effects, and did not have the same cholesterol elevations. Nervous system and psychiatric events were the most common side effects but higher in the Atripla group. Concerns about switching from Atripla to Complera were eased when decreases in Complera levels were only seen in the first few weeks of a 12-week study (when Atripla levels were still high enough to be effective against HIV), and participants maintained their undetectable viral loads. All the drugs in Complera have long half-lives (the 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 Emtriva). Two of the components in Complera also work against hepatitis B (HBV), thus patients who have both HIV and HBV should be monitored closely if Complera is discontinued, because of the risk of flare-up. Some government programs may not pay for Complera but require that patients take its components separately. See package insert for more complete information on potential side effects and drug interactions.

DOCTOR'S COMMENTS

The primary benefit of Complera is fewer CNS side effects compared with Atripla. It should only be prescribed for people with lower baseline viral loads (below 100,000 copies/mL) and higher CD4 cells (greater than 200/mL), but it is well tolerated and successful in this population, as well as those who switch from Atripla without having had virologic failure. The rilpivirine component makes its activity vulnerable to acid blockers and requires administration with food. A newer formulation substituting TAF for TDF began clinical trials in February.

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Complera was poised to be the answer to Atripla's side effects, notably the central nervous system issues of efavirenz. Unfortunately, it fell somewhat short. It doesn't work as well as Atripla in people starting treatment with high viral loads (more than 100,000 copies) and, if resistance to rilpivirine occurs, switching to the non-nuke Intelence might not be fruitful. Plus, Complera must be taken with food, whereas Atripla comes without a dietary requirement. All of that said, Complera is a strong option for those who start treatment on Atripla, push their viral loads to undetectable, and experience ongoing central nervous system troubles. It's good to have kinder, gentler options that can step in after a slightly more potent regimen has done the heavy lifting. A newer version of Complera that swaps out the older version of tenofovir for TAF is being developed.

—TIM HORN

Isentress

DHHS RECOMMENDED WITH TRUVADA; ALTERNATIVE WITH EPZICOM

raltegravir, or RAL

POTENTIAL SIDE EFFECTS AND TOXICITY

Very tolerable and infrequent side effects. Those reported included diarrhea, insomnia, nausea, headache, dizziness, and fatigue. The side effect profile in children is comparable to adults. Rare side effects include abdominal pain, vomiting, weakness, mild to moderate rash, anxiety, anemia (low red blood cells), neutropenia (low white blood cells), and lipodystrophy (abnormal fat distribution). Isentress may cause elevated levels of creatine kinase (a muscle enzyme). Contact your health care provider if you experience dark or tea-colored urine, or if you experience unexplained muscle pain, tenderness, or weakness. Increases in ALT, AST, and total bilirubin (signs of liver toxicity) can be seen in around 8% of people taking Isentress, especially those co-infected with hepatitis B or C. Although very rarely seen, side effects can include severe and potentially fatal skin and hypersensitivity (allergic) reactions, such as Stevens-Johnson Syndrome, 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: 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 (such as 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. If you have severe liver injury or impairment, your dose may need to be adjusted by your provider. See page 67 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. Alert your provider or pharmacist to any history of rhabdomyolysis, myopathy, or increased creatine kinase. Like Isentress, some medications, such as statins, fenofibrate, gemfibrozil, or zidovudine, have been known to cause these conditions and should be used cautiously with Isentress. Use caution with rifampin as it decreases the levels of Isentress in the body—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. There are no data on dosing of the chewable tablets with rifampin. There is no need to increase the Isentress dose with rifabutin. Avoid Gaviscon and other antacids containing aluminum or magnesium. Calcium-containing antacids like Tums (calcium carbonate) can be used. Prilosec (omeprazole) can increase concentrations of Isentress, but no dose adjustment is recommended. There is no interaction with methadone. Isentress can be used with Harvoni, Olysio, Sovaldi, or Viekira Pak.

MORE INFORMATION

According to DHHS HIV treatment guidelines, all three INSTIs on the market are recommended drugs. Long-term Isentress data show efficacy with great tolerability in both first-time therapy and in treatment-experienced people with resistance to other antiretroviral drug classes. When taken with Truvada, it was found to be superior to and more tolerable than Atripla. The combo is a potential option for those whose virus has developed drug resistance to the NNRTIs and PIs. When compared with a boosted-PI or NNRTI regimen, treatment-naïve individuals achieved faster viral suppression on Isentress. For combined virologic efficacy and tolerability, Isentress was shown to be superior to two boosted-PI regimens. DHHS guidelines note drawbacks with the use of Isentress: twice-a-day dosing and a lower barrier to drug resistance than boosted PIs. Greater tolerability may help overcome those issues and result in greater adherence. A 1,200 mg once-daily Isentress tablet is under development, which would help improve adherence and would offer a third once-daily INSTI option. Adherence is important because of the drug's short half-life and its low genetic barrier to drug resistance (meaning that it may only take very few missed doses for this medication to stop working). The guidelines state that before prescribing Isentress, providers may want to order a resistance test that can measure INSTI resistance (standard tests cannot). If resistance to Isentress develops, elvitegravir (part of Stribild) will likely not work. However, Tivicay, part of the recently introduced single-tablet regimen Triumeq, may still be an effective option due to Tivicay's higher barrier for resistance. See package insert for more complete information on potential side effects and interactions.

STANDARD DOSE

One 400 mg film-coated tablet twice a day, with or without food, with no dietary restrictions. The tablets may be taken by children weighing at least 55 pounds. Dosing is based on weight for children less than 55 pounds.

Take a 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.

Pediatric formulations are available as an oral suspension and chewable tablet. The suspension may be used for children ages four weeks and up, weighing at least seven pounds (3 kg). The chewable tablet, which may also be swallowed, is available in a 25 mg and 100 mg banana-orange-flavored formulation, and may be taken with or without food. The chewable tablets and oral suspension are not bioequivalent to the film-coated tablets; therefore, do not substitute chewable tablets for film-coated tablets.

MANUFACTURER

Merck and Co.
isentress.com
(800) 622–4477

AWP

$1,445.34 / month

DOCTOR'S COMMENTS

The first of the integrase strand transfer inhibitors, Isentress (raltegravir) showed the most rapid viral suppression ever seen, a characteristic that is now known to be a class effect. Its short- and long-term toxicity profile has been remarkably clean. Major negatives are twice-daily dosing, the lack of any co-formulations to simplify dosing, and a relatively fragile genetic barrier to resistance. Still, it is recommended for initial therapy as well as for treatment of multi-class resistant virus. It remains to be seen whether the new formulation in development can turn RAL into a once-daily drug.
—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Integrase inhibitors spent a long time in the making, but their arrival—beginning with Isentress in 2007—made it very much worth the effort. At first, Isentress was embraced for being the first in a new class of drugs to help manage drug-resistant HIV. And even though it needs to be taken twice a day, raltegravir has found a spot in the medicine cabinets of first-time treatment takers as well. It remains a very well tolerated option and manufacturer Merck is currently developing a new tablet for once-daily dosing. —TIM HORN

Tivicay

DHHS RECOMMENDED FOR FIRST-LINE USE

dolutegravir, or DTG

STANDARD DOSE

One 50 mg tablet once daily for people on HIV therapy for the first time or treatment-experienced people with no previous INSTI drug resistance. One 50 mg tablet twice daily when also taking efavirenz (Sustiva), Lexiva/Norvir, Aptivus/Norvir, or rifampin, or in people with INSTI (Isentress or Vitekta [found in Stribild]) drug resistance or suspected resistance. Take with or without food. Tivicay is approved for patients 12 years and older weighing at least 88 pounds, but a pediatric formulation is being studied in children 6 weeks and older.

Take a missed dose as soon as possible, unless it is within 4 hours of your next dose, then skip the missed dose. Do not double up on your next dose. Not recommended for people with severe liver impairment. Use with caution in people with severe kidney impairment who have INSTI drug resistance or suspected resistance, because Tivicay levels may be decreased.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$1,479.59 / month

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common moderate to severe side effects in clinical studies were insomnia (3%), headache (2%), and fatigue (2%). Mild insomnia was seen in 7% of participants in one study. Rarely, hypersensitivity (an allergy-like reaction) may occur. Stop taking Tivicay if signs or symptoms of hypersensitivity occur (including but not limited to severe rash or rash with: a fever, feeling ill, muscle or joint aches, blisters or skin peeling, blisters or sores in the mouth, redness or swelling of the eyes, facial swelling, liver inflammation, angioedema [swelling under the skin], and difficulty breathing). Associated with a small increase in creatinine (a marker of kidney function; this has been a laboratory increase not found to be a sign of kidney toxicity). Liver enzymes should be monitored in people with hepatitis B or C. Stop taking Tivicay if you experience signs of liver problems (yellowing of the skin or whites of the eyes; dark or tea-colored urine; pale-colored bowel movements; nausea or vomiting; loss of appetite; and pain, aching, or tenderness on the right side below the ribs). See page 67 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. Do not take with the anti-arrhythmic dofetilide (Tikosyn), due to the potential for serious or life-threatening reaction. Intelence decreases Tivicay levels by 88%. This interaction must be counteracted by the addition of Kaletra, ritonavir-boosted Prezista, or boosted Reyataz. Tivicay should be taken two hours before or six hours after taking laxatives or antacids containing aluminum, magnesium (such as Maalox), or calcium; the ulcer medication sucralfate; oral iron or calcium supplements; or buffered medications. When taken together, these medications can reduce the absorption of Tivicay; however, it can be taken with iron or calcium-containing supplements if taken together with food. Acid reducers and proton pump inhibitors (such as Prilosec) are okay to use as no change in Tivicay levels was seen. Avoid taking with oxcarbazepine, phenytoin, phenobarbital, carbamazepine, and St. John's wort. Metformin levels are increased by Tivicay and a dose reduction in metformin should be considered. Use alternatives to rifampin, efavirenz, Aptivus/Norvir, and Lexiva/Norvir when possible in people with INSTI drug resistance patterns or clinically suspected resistance. Should be okay to take with Harvoni, Olysio, and Sovaldi. Taking with Viekira Pak is not recommended.

MORE INFORMATION

According to DHHS HIV treatment guidelines, all three INSTIs on the market are recommended drugs. Tivicay is a second-generation INSTI, meaning that it may work in many individuals whose virus has developed resistance to the other drugs in its class, Isentress and Vitekta (in Stribild), but it needs to be dosed twice daily in these people. This could have financial impact. Tivicay is part of the single-tablet regimen Triumeq. See data at positivelyaware.com/tivicay.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Tivicay (dolutegravir) caused an unexpected stir of excitement in the field not only as the first integrase inhibitor approved for once-daily dosing without boosting, but because of its stellar clinical trial performance against our gold-standard drugs. It has beaten both efavirenz (SINGLE) and darunavir/ritonavir (FLAMINGO) as initial therapy, and was non-inferior to raltegravir. Its activity against many (not all) integrase-resistant viruses was shown in the VIKING study. Because it is primarily metabolized by UGT1A1 instead of CYP 3A4, the drug interactions we commonly have seen with protease inhibitors and NNRTIs are not frequent (except for a contraindication against use with etravirine without a booster) but a few others have emerged. There is a "black box" warning in the package insert against taking dolutegravir with dofetilide (for atrial fibrillation). As with all integrase inhibitors, use with divalent metal cations such as calcium and magnesium can substantially lower activity (Maalox reduces levels by 77%). Dolutegravir, like cobicistat, causes elevations in creatinine "on paper" that do not translate into an actual change in kidney function. All of this excitement bears a very high price tag, however, and the marketplace will likely have a say in the uptake of Tivicay and Triumeq. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Approved in August 2013, Tivicay has certainly made a strong impression on providers and people living with HIV. Like other integrase inhibitors, it is potent and well tolerated, with the addition of being active against some, but not all, HIV strains that become resistant to Isentress or Vitekta. Unlike Isentress and Vitekta, it can be taken once a day (twice daily for people combining it with certain medications [e.g., efavirenz] or treatment-experienced individuals with previous integrase resistance) without any boosting agent. Plus, it's now available in the single-tablet regimen Triumeq. Though the package insert states that it can be taken independent of mealtime, food moderately increases dolutegravir concentrations in the blood, which might help maximize effectiveness, particularly for integrase inhibitor-experienced patients. One concern has been the price—a wholesale cost of $14,000-plus (double that for twice-daily dosing), which, despite its much lower milligram dosing and huge market share expectations, is more expensive than Isentress and Vitekta and one of the most expensive single agents now on the market. Upward pricing trends are no longer sustainable in the U.S.—or anywhere, for that matter.
—TIM HORN

Vitekta

RECENTLY APPROVED; NOT YET RATED AS A SINGLE DRUG. DHHS RECOMMENDED AS PART OF THE SINGLE-TABLET REGIMEN STRIBILD

elvitegravir, or EVG

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects are nausea, diarrhea, headache, and fatigue. Laboratory abnormalities indicating potential liver damage were lower with Vitekta than with Isentress. Liver enzymes (ALT, AST, and GGT) can also be elevated as Vitekta is processed through the liver (but the incidence is not higher than with PIs or NNRTIs). Available data are limited due to the recent approval of this medication as a stand–alone medication. See page 67 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See package insert for most complete list of interactions. Tell your provider or pharmacist about all medications, herbal products, and supplements you are taking or thinking of taking, prescribed or not. It is co-formulated with emtricitabine, tenofovir, and cobicistat (Tybost) in the combination tablet Stribild and on its own it needs to be boosted by Norvir. Tybost has not been studied yet to be used as a booster for Vitekta except in Stribild. Vitekta is not recommended to be used in combination with Sustiva, Viramune, bosentan, rifampin, some of the seizure medications (such as Dilantin and Tegretol), St. John's wort, or dexamethasone, because these agents decrease Vitekta's concentration. Antacids (medications like Mylanta, Maalox, Rolaids, and Tums) have to be separated from Vitekta by at least 2 hours. Multiple drug interactions are possible with Norvir, which must be used to boost Vitekta dose, so also check the Norvir package insert for the most complete drug interaction list.

MORE INFORMATION

According to DHHS HIV treatment guidelines, all three INSTIs on the market are recommended drugs. Elvitegravir is also part of the single-tablet regimen Stribild (again, a recommended therapy in the guidelines). As part of Stribild, elvitegravir was compared with Atripla and boosted Reyataz plus Truvada in patients who had never had HIV treatment. In both studies, it was shown to be non-inferior (no better, no worse) to the other regimen. When used by treatment-experienced people without INSTI resistance and paired with a Norvir-boosted PI, Vitekta was also shown to be as effective as Isentress. Other data showed it to be as effective as Isentress. Providers may want to order a resistance test that can measure INSTI resistance (standard tests cannot), such as Monogram's Genosure, prior to initiating a regimen containing elvitegravir. Individuals who have resistance to Isentress are likely to also have resistance to Vitekta. Vitekta is not yet FDA approved to be taken with the booster Tybost unless taken as part of Stribild. As this issue went to press, Vitekta was not yet available in pharmacies.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Finally approved for use with a ritonavir-boosted protease inhibitor, elvitegravir is another integrase option but one that requires PK boosting for once-daily dosing. It should be noted that the dose of Vitekta is 85 or 150 mg, depending on the protease inhibitor. The stand-alone approval allows combination with abacavir for those who cannot tolerate TDF, but given the availability of the dolutegravir/abacavir/lamivudine combination Triumeq, it will be interesting to see whether it can actually find a niche outside of the single-tablet regimen Stribild and (soon) E/C/F/TAF, a version of Stribild using TAF instead of TDF. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Though Vitekta was approved in September 2014 as a stand-alone tablet for use in combination with other antiretrovirals, it has been available as a component of Stribild since 2012. In fact, Stribild remains the best vehicle for elvitegravir, given that it needs a booster and is well paired with tenofovir and emtricitabine—all components of the single-tablet regimen. Like other integrase inhibitors, elvitegravir is potent and well tolerated. —TIM HORN

STANDARD DOSE

85 mg once a day when taken with Reyataz 300 mg/Norvir 100 mg or Kaletra; 150 mg once a day when taken with Prezista 600 mg/Norvir 100 mg twice daily, Lexiva 700 mg/Norvir 100 mg twice daily, or Aptivus 500 mg/Norvir 200 mg twice daily, in antiretroviral treatment-experienced adults. Take with food.

Take a missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose.

MANUFACTURER

Gilead Sciences, Inc.
gilead.com
(800) GILEAD-5
(445–3235)

AWP

Vitekta was not available in the pharmacy at press time.

Prezista

DHHS RECOMMENDED WITH TRUVADA; ALTERNATIVE WITH EPZICOM

darunavir, or DRV

STANDARD DOSE

One 800 mg tablet with 100 mg Norvir or 150 mg Tybost (cobicistat; not yet approved for pediatric patients) once daily with food for first-time therapy and treatment-experienced adults without Prezista-related resistance. One 600 mg tablet with 100 mg Norvir twice daily with food for pregnant women and those whose HIV therapy has failed in the past and who have at least one Prezista-related resistance mutation. Prezista should never be taken without Norvir or Tybost. 75 mg and 150 mg tablets available for children older than three, dose based on weight. The dose for children should never exceed the adult dose. An oral suspension for children three and older and adults who can't swallow pills is available. New fixed-dose tablet containing Prezista and Tybost available; see Prezcobix.

See the package insert for specific dose of oral suspension based on weight. As with the tablet, Prezista oral suspension needs to be taken with Norvir or Tybost.

Take a missed dose as soon as possible, but not if closer to the time of your next dose. Do not double up on your next dose.

MANUFACTURER

Janssen Therapeutics
prezista.com
(800) JANSSEN
(526-7736)

AWP

$1,509.79 / month for all strengths for 600 mg, 800 mg tablets, and 360 mL suspension

POTENTIAL SIDE EFFECTS AND TOXICITY

As Prezista contains a sulfa component, use with caution in patients with sulfa allergies. Most common side effects may include diarrhea, nausea, headache, rash, vomiting, and abdominal pain. Measure liver function before starting and then monitor, with perhaps closer monitoring for those with underlying liver problems, especially during the first several months. No dose adjustment necessary with mild to moderate liver disease, but Prezista/Norvir is not recommended for those with severe liver impairment. While very rare, severe rash (in less than 0.4% of those taking it), accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek medical attention immediately. When used with Tybost a small decrease in kidney function may be seen and Tybost is not recommended in individuals with a creatinine clearance less than 70 mL/min. See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See package insert for the most complete list of interactions. Drug interactions of Prezista/Norvir may be different than those for Prezista/Tybost. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. May decrease levels of phenytoin and phenobarbital, and increase levels of carbamazepine; levels should be monitored. Reduced dose of rifabutin is recommended. Do not use lovastatin (Mevacor, Altoprev) or simvastatin (Zocor), or co-formulations containing these drugs (Advicor and Vytorin), for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor (rosuvastatin), Lipitor (atorvastatin) (should not exceed 20 mg a day), and Pravachol (pravastatin), but should be used with caution and started at the lowest dose possible. Monitor closely for increased side effects from these medications. Reduce clarithromycin dose by 50 to 70% in kidney impairment. The antifungal drugs such as itraconazole or ketoconazole and Prezista may increase each other's levels, so caution must be exercised when used together (maximum dose is 200 mg a day for the antifungals). Voriconazole should not be used unless the benefits outweigh the risks. Cialis (tadalafil), Levitra (vardenafil), and Viagra (sildenafil) 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 (like Norvasc) and beta-blockers; 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) and budesonide (found in Pulmicort and Rhinocort); use only if the benefits outweigh the risks, and monitor for signs of Cushing's syndrome (increased abdominal fat, hump between the shoulders, rounded face, red/purple stretch marks, bone loss, high blood pressure, and sometimes diabetes). Effectiveness of birth control pills may be decreased; consider other methods of contraception. Use lowest dose of digoxin; monitor and titrate. No dose adjustment required with buprenorphine or methadone. Monitoring of antidepressant response is recommended with selective serotonin reuptake inhibitors (such as paroxetine and sertraline). Use cautiously with bosentan, salmeterol, immunosuppressants, and colchicine; use lower dose of colchicine. No dose adjustment needed with Sovaldi. Taking with Olysio is not recommended. Do not take with Viekira Pak.

MORE INFORMATION

Prezista is one of two recommended PIs for initial therapy in U.S. HIV treatment guidelines, but may soon become the only one. A single-tablet, once-daily regimen containing Prezista, Tybost, TAF, and Emtriva is under investigation and will be the first one tablet, once-daily PI-containing regimen. It worked as well as a similar regimen containing the older tenofovir disoproxil fumarate (Viread) formulation, but it had less detrimental effects on kidney function and bone density. Prezista/Norvir is as lipid friendly as Reyataz/Norvir, which may make metabolic problems such as diabetes, high cholesterol, and body shape changes less likely.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Prezista (darunavir) boosted with ritonavir is one of the best-tolerated and most effective PIs ever in our toolbox, and a versatile option for treatment-experienced as well as naïve patients. Once-daily dosing works for most patients unless there are darunavir-associated mutations requiring twice-daily dosing. Darunavir also is co-formulated with cobicistat as a booster, making it even easier to take. Major toxicity is not common although lipid elevations are frequent, and occasionally rash and elevation of liver enzymes occur.

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Initially approved in 2006 for protease inhibitor-experienced patients and then in 2008 for first-time treatment takers, Prezista is the newest member of this drug class and the most commonly prescribed. For most people living with HIV, regimens containing one 800 mg darunavir tablet combined with one 100 mg ritonavir tablet or 150 mg cobicistat, once a day, will suffice. Though twice-daily ritonavir-boosted darunavir is necessary for some people with HIV harboring protease mutations that confer resistance to darunavir, this is mostly limited to those who experienced treatment failure on an amprenavir or fosamprenavir-based regimen in the past. Ritonavir-boosted darunavir is potent and has one of the better tolerability profiles of the protease inhibitors. It's been well studied, including in women. —TIM HORN

Reataz

DHHS RECOMMENDED FOR FIRST-LINE USE

atazanavir sulfate (atazanavir), or ATV

POTENTIAL SIDE EFFECTS AND TOXICITY

Dizziness, nausea, and possible jaundice (yellowing of the skin or eyes), which should be reported to your medical provider right away. Other side effects may include rash, kidney stones, gall stones, abnormal heart rhythm, and elevated liver enzymes (more common in people with hepatitis B or C). Reyataz is less likely to increase lipid levels compared to other PIs, but higher lipid levels may be seen when taken with Norvir or Tybost. Capsules do not contain phenylalanine but oral powder does; thus use with caution in individuals with phenylketonuria (PKU). See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See package inserts for Reyataz, Norvir, and Tybost for the most complete list of interactions. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. Do not use lovastatin (Mevacor, Altoprev), simvastatin (Zocor), or the co-formulations containing them (Advicor and Vytorin) for treatment of high cholesterol. Alternatives for these are Crestor, Lescol, Lipitor, and Pravachol, but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects. Proton pump inhibitors (PPIs, like Protonix, Nexium, and Prevacid) and H2-receptor antagonists (H2RAs, like Pepcid, Zantac, and Tagamet) can stop Reyataz from being absorbed. Treatment-experienced people should not take PPIs while on Reyataz. Treatment-naïve people can take a PPI at a low dose (such as 20 mg Prilosec OTC) 12 hours before Reyataz/Norvir. Acid reducers like Pepcid may be taken (no more than 20 mg twice a day if treatment-experienced or 40 mg twice a day if treatment-naïve) at the same time as Reyataz/Norvir or at least 10 hours later. When taking Reyataz without Norvir, the dose can be taken at least two hours before and at least 10 hours after an acid reducer. If taking chewable antacids like Rolaids and Tums, take Reyataz two hours before or one hour after. Treatment-naïve people should take 400 mg Reyataz with Norvir 100 mg or Tybost 150 mg when taking with Sustiva, but treatment-experienced people should not take Reyataz with Sustiva at all. Viread decreases the levels of Reyataz and Reyataz increases Viread levels; monitor for adverse events. Reyataz can be taken unboosted with Epzicom if necessary. Bepridil, Cordarone, quinidine, and lidocaine should be used cautiously because of the risk of worsening heart rhythm. Monitoring may be required when used with warfarin. Calcium channel blockers should be monitored. Use caution when using the antifungals itraconazole or ketoconazole. Voriconazole is not recommended. Reducing dose and frequency of rifabutin to 150 mg every other day or three times a week is recommended. Reyataz increases levels of fluticasone (found in Advair, Flonase, and Flovent); monitor for signs of Cushing's syndrome, including rounded face. Reyataz can be taken with birth control pills that contain no more than 30 mcg of ethinyl estradiol if taking Reyataz without Norvir and at least 35 mcg if taken with Norvir. Use caution with carbamazepine, phenobarbital, and phenytoin. ED drugs should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. A lower dose of trazodone is recommended. Use with caution with bosentan, salmeterol, and immunosuppressants, and use lower dose of colchicine. Use with Norvir when taking buprenorphine. Monitor before sedation. Taking with Olysio is not recommended. Sovaldi taken with Reyataz may cause elevated total bilirubin. Take Viekira Pak in the morning, without an extra dose of Norvir.

MORE INFORMATION

Norvir-boosted Reyataz is one of two recommended PIs in U.S. HIV treatment guidelines for people starting HIV therapy, and is also recommended for pregnancy. It is now available as a boosted tablet; see EvoTaz. The booster Tybost should only be used in pregnancy if the benefits justify the risks—there is only animal data in pregnancy.

See package insert for details of potential side effects and interactions.

DOCTOR'S COMMENTS

Atazanavir was the first protease inhibitor to combine the ease of once-daily dosing with a favorable lipid profile, in spite of ritonavir boosting. Although unboosted atazanavir 400 mg can be given to naïve patients (without tenofovir), this is not recommended by guidelines. Atazanavir/ritonavir is recommended for first-line therapy, but there are challenges. Acid blockers, especially proton pump inhibitors, interfere with atazanavir absorption. Drug interactions must be checked, as atazanavir has intrinsic boosting activity in addition to that of ritonavir. Its most common side effect is hyperbilirubinemia that is harmless, but "muddy" eyes and orange skin tint can be cosmetically bothersome unless you are John Boehner. Also, atazanavir, like Crixivan (indinavir), can cause kidney stones and gallstones. Co-formulated atazanavir/cobicistat (EvoTaz) was recently approved by the FDA. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Like Prezista, Reyataz has enjoyed popularity in the modern-day treatment era as a safe and effective once-daily protease inhibitor option requiring a low-dose ritonavir boost (it can also be used once daily without ritonavir, but not if Truvada is also prescribed). Reyataz doesn't cause the same cholesterol and triglyceride increases as first-generation protease inhibitors, though it does come with a unique tolerability issue: bilirubin increases that are physically harmless—in fact, study data suggest it may be protective against cardiovascular disease—but can cause cosmetically troubling yellowing of the eyes and skin in around 5% of those taking it. So much so that a recent clinical trial (ACTG 5257) saw more people discontinue an atazanavir-based regimen, compared with once-daily darunavir/ritonavir and twice-daily raltegravir-based regimens. Drug interactions can also be a challenge, particularly for those using medications for acid reflux. —TIM HORN

STANDARD DOSE

One 300 mg capsule plus 100 mg Norvir or 150 mg Tybost (cobicistat; not yet approved for pediatric patients), once daily with food (this dose must be used if taking Viread or Truvada). Two 200 mg capsules (without Norvir or Tybost), once daily with food can be considered for treatment-naïve adults. If pregnant, dosing depends on stage of pregnancy, previous ARV experience, and drug interactions—ask your doctor. Reyataz should not be taken without Norvir by pregnant women. New fixed-dose tablet combining Reyataz and Tybost available; see EvoTaz. Take with food.

Take a 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. Swallow capsules whole—do not open or mix with anything. Take Norvir or Tybost pill when you take Reyataz.

With end stage kidney or liver disease, use 300 mg Reyataz/100 mg Norvir or 150 mg Tybost. Reyataz should not be taken by treatment-experienced patients on hemodialysis.

See dosing information for patients under age 18 at positivelyaware.com/reyataz.

Also available in 150 and 200 mg capsules, and 50 mg oral powder packets.

MANUFACTURER

Bristol-Myers Squibb
reyataz.com
(800) 321–1335

AWP

$1,520.72 / month for 300 mg capsules;
$1,535.23 / month for 200 mg capsules

Kaletra

NOT DHHS RECOMMENDED FOR FIRST-LINE USE

lopinavir / ritonavir, or LPV / r

STANDARD DOSE

Four tablets (200 mg lopinavir / 50 mg ritonavir) once a day for people with less than three lopinavir resistance-related mutations; or two 200 / 50 mg tablets twice daily. Do not use once daily if taken with Sustiva or Viramune, or anticonvulsants. Three tablets twice a day may be considered for treatment-experienced people, pregnant women during the second and third trimesters, or those taking it in combination with Sustiva or Viramune. Pregnant women with no lopinavir resistance-related mutations may use two tablets (400 mg lopinavir/100 mg ritonavir) twice a day. Avoid oral solution in pregnant women. Kaletra should not be taken once a day by children under 18. Solution cannot be given to premature babies until 14 days after their due date because it contains propylene glycol. Other available formulations include: 100 mg lopinavir / 25 mg ritonavir tablets and an oral solution lopinavir 80 mg/mL / ritonavir 20 mg/mL.

Take a 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.

MANUFACTURER

AbbVie
kaletra.com
(800) 222–6885

AWP

$977.22 / month for tablets; $488.60 for 160 mL oral solution

POTENTIAL SIDE EFFECTS AND TOXICITY

Diarrhea is the most common and can be severe, but generally less severe with tablets than liquid. Associated with high incidence of elevated cholesterol and triglycerides, as well as insulin resistance. Rash, nausea, vomiting, stomach pain, headache, muscle weakness, lipodystrophy, and elevated liver enzymes (a sign of liver damage—may be more common in people with hepatitis B or C). Four tablets once daily can increase side effects, especially diarrhea. See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See package insert for the most complete list of interactions. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or are considering taking, prescribed or not. Do not take with alfuzosin, Revatio (sildenafil), Tambocor, Rythmol, Cordarone, midazolam (oral Versed), rifampin, pimozide, Priftin, triazolam, garlic supplements, or the herb St. John's wort. Do not use lovastatin and simvastatin or co-formulations containing these drugs (Advicor and Vytorin). Alternatives are Crestor, Lescol, Lipitor, and Pravachol, but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects. Oral solution contains alcohol, so do not use with Antabuse or Flagyl. Use calcium channel blockers with caution. Dosage of methadone may need to be increased. Current U.S. HIV treatment guidelines state the Kaletra dose should total 500 mg lopinavir and 125 mg ritonavir twice daily when used with Sustiva or Viramune. Not recommended with Lexiva. May lower levels of AZT and Ziagen. See positivelyaware.com/videx for that drug. If taking Kaletra with Viread or other combinations containing tenofovir, monitor for side effects from tenofovir. Kaletra should not be taken with Stribild; however, Kaletra may be taken as once- or twice-daily dosing with Tivicay. Rifabutin dose 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 other contraception. Mepron 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 Noxafil. Decreases voriconazole levels. People with kidney impairment may require lower clarithromycin doses with Kaletra. Kaletra may alter warfarin levels; additional monitoring may be required. Steroids, especially Decadron, may decrease Kaletra levels. Kaletra increases levels of steroids, particularly fluticasone (Advair, Flonase, Flovent, etc.). Monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, and more) as well as for signs of liver inflammation (elevated liver enzymes, yellowing of the eyes or skin, etc.) if you have a history of hepatitis B infection. Kaletra increases levels of trazodone. Use caution with anti-convulsants carbamazepine, phenobarbital, and phenytoin, as they may lower levels of Kaletra. Bupropion levels are lowered; titrate dose based on clinical response. Doses of certain erectile dysfunction drugs 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 immunosuppressants, and use lower dose of colchicine. Monitor blood levels of immunosuppressants because levels may increase. Kaletra can decrease the effects of Malarone. Kaletra may be taken with Sovaldi and should be taken with caution when tenofovir (Viread) in addition to Kaletra are prescribed with Harvoni, due to potential increased tenofovir levels. Kaletra should not be taken with other hepatitis C drugs like Olysio or Viekira Pak.

MORE INFORMATION

According to U.S. treatment guidelines, the 200 mg of Norvir and the higher rate of gastrointestinal side effects compared to other PIs using 100 mg Norvir, make Kaletra an alternative (instead of "recommended") drug for first-time therapy. It is recommended for pregnancy and pediatrics (as is boosted Reyataz), but data from 2012 adds to concerns about a link to premature births with Kaletra and other Norvir-boosted PIs. Taking with food and anti-diarrheal medicine helps lessen diarrhea. See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Kaletra was the first co-formulated boosted PI and played an important role in HAART history, in spite of its GI and lipid toxicities and higher pill burden. Its high resistance barrier has helped many patients sustain viral suppression. It is generally given as two or three capsules twice daily but can be given as four tablets once daily if three or fewer lopinavir resistance mutations are present. Either way, the daily dose of ritonavir is 200 mg. That is a lot of pills and a lot of ritonavir. Monotherapy Kaletra trials were popular for a while, but efficacy was disappointing and the strategy is not recommended. While Kaletra is still popular in global settings, it is domestically demoted to alternative status behind boosted Prezista (darunavir) and Reyataz (atazanavir), both of which require fewer pills and only 100 mg of ritonavir. When darunavir and atazanavir are co-formulated with cobicistat, there will be even fewer reasons to use Kaletra. Currently Kaletra is recommended as alternative initial therapy by the DHHS and IAS-USA panels. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Once it was determined that ritonavir boosting was standard practice for protease inhibitor-based regimens, Abbott Laboratories (now AbbVie) moved full steam ahead with the development of its lopinavir/ritonavir fixed-dose combination, which was approved in 2000. Originally sold as capsules that required refrigeration and twice-daily dosing, a heat-stable tablet formulation and data supporting once-daily administration was eventually approved. The fact that it was effective and easy to take made it a leading protease inhibitor option for several years, at least until better-tolerated Reyataz and Prezista were approved (both require half the amount of ritonavir boosting). —TIM HORN

Aptivus

NOT DHHS RECOMMENDED FOR FIRST-LINE USE; USED ONLY IN MULTI-DRUG RESISTANCE

tipranavir, or TPV

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common are 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, happens in 1 out of 10 patients (commonly among children). Rash may occur with 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. Stop using Aptivus if a severe rash occurs or if rash appears with the symptoms listed above and call your medical provider immediately. The Aptivus label contains a black box warning regarding liver abnormalities and bleeding in the brain. Use with caution in people who may be at risk of increased bleeding or who are taking medications that may increase the risk of bleeding. Many of the patients were also taking other drugs that may have caused or added to the bleeding risk. Caution should be used for people with mild liver impairment; don't use with moderate to severe liver disease. Liver function should be checked before taking this drug. If you have hepatitis B or C, it may worsen when using Aptivus. Use with caution in patients with allergies to sulfa drugs. Aptivus may also increase blood sugar, cholesterol, and triglycerides. See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

Tell your provider or pharmacist about all the medications, herbs, supplements, and over-the-counter (OTC) products you are taking or thinking of taking. Do not take with alfuzosin, Revatio (sildenafil), Tambocor (flecainide), Rythmol (propafenone), Cordarone (amiodarone), quinidine, midazolam, pimozide, triazolam, or the herb St. John's wort. Do not use lovastatin (Mevacor, Altoprev), simvastatin (Zocor), or the co-formulations containing them (Advicor and Vytorin) for treatment of high cholesterol. Cholesterol-lowering alternatives Crestor (rosuvastatin), Lescol (fluvastatin), Lipitor (atorvastatin), and Pravachol (pravastatin) should be used with caution and started at the lowest dose possible; monitor closely for increased side effects. Increases levels of fluticasone (found in Advair, Flonase, and Flovent); use with caution and only if the benefits outweigh the risks, and monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, bone loss, and more). Aptivus can lower blood levels of Intelence, Ziagen, Videx EC, and Retrovir and they should not be combined. Take Videx EC and Aptivus two hours apart. Aptivus should not be taken with other protease inhibitors because it greatly lowers their blood levels. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Effectiveness of birth control pills may be decreased; consider the use of other contraception. Methadone doses may need to be increased. Buprenorphine and naloxone can lower Aptivus levels significantly; dose adjustments are not recommended. A lower dose of trazodone is recommended. Calcium channel blockers should be monitored for side effects. Avoid use of ergot derivatives (dihydroergotamine, ergonovine, ergotamine, and methylergonovine). Additional monitoring may be required when taking Coumadin (warfarin). Seizure medicines carbamazepine, phenobarbital, or phenytoin (Dilantin) may decrease Aptivus levels; alternate seizure medications, such as levetiracetam, should be used if possible, and monitoring of Aptivus levels is recommended. Use caution when taking itraconazole or fluconazole. Rifampin and rifapentine should not be used; reduce the dose and frequency of rifabutin, the recommended alternative. Use with caution with bosentan, salmeterol, immunosuppressants, and colchicine. Norvir and Aptivus capsules contain alcohol (should not be enough to trigger relapse), so be cautious with Antabuse or Flagyl (metronidazole). Oral solution contains vitamin E; do not take more vitamin E than found in a multivitamin. Aptivus should be taken two hours before or one hour after antacids. Prilosec dose may need to be increased. Taking with Olysio or Sovaldi is not recommended. Do not take with Harvoni.

MORE INFORMATION

Aptivus is not as commonly used as other PIs, and is approved for patients whose virus is resistant to other PIs. It is not FDA approved for treatment-naïve patients. Take with food to minimize stomach problems. Refrigerate capsules before opening, but Aptivus capsules can be stored at room temperature (up to 77˚F) if used within 60 days. The oral solution should be stored at room temperature and used within 60 days of opening bottle. See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Tipranavir's resistance profile offered an advantage over other older PIs, but it was simply not a user-friendly drug, with multiple drug interactions, twice-daily dosing, high pill burden, and the requirement for boosting with higher dose ritonavir. It had a brief moment in the sun but retreated to rarely-used status once Prezista (darunavir) emerged as a potent and well tolerated option for PI-experienced patients. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

One of only a few antiretrovirals approved solely for the management of drug-resistant HIV, but even here its value is unclear. It must be co-administered with a relatively high dose of ritonavir—200 mg twice daily—which undoubtedly contributes to a less-than-favorable side effect profile, including gastrointestinal problems, cholesterol and triglyceride increases, and elevated liver enzymes. Though it has played an important role for people with a history of drug resistance to first-generation protease inhibitors, the less-toxic Prezista and newer drugs in other classes may work just as well in many cases. —TIM HORN

STANDARD DOSE

Two 250 mg capsules with two 100 mg tablets of Norvir, both twice daily at the same time.

Take a 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. Must be taken at the same time as ritonavir (Norvir). Must take with food when using Norvir tablets; no food restrictions with Norvir capsules or solution, but preferably taken with food to improve Norvir tolerability. Oral solution is available; both formulations available for children ages 2 years and older. Swallow Aptivus capsules whole, do not crush or chew the capsule.

MANUFACTURER

Boehringer Ingelheim
(800) 542–6257

AWP

$1,590.18 / month for capsules;
$530.04 for 95 mL solution

Lexiva

NOT DHHS RECOMMENDED FOR FIRST-LINE USE; RARELY USED

fosamprenavir calcium (fosamprenavir), or FPV

STANDARD DOSE

For people on a PI for the first time: two 700 mg tablets with either one 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.

Take a 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. Available for children ages four weeks 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. Adults must take suspension without food. Tablets can be taken with or without food, with no dietary restrictions.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$1,126.69 / month for tablets;
$172.62 for 225 mL suspension (50 mg/mL)

POTENTIAL SIDE EFFECTS AND TOXICITY

As Lexiva contains a sulfa component, use with caution in patients with sulfa allergies. 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 provider. For mild or moderate rashes, your provider 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. A 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 page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

PIs interact with many other drugs. See package insert for the most complete list of interactions. Tell your provider or pharmacist about all medications, herbs, supplements, and over-the-counter (OTC) products 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 (1,400 mg once daily) with 300 mg of Norvir. Do not take with alfuzosin, Revatio, Tambocor (flecainide), Rythmol (propafenon), midazolam (Versed), triazolam (Halcion), rifampin, Orap (pimozide), Priftin (rifampetine), or the herb St. John's wort. Do not use lovastatin (Mevacor, Altoprev) and simvastatin (Zocor) or co-formulations containing these drugs (Advicor and Vytorin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor (rosuvastatin), Lescol (fluvastatin), Lipitor (atorvastatin), and Pravachol (pravastatin), but use with caution and start at the lowest dose possible; monitor closely for increased side effects from these medications. Calcium channel blockers (amlodipine, nifedipine, and others) should be used with caution and careful monitoring. Lexiva should be taken two hours before H2 blockers (Zantac/ranitidine, Pepcid/famotidine, 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 (dexamethasone), can decrease levels of Lexiva. Lexiva increases levels of fluticasone (found in Advair, Breo Ellipta, Flonase, Flovent, and Veramyst), and budesonide (found in Pulmicort and Rhinocort, for example); use only if the benefits outweigh the risks, and monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, bone loss, possible high blood pressure, and sometimes diabetes). Trazodone concentrations may increase; a lower dose of trazodone is recommended. Drug levels of Paxil (paroxetine) are lowered; titrate dose based on clinical response. Use with caution with anti-convulsants carbamazepine, phenobarbital, and phenytoin. Lexiva may alter Coumadin (warfarin) levels; additional monitoring may be required. Effectiveness of birth control pills may be decreased; consider the use of other contraception methods. 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 (Tracleer), clarithromycin (Biaxin), Cordarone (amiodarone), Nizoral (ketoconazole), salmeterol, Sporanox (itraconazole), immunosuppressants (including transplant drugs), and colchicine (lower the colchicine dose). Lexiva may be taken with Sovaldi and should be taken with caution when tenofovir (Viread) in addition to Lexiva are prescribed with Harvoni, due to potential increased tenofovir levels. Lexiva should not be taken with other hepatitis C drugs like Olysio or Viekira Pak.

MORE INFORMATION

U.S. HIV treatment guidelines recommend against Lexiva without Norvir as an option for first-time therapy because of inferior potency and the potential for developing cross-resistance to Prezista (darunavir), a recommended protease inhibitor for first-time treatment. The lower dose of Norvir may cause less of an increase in cholesterol and triglycerides, but it is uncertain. 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 provider instructs, and not to change dosing without discussing it with your provider. There may be an association between Lexiva and heart attacks, heart disease, and stroke. See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Lexiva (fosamprenavir) is the prodrug of amprenavir and replaced amprenavir by offering improved bioavailability and tolerability (and smaller capsules). In clinical trials, it was better than nelfinavir (a low bar) and comparable to Kaletra when dosed twice daily. It was one of the few PIs that could be given without boosting, but a high pill burden hampered its utility, and other drugs emerged with better tolerability and potency. Fosamprenavir is rarely used today and is no longer recommended as an alternative regimen by DHHS or IAS-USA guidelines.
—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Lexiva is an improved version of Agenerase (amprenavir), an older protease inhibitor that suffered from potency problems and a significant pill burden (a total of eight pills either once or twice a day, depending on whether ritonavir was used). Though Lexiva can be taken once or twice daily, either with or without food, its approval in 2003 was soon overshadowed by the arrival of Reyataz and Prezista, with their safety, efficacy, and dosing advantages. —TIM HORN

Invirase

NOT DHHS RECOMMENDED FOR FIRST-LINE USE; RARELY USED

saquinavir, or SQV

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common are diarrhea, abdominal discomfort, vomiting, and nausea. Drug label warning states that Invirase combined with 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 rhythm problems, or low potassium or magnesium levels, are at greatest risk and should take Invirase plus Norvir with caution. Symptoms may include lightheadedness and fainting. A medication guide is required when Invirase is prescribed. See page 64 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, supplements, and over-the-counter (OTC) products you are taking or thinking of taking, prescribed or not. Viramune and Sustiva decrease Invirase levels. Not recommended to be used with other PIs (besides Norvir for boosting). Rescriptor and Norvir both significantly increase Invirase concentrations, which is why they are "boosting" Invirase (Norvir preferred, or Rescriptor if Norvir cannot be prescribed). Invirase is contraindicated (cannot be taken) with alfuzosin, Revatio (sildenafil), Tambocor (flecainide), Rythmol (propafenone), amiodarone (Cordarone), midazolam (oral Versed), triazolam (Halcion), pimozide (Orap), quinidine, trazodone, dofetilide (Tykosyn), lidocaine (systemic), rifampin, and ergot derivatives. Colchicine levels may be increased and dose reduction is necessary. Do not use lovastatin (Mevacor, Altoprev) and simvastatin (Zocor) or co-formulations containing these drugs (Advicor and Vytorin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor (rosuvastatin), Lescol (fluvastatin), Lipitor (atorvastatin), and Pravachol (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. Invirase cannot be taken with Priftin (rifapentine) or rifampin. Rifabutin can be used as an 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) and budesonide (found in Pulmicort and Rhinocort); use only if the benefits outweigh the risks, and monitor for signs of Cushing's syndrome (increased abdominal fat, hump between the shoulders, rounded face, red/purple stretch marks, bone loss, possible high blood pressure, and sometimes diabetes). Use calcium channel blockers with caution. Monitor digoxin levels; digoxin dose may need to be decreased. Use caution with anticonvulsants carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin), as these medications will decrease Invirase levels. Invirase may increase dapsone levels and alter Coumadin (warfarin) 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. Prilosec (omeprazole), Prevacid (lansoprazole), or any other proton pump inhibitor (PPI—a type of medication 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). Invirase may be taken with Sovaldi and should be taken with caution when tenofovir (Viread) in addition to Invirase and Norvir are prescribed with Harvoni, due to potential increased tenofovir levels. Invirase should not be taken with other hepatitis C drugs like Olysio. Refer to the package insert for the complete guide to drug interactions.

MORE INFORMATION

Rarely used, Invirase has efficacy similar to Kaletra with less hyperlipidemia (elevated cholesterol and triglycerides). Invirase plus Norvir has been added to the "Antiretroviral Components or Regimens Not Recommended as Initial Therapy" as of the U.S. HIV treatment guidelines in November 2014, due to a high total pill burden and risk for QT and PR prolongation. Invirase must be taken with food and always with Norvir. Invirase was the first PI to lose its patent (May 2011), however, there is no generic available.

See package insert for more complete information on potential side effects and interactions.

STANDARD DOSE

Two 500 mg film-coated tablets with 100 mg Norvir (ritonavir) two times a day with food, or within two hours of a meal for patients over 16 years old. Must be taken with Norvir. Invirase 200 mg hard gel capsules available.

Take a 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.

MANUFACTURER

Genentech
genentech.com
(800) 626-3553

AWP

$1,260.01 / month
for 500 mg tablets

DOCTOR'S COMMENTS

The first protease inhibitor, Invirase (saquinavir), was very potent in the lab, but went through multiple incarnations before dropping off the list of recommended therapies entirely. The original hard gel cap formulation (Invirase) was badly absorbed and reformulated into soft gel caps (Fortovase) with more bioavailability but less tolerability. When saquinavir was boosted with Norvir (ritonavir), it turned out that the older formulation, Invirase, was better tolerated. Fortovase is no longer manufactured, and Invirase is used rarely and only when boosted by ritonavir. In the U.S., newer PIs with longer half-lives and better tolerability quickly pushed saquinavir off to the history books. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Though Invirase was the first to emerge from the protease inhibitor kitchen in the mid-1990s, it was half-baked. It suffered from very poor absorption, requiring stopgap measures such as taking it with grapefruit juice while awaiting the development of a newer formulation (Fortovase). Soon after the arrival of Fortovase, we reverted back to Invirase, once it was concluded that the original formulation is better absorbed with a low dose of ritonavir added to the mix. By the time this was all sorted out, newer, easier-to-use protease inhibitor options had become available. —TIM HORN

Norvir

USED ONLY AS A BOOSTER FOR OTHER DRUGS

ritonavir, or RTV

STANDARD DOSE

Used as a boosting agent for other PIs (increases the levels of other PIs), at smaller doses of 100 to 200 mg, taken either once or twice a day with a meal.

Take a 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. Do not crush or chew tablets, always swallow whole. See drug label of the other PIs. Always take Norvir at the same time as the other PI prescribed. Approved for children ages one month and older. Capsule formulation requires refrigeration. Tablet formulation is better tolerated than the capsule and does not require refrigeration. Liquid formulation available, but it tastes horrible. Liquid formula should not be taken by pregnant women, as it contains 43% alcohol.

MANUFACTURER

AbbVie
norvir.com
(800) 633-9110

AWP

$308.60 / month for 30 tablets; $1,728.24 for 240 mL solution (80 mg/mL)

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects include weakness, stomach pain, 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 an increase in liver enzymes (AST, ALT, and GGT), hepatitis (liver inflammation), jaundice (yellowing of skin or eyes), increased muscle enzyme (CPK), and uric acid. People with hepatitis B or C may be at increased risk for liver toxicity. See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

Norvir interacts with many drugs, because as a booster it inhibits liver enzymes involved in drug metabolism. See package insert for the most complete list of interactions. Tell your provider or pharmacist about all medications, herbals, supplements, or over-the-counter (OTC) products you are taking or thinking of taking, prescribed or not, as there are many other drug interactions which are not listed here. Do not take with alfuzosin, Revatio (sildenafil), Tambocor (flecainide), Rythmol (propafenone), Cordarone (amiodarone), oral midazolam (Versed), Halcion (triazolam), pimozide, Priftin, Rifadin, voriconazole, garlic supplements, or the herb St. John's wort. Do not use lovastatin (Mevacor, Altoprev) and simvastatin (Zocor) or co-formulations containing these drugs (Advicor and Vytorin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are Crestor (rosuvastatin), Lescol (fluvastatin), Lipitor (atorvastatin), Livalo (pitavastatin), and Pravachol (pravastatin), but should be used with caution and started at the lowest dose possible; monitor closely for increased side effects. Increases levels of fluticasone (found in Advair, Flonase, and Flovent) and budesonide (found in Pulmicort and Rhinocort); monitor for signs of Cushing's syndrome (increased abdominal fat, fatty hump between the shoulders, rounded face, red/purple stretch marks, bone loss, possible high blood pressure, and sometimes diabetes). Trazodone concentrations may increase; a lower dose of trazodone is recommended. Norvir may decrease levels of methadone, which may need to be increased. Use caution with anti-convulsants such as carbamazepine, phenobarbital, and phenytoin. Use calcium channel blockers (amlodipine, nifedipine, and others) with caution. Norvir may alter Coumadin (warfarin) levels; additional monitoring may be required. Do not take Xarelto (rivaroxaban) as Norvir can increase Xarelto concentrations and increase risk of bleeding. 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 other contraception. Levels of the street drug ecstasy are greatly increased by Norvir, and at least one death has been attributed to the combination. GHB, another street drug, is also dangerous with Norvir. Tobacco and alcohol may lower blood levels of Norvir. Clarithromycin levels can increase by up to 80%. Use with caution with bosentan (Tracleer), salmeterol, and immunosuppressants; use a lower colchicine dose. Norvir, when combined with another PI (Norvir + PI) may be taken with Sovaldi and should be taken with caution when tenofovir (Viread) in addition to Norvir + PI are prescribed with Harvoni, due to potential increased tenofovir levels. Norvir + PI should not be taken with other hepatitis C drugs like Olysio.

MORE INFORMATION

The real strength of Norvir is its use with other PIs as a boosting agent. An alternative to Norvir was approved in 2014 (see Tybost page). Stomach side effects are reduced by taking Norvir with high-fat foods—however, some other HIV medicines should not be taken with high-fat foods. You can mix liquid solution one hour before taking in ice cream, milk (especially chocolate), or pudding to hide the taste. See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

It's hard to imagine that anyone ever took Norvir (ritonavir) at 600 mg twice daily in a nasty liquid formulation. But its impact was revolutionary, first for its own antiviral effect and then for its use as the CYP 3A4 inhibitor needed to boost almost all other PIs. This boosting activity also leads to multiple drug interactions. The formulation has improved over the years, first to gel caps and then to tablets, but its Achilles heel is its toxicity. It is never used as a PI by itself, but even as a booster, it raises triglyceride and cholesterol levels and adds to GI symptoms. Although cobicistat appears to have the same toxicity issues, its availability for co-formulation with darunavir and atazanavir might make the demise of ritonavir imminent, except for the fact that the ritonavir patent expires soon and lower cost may tempt the marketplace. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Much can be written about Norvir's storied history. Originally approved as a therapeutic drug in its own right—it was among the first protease inhibitors to demonstrate that combination antiretroviral therapy improved survival among people living with HIV—ritonavir's debilitating side effects at its approved dose (six pills twice daily), coupled with its ability to increase blood levels of other drugs, paved the way for its future as a low-dose boosting agent to simplify dosing and improve the efficacy of other protease inhibitors. With fewer Norvir pills being prescribed, Abbott decided to raise the price of the drug by 400% in December 2003 and ignored requests from other protease inhibitor manufacturers to develop ritonavir-inclusive fixed-dose combinations, both of which earned the ire of activists. Compounded by the fact that even low-dose ritonavir comes with side effects, all eyes have been on the development of Gilead's boosting agent cobicistat (Tybost), which addresses some—but not all—of ritonavir's drawbacks. —TIM HORN

Tybost ✚ USED ONLY AS A BOOSTER FOR OTHER DRUGS

cobicistat, or COBI

POTENTIAL SIDE EFFECTS AND TOXICITY

Side effects seen in clinical studies include diarrhea, nausea, increases in cholesterol and triglycerides, and red blood cells in the urine. Does not appear to impact kidney health, although there may be a modest increase in serum creatinine (SCr) and decreases in estimated creatinine clearance (CrCl) due to inhibition of tubular secretion of creatinine without affecting actual renal glomerular function. Decreases seen in estimated glomerular filtration rate (eGFR). The SCr increase occurred within weeks of starting cobicistat and was reversible. SCr returned to normal within a few days after stopping Tybost. The coadminstration of Tybost and Viread (tenofovir DF or TDF, also found in Atripla, Complera, Truvada, and Stribild) is not recommended if the CrCl is less than 70 mL/min.

POTENTIAL DRUG INTERACTIONS

Tybost interacts with many drugs, because as a booster it inhibits liver enzymes involved in drug metabolism. See the package insert for the most complete list of interactions. Tell your provider or pharmacist about all medications, herbals, and supplements that you're taking or thinking of taking, prescribed or not, before starting on a regimen that contains cobicistat. Tybost may increase levels of certain calcium channel blockers, beta-blockers, HMG-CoA reductase inhibitors (statins), antiarrhythmics, antidepressants, sedative-hypnotics, erectile dysfunction agents, inhaled corticosteroids, and norgestimate. Caution should be taken, with possible dose adjustments of these medications, when used with Tybost. Tybost-boosted Reyataz is contraindicated (cannot be taken) in individuals who need irinotecan (a chemo drug). Tybost increases serum levels of elvitegravir (as part of Stribild), and several protease inhibitors, including Prezista and Reyataz. Sporonox (antifungal) and Biaxin (antibiotic) may increase Tybost concentrations. Tybost may increase Biaxin levels. Rifabutin and some anti-seizure medications, such as carbamazepine (Tegretol) and phenytoin (Dilantin) may decrease Tybost levels. Taking with Olysio is not recommended. Tybost is metabolized by the same drug breakdown pathways as Norvir, but they are not interchangeable and there may be some drug interactions with Tybost that are not seen with Norvir. When Tybost is given with Reyataz, antacids which contain aluminum or magnesium should be taken 2 hours before or after; other medications used for heartburn or reflux need to be taken 10–12 hours after EvoTaz.

MORE INFORMATION

Tybost is not an HIV medication. It is used to boost blood levels of Prezista and Reyataz, and is available in fixed-dose tablets with those medications (see EvoTaz and Prezcobix). Cobicistat is also part of the single-tablet regimen Stribild, a recommended therapy in U.S. HIV treatment guidelines. It is not, however, yet been studied or FDA approved to boost elvitegravir levels when not taken as part of Stribild. As an alternative to Norvir, Tybost's development has created a lot of excitement. Note, Tybost shares some of the same side effects of increased cholesterol, increased triglycerides, and stomach upset as Norvir.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Tybost (cobicistat) is a first-in-class drug that boosts like Norvir (ritonavir), but has no antiviral activity of its own. Like ritonavir, it raises triglycerides and cholesterol. It also interacts with a host of drugs metabolized by the cytochrome system, particularly 3A4, but unlike ritonavir, it is being made available for co-formulation with drugs from other manufacturers. Co-formulations have been approved with the protease inhibitors atazanavir and darunavir, and are planned with darunavir, TAF, and FTC. At present cobicistat is approved only for combination with atazanavir 300 mg and darunavir 800 mg because of lack of data with other drugs and doses. A quirk of cobicistat is that it raises levels of creatinine in the blood by inhibiting its tubular secretion. It is typical to see a change "on paper" of 0.4 mg/dL or less within the first 12 weeks of dosing, but actual kidney function is not affected. Higher levels or late onset increases should be evaluated for renal toxicity. Just as ritonavir nears generic status, co-formulated COBI will be everywhere and the battle truly will be on.

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Truthfully, we were hoping for a bit more from cobicistat. Even at low doses, ritonavir can cause side effects, notably minor gastrointestinal problems. Unfortunately, cobicistat didn't provide much in the way of a tolerability advantage over ritonavir. It also causes many (but not all) of the same drug interactions as ritonavir, which demands careful attention when prescribing other medications. One advantage is that Gilead is licensing the drug for use in fixed-dose combinations with other manufacturers' products—something Abbott (now AbbVie) wouldn't allow for ritonavir—such as Bristol-Myers Squibb's atazanavir and Janssen's darunavir. —TIM HORN

STANDARD DOSE

150 mg once a day with food taken at the same time with either Prezista 800 mg or Reyataz 300 mg.

Tybost is not an HIV drug, but is a "booster" used to increase the levels of Prezista 800 mg once daily or Reyataz 300 mg once daily. Tybost is not interchangeable with Norvir when used to increase the levels of other HIV medications.

Take a missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose.

Tybost should only be used in pregnancy if the benefits justify the risks. There are only animal data in pregnancy. Tybost has not been studied in individuals under 18 years of age, thus it should not be used in pediatric patients.

MANUFACTURER

Gilead Sciences, Inc.
gilead.com
(800) GILEAD-5
(445–3235)

AWP

$216.00 / month

EvoTaz

RECENTLY APPROVED AND NOT YET DHHS RATED AS A FIXED-DOSE DRUG; HOWEVER, THE INDIVIDUAL DRUGS IN THIS MEDICATION ARE DHHS RECOMMENDED FOR FIRST-LINE USE, AS REYATAZ (WHEN BOOSTED BY NORVIR) AND IN STRIBILD (CONTAINING COBICISTAT)

atazanavir / cobicistat, or ATV / COBI

STANDARD DOSE

One tablet (300 mg atazanavir/150 mg cobicistat) once daily with food. Use in treatment-experienced patients depends on protease inhibitor drug resistance substitutions. Coadministration with Viread is not recommended if kidney function is below 70 mL/min.

Take a 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.

Cobicistat should be used in pregnancy only if the benefits justify the risks. There is only animal data in pregnancy.

Cobicistat has not been studied in individuals under 18 years of age, thus EvoTaz should not be used in pediatric patients.

MANUFACTURER

Bristol-Myers Squibb
evotaz.com
(800) 321–1335

AWP

Price not available at press time.

POTENTIAL SIDE EFFECTS AND TOXICITY

See the pages for the individual drugs contained in this medication—Reyataz and Tybost. The most common side effects seen in research were nausea (2%), ocular icterus (yellowing of the eyes; 3%), jaundice (5%), and rash (5%). Serum phosphorus in patients with or at risk for renal (kidney) impairment should also be monitored. Renal impairment, including cases of acute renal failure and Fanconi syndrome, have been reported in patients taking both cobicistat and Viread (tenofovir DF or TDF, also found in Truvada). When used with TDF, a baseline CrCL, urine glucose and urine protein is needed; CrCr, urine glucose, and urine protein should be monitored regularly while taking Tybost-containing regimens. Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. EvoTaz has not been studied in individuals with liver impairment and is not recommended to be used in these individuals. It is also not recommended in those on dialysis who are HIV-treatment-experienced.

POTENTIAL DRUG INTERACTIONS

See the pages for the individual drugs contained in this medication—Reyataz (atazanavir) and Tybost (cobicistat). Do not take with Kaletra, Norvir, Prezcobix, Reyataz, Stribild (not recommended to be taken with EvoTaz), or Tybost; all or part of these medications are already in EvoTaz or contain equivalent medication. Use with other protease inhibitors or with Intelence, Sustiva, or Vitekta is not recommended. EvoTaz is contraindicated (cannot be taken) in individuals who need irinotecan (a chemo drug). Do not use with Viekira Pak.

MORE INFORMATION

See the pages for the individual drugs contained in this medication—Reyataz and Tybost. EvoTaz received FDA approval in January of this year as this issue went to press. Reyataz is one of two recommended PIs for first-time therapy in Department of Health and Human Services (DHHS) HIV treatment guidelines. Since some people who take Reyataz must use it with a PK enhancer like cobicistat (Tybost) or ritonavir (Norvir), this formulation makes for greater convenience, one less pill, and one less co-pay. Tybost was FDA approved in November. It is not an HIV medication; like ritonavir, it is used to boost blood levels of other drugs. The two PK enhancers have a long list of drug interactions. As an alternative to Norvir, Tybost has created a lot of excitement. Tybost is also found in a single-tablet regimen, Stribild.

See package insert for more information on side effects and interactions.

DOCTOR'S COMMENTS

Co-formulated atazanavir/COBI was approved based upon a clinical trial demonstrating virologic non-inferiority. Sadly, the safety profiles were similar with no apparent benefit of COBI over ritonavir. Still, a co-formulated PI and booster has not been seen since Kaletra because of Abbott's unwillingness to play with others. Fewer pills, fewer individual prescriptions to keep in sync, and fewer co-pays will be a welcomed benefit if the drug is affordably priced. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

This fixed-dose combination tablet is a moderate improvement over previous ritonavir/Reyataz-based combinations. Cobicistat is a comparable swap for ritonavir—not much better, and definitely no worse. The benefit here is one fewer tablet in a multi-tablet regimen. Those currently using ritonavir-boosted Reyataz plus Truvada will see their daily pill count decrease from three to two, which for those with private insurance also means one less co-payment or co-pay assistance program to deal with. Even minor treatment simplifications can make a difference. —TIM HORN

Prezcobix

RECENTLY APPROVED AND NOT YET DHHS RATED AS A FIXED-DOSE DRUG; HOWEVER, THE INDIVIDUAL DRUGS IN THIS MEDICATION ARE DHHS RECOMMENDED FOR FIRST-LINE USE, AS PREZISTA (WHEN BOOSTED BY NORVIR) AND IN STRIBILD (CONTAINING COBICISTAT)

darunavir / cobicistat, or DRV / COBI

POTENTIAL SIDE EFFECTS AND TOXICITY

See the pages for the individual drugs contained in this medication—Prezista and Tybost. The most common side effects seen in research of at least moderate intensity in 5% or more of participants taking it were diarrhea, nausea, rash, headache, abdominal pain, and vomiting. Serum phosphorus in patients with or at risk for renal (kidney) impairment should also be monitored. The coadministration of Tybost and Viread (tenofovir DF, TDF, brand name Viread, also found in Truvada) is not recommended if the CrCl (creatinine clearance) is less than 70 mL/min. A baseline CrCL, urine glucose, and urine protein are needed when used with TDF; CrCr, urine glucose, and urine protein should be monitored regularly while taking Tybost-containing regimens.

Renal impairment, including cases of acute renal failure and Fanconi syndrome, have been reported in patients taking both Tybost and TDF. Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. As Prezista contains a sulfa component, use with caution in patients with sulfa allergies.

POTENTIAL DRUG INTERACTIONS

See the pages for the individual drugs contained in this medication—Prezista (darunavir) and Tybost (cobicistat). Do not take with EvoTaz, Kaletra, Norvir, Prezista, Stribild (not recommended to be used with Prezcobix), or Tybost; all or part of these medications are already in Prezcobix or contain equivalent medication. Use with other protease inhibitors or with Vitekta is not recommended. Do not use with Viekira Pak.

MORE INFORMATION

See the pages for the individual drugs contained in this medication—Prezista and Tybost. Prezcobix received FDA approval in January of this year as this issue went to press. Prezista is one of two recommended PIs for first-time therapy in Department of Health and Human Services (DHHS) HIV treatment guidelines. Since Prezista must be used with a PK enhancer like cobicistat (Tybost) or ritonavir (Norvir), this formulation makes for greater convenience, one less pill and one less co-pay. Tybost was FDA approved in November. It is not an HIV medication; like Norvir, it is used to boost blood levels of other drugs. The two PK enhancers have a long list of drug interactions. As an alternative to Norvir, Tybost has created a lot of excitement. Tybost is also found in a single-tablet regimen, Stribild.

See package insert for more information on side effects and interactions.

DOCTOR'S COMMENTS

Co-formulated darunavir/COBI is now available in the U.S. Darunavir/COBI was non-inferior to ritonavir-boosted darunavir but without any additional safety benefit from COBI. As with atazanavir/COBI, the advantage of co-formulation is mainly about fewer pills, fewer individual prescriptions to manage, and perhaps fewer drug co-pays. Whether there is a financial benefit, however, will depend on the price point. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

This fixed-dose combination tablet is a moderate improvement over previous ritonavir/Prezista-based combinations. Cobicistat is a comparable swap for ritonavir—not much better, and definitely no worse. The benefit here is one fewer tablet in a multi-tablet regimen. Those currently using ritonavir-boosted Prezista plus Truvada will see their daily pill count decrease from three to two, which for those with private insurance also means one less co-payment or co-pay assistance program to deal with. Even minor treatment simplifications can make a difference. —TIM HORN

STANDARD DOSE

One tablet (800 mg darunavir/150 mg cobicistat), once daily with food, in patients with no darunavir drug resistance. When coadministered with Viread the kidney function should be above 70 mL/min.

Take a 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.

Cobicistat should be used in pregnancy only if the benefits justify the risks. There is only animal data in pregnancy.

Cobicistat has not been studied in individuals under 18 years of age, thus Prezcobix should not be used in pediatric patients.

MANUFACTURER

Janssen Therapeutics
prezcobix.com
(800) JANSSEN
(526-7736)

AWP

Price not available at press time.

Sustiva

DHHS RECOMMENDED (A COMPONENT OF ATRIPLA)

efavirenz, or EFV

STANDARD DOSE

One 600 mg tablet, once a day, typically at bedtime, on an empty stomach or with a light, low-fat snack. However, to minimize potential side effects it is often recommended to take Sustiva (efavirenz) on an empty stomach at bedtime.

Take a missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose. Also available in smaller 50 mg and 200 mg capsules. Strawberry/mint flavored 30 mg/mL solution available for children under expanded access program.

Approved for children 3 months and older weighing at least 7.7 lbs. (3.5 kg). For those who can't swallow capsules, administer by capsule sprinkle method. See below or drug label for instructions or watch video at sustiva.com.

MANUFACTURER

Bristol-Myers Squibb
bms.com
(800) 321-1335

AWP

$1,011.97 / month for 600 mg tablets

POTENTIAL SIDE EFFECTS AND TOXICITY

Central nervous system (CNS) or psychiatric symptoms (dizziness, insomnia, impaired concentration, abnormal dreams and hallucinations, depression, suicidal thoughts or actions, aggression, paranoid/manic reactions), usually diminishing within four weeks. Bedtime dosing may help reduce symptoms. Other side effects may include rash, nausea, vomiting, diarrhea, and fever. Rash in children is more common and more severe. Efavirenz may raise levels of triglycerides (fat in the blood) and cholesterol. It also may lead to false positive urine tests for marijuana; a confirmatory test is available. Risk of birth defects (see Atripla). Close monitoring for increased liver enzyme levels is recommended initially with regular check-ups for people with hepatitis B/C or liver disease. Use with caution in mild liver impairment; not recommended with moderate or severe liver impairment. See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbals, supplements, and over-the-counter products you are taking or thinking of taking. Sustiva should not be taken with other NNRTIs or medications that contain them (Atripla and Complera). Do not take avanafil, Gingko biloba, midazolam, pimozide, rifapentine, St. John's wort, or triazolam. Sustiva may affect warfarin levels. Sustiva can decrease levels of buprenorphine and methadone—monitor for withdrawal. Increase Kaletra to three tablets twice daily with food when taken with Sustiva by treatment-experienced people. Kaletra cannot be taken once daily with Sustiva. Monitor liver enzymes closely if Sustiva and Norvir are used together. When using with Tivicay, increase the Tivicay dose to 50 mg twice daily. Treatment-experienced people should not take Reyataz with Sustiva, but for treatment-naïve people, Reyataz once-daily dose should be 400 mg with Norvir boost. Boost once-daily Lexiva with 300 mg Norvir. Increase the Sustiva dose to 800 mg once daily with rifampin for people weighing 132 pounds (60 kg) or more. Rifabutin can be used as an alternative, but dose adjustment is needed when it is used two or three times a week. When taken with anticonvulsants carbamazepine, phenobarbital, or phenytoin, periodic monitoring of anticonvulsant and Sustiva levels should be done or alternative anti-seizure drugs, such as levetiracetam, should be considered. Effectiveness of birth control pills may be decreased; consider the use of other contraceptives. Closer monitoring and dose adjustments may be required with azole antifungal agents posaconazole (avoid unless benefit outweighs potential risk) and itraconazole (should consider an alternative, as no dose recommendation can be made). The dose of voriconazole should be increased to 400 mg every 12 hours and the Sustiva dose should be decreased to 300 mg once daily using capsules; tablets should not be broken. Monitor effectiveness of clarithromycin or consider azithromycin. Levels of immunosuppressants should be monitored when starting or stopping Sustiva. Cardizem, Lipitor, Pravachol, Zocor, and Zoloft doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. No dose adjustment with Harvoni or Sovaldi. Don't take with Olysio.

MORE INFORMATION

According to DHHS HIV treatment guidelines, Sustiva is the recommended NNRTI for NNRTI-based regimens without any limitations (viral load or CD4 requirements). It is usually taken as a component of the Atripla single-tablet regimen. Avoid driving or operating heavy machinery for a few hours after dose. If you can't sleep, ask about switching the timing of your dose little by little until it's taken in the daytime. A rare genetic trait affecting drug metabolism of Sustiva, leading to a higher rate of side effects, occurs more in African Americans. See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Efavirenz, the anchor drug of Atripla, has been one of the most widely-used components of initial therapy for over a decade. While potent and long acting, some people have difficulty tolerating the neuropsychiatric effects of efavirenz (vivid dreams, mood changes, dizziness) even when taken at bedtime. One study showed 400 mg of efavirenz to be virologically non-inferior to 600 mg daily, with fewer side effects, but that dose is not yet recommended and there are no co-formulated regimens using the lower dose at present. The long half-life of efavirenz can become problematic for persons, most commonly in African Americans, who have a genetic mutation that extends its presence in the blood. This means that, on stopping an efavirenz-based regimen, high levels of efavirenz may persist in the system even for weeks and potentially select for resistance because the backbone is gone. If efavirenz-based regimens for some reason are to be stopped (rather than switched), a boosted PI should be substituted until efavirenz is out of the blood. A generic efavirenz was expected soon; however, its patent was extended again this year.

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Full disclosure: I have been on an efavirenz-based regimen since the drug was first approved in 1998. It is very potent, can be taken with or without food, and I tolerate it extremely well. Many others, however, haven't been so lucky, particularly in the side effects department. It can cause rash and central nervous system (CNS) disturbances, including truly bizarre dreams, muddled thinking, and depression. Fortunately, newer drugs and regimens have yielded comparable efficacy—efavirenz has, for many years, been the drug to beat—with far fewer CNS side effects. In turn, the popularity of efavirenz as a leading option for people starting therapy for the first time is rapidly diminishing. For people like me, however, many doctors seem to agree: don't feel pressured to fix something that isn't broken. —TIM HORN

Edurant

DHHS RECOMMENDED WITH LIMITATIONS AND ONLY WITH TRUVADA

rilpivirine hydrochloride (rilpivirine), or RPV

POTENTIAL SIDE EFFECTS AND TOXICITY

Insomnia, headache, rash, and depressive disorders. Tell your doctor right away if you experience negative or suicidal thoughts or actions. Nephrotic syndrome (a kidney disorder) was added to the label, noting that the level of risk is unknown, and that the syndrome may not even be related to rilpivirine (Edurant). Two different studies comparing Edurant to Sustiva showed that Edurant was slightly better tolerated. Edurant also has minimal negative effects on "bad" cholesterol, total cholesterol, and triglycerides when compared to Sustiva. Edurant improved "good" cholesterol slightly less than Sustiva. Liver problems can occur with Edurant (even in patients without a history of liver disease). See page 64 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. Edurant should not be taken with other non-nukes or Complera, as the latter contains rilpivirine. Can be taken with Isentress without dose adjustments. Antacids should be taken two hours before or at least four hours after Edurant. Acid-reducing drugs (Pepcid, Tagamet, Zantac, and Axid) should be taken 12 hours before or four hours after an Edurant dose. Proton pump inhibitors (Aciphex, Nexium, Prevacid, Protonix, and Prilosec) should not be taken. Cannot be taken with the anti-seizure medications carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the anti-TB drugs rifampin and rifapentine; or the herb St. John's wort. If administered with rifabutin, the dose should be increased to two 25 mg tablets once daily with a meal. When rifabutin is stopped, Edurant dose should be decreased to 25 mg daily. Do not take with more than one systemic dose of the steroid dexamethasone (repeated topical use is okay and tablets are available). Monitor for worsening of any fungal infections when Edurant is used with anti-fungal medications like fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole; dose adjustment for these medications may be needed. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, and telithromycin. 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 abnormal heart rhythms can make the heart stop). No dose adjustment needed with hepatitis C medications Olysio (simeprevir) and Sovaldi (sofosbuvir). Cannot be taken with Viekira Pak.

MORE INFORMATION

Edurant is not recommended for patients with a viral load of greater than 100,000. ECHO and THRIVE studies showed that Edurant is non-inferior (a term used in scientific research that means the drug is no better or worse than those it's compared to) to Sustiva in efficacy—76% vs. 77% of patients achieved a viral load of less than 50 copies (undetectable) and CD4 count increases of 228 vs. 219 when comparing Edurant and Sustiva, respectively. While its tolerability and safety profiles are advantages for Edurant, the greater potential for virologic failure in patients with high viral loads, and cross-resistance to the other NNRTIs puts Edurant at a disadvantage for first-time treatment (because patients may not be able to switch to another NNRTI if their HIV develops NNRTI resistant mutations to Edurant). 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 human studies have been conducted. Edurant should be used in pregnancy only if the potential benefit justifies the potential risk. Most HIV medications are Pregnancy Category B and carry the same warning.

See package insert for more complete information on potential side effects and interactions.

STANDARD DOSE

One 25 mg tablet once daily with a meal.

Take a 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. For proper absorption, it must be taken with a meal that you chew, not nutritional drinks or protein shakes, and it should have some fat. Meal examples include two slices of whole wheat toast with peanut butter and fresh fruit; a roast beef sandwich on a hard roll with mayo; or pasta and meat sauce with salad. Taking Edurant without food could result in a 40% decrease in the drug absorption and may lead to HIV resistance.

MANUFACTURER

Janssen Therapeutics
janssentherapeutics.com
(800) JANSSEN
(526-7736)

AWP

$996.43 / month

DOCTOR'S COMMENTS

Edurant (rilpivirine), a once-daily drug, emerged as a competitor to Sustiva (efavirenz) largely due to its better central nervous system (CNS) tolerability (and lower incidence of rash and lipid elevations) as well as its more robust resistance profile. Yet, there are disadvantages. Rilpivirine performs better at viral loads less than 100,000 copies/mL and with CD4 counts above 200/mL. It is better absorbed when given with food, and proton pump inhibitors interfere with activity and should not be used. The good news is that persons who have well-suppressed virus on efavirenz regimens can probably safely switch to the single-tablet regimen that includes rilpivirine, TDF, and FTC (Complera) as long as they have not had prior virologic failure.

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Rilpivirine is most often used in the single-tablet regimen Complera, which also contains tenofovir and emtricitabine. It has a favorable side effect profile and has proven to be a decent alternative to efavirenz, but with some caveats: it's not as effective in people starting therapy with viral loads above 100,000 and, if resistance to rilpivirine occurs, switching to Intelence might not be beneficial. It also needs to be taken with food.

—TIM HORN

Intelence

ONLY FOR TREATMENT-EXPERIENCED INDIVIDUALS

etravirine, or ETR

STANDARD DOSE

One 200 mg tablet, or two 100 mg tablets, twice a day, with food. 25 mg tablets available for children 6–18 years old (dose based on weight).

Take a 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. People unable to swallow pills (Intelence tablets are chalky) can dissolve tablets in 5 mL (1 teaspoon) of water, or at least enough liquid to cover the medication, stir well until the water looks milky, add more water if desired—can use orange juice or milk as an alternative (always placing tablets in water first). Avoid grapefruit juice and warm (over 104° F) or carbonated beverages. Drink it immediately, rinse the glass several times with water, orange juice, or milk and completely swallow the rinse each time to make sure the entire dose is taken. See commentary in the More Information section at positivelyaware.com/intelence.

MANUFACTURER

Janssen Therapeutics
janssentherapeutics.com
(800) JANSSEN
(526-7736)

AWP

$1,212.29 / month

POTENTIAL SIDE EFFECTS AND TOXICITY

Generally tolerable, but most common are mild rash and increased cholesterol. Rare side effects include severe rash and peripheral neuropathy. The FDA advises, "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 NNRTIs, but if you develop a rash from Intelence, you may still be able to take one of the other NNRTIs. See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

NNRTIs have the potential to interact with many other drugs. Refer to package insert for complete list. Tell your provider or pharmacist about all medications, herbal products, and supplements you are taking or thinking of taking, prescribed or not. Intelence should not be taken with other NNRTIs or medications that contain them (Atripla and Complera). If Intelence is taken in combination with a protease inhibitor, it must be boosted with low-dose Norvir. Avoid Intelence in combination with the following PIs: Aptivus, Lexiva, Reyataz, or full-dose Norvir. It can be taken with the integrase inhibitor Isentress with no adjustments necessary, however, should be avoided with Tivicay unless administered with one of the following combinations: Reyataz/Norvir, Prezista/Norvir, or Kaletra. Taking it in combination 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 a Norvir-boosted PI. In people who've failed therapy with other NNRTIs, Intelence should not be taken with NRTIs alone. Do not take Intelence with Tegretol, Luminal, Dilantin, Priftin, Rifadin, or the herb St. John's wort. Use with caution when combined with antifungals (Diflucan and Vfend). Dosage adjustments of certain cholesterol medications may be needed based on clinical response, including Lipitor, Lescol, Mevacor, Livalo, and Zocor.

Monitor the effectiveness of Coumadin (warfarin) and adjust dose as needed based on clinical response. Alternatives to Plavix should be considered when used with Intelence. Alternatives to clarithromycin, such as azithromycin, should be considered for treatment of MAC. Lower Valium dose may be needed. Use caution with systemic dexamethasone or consider alternatives. Intelence can be taken with Mycobutin 300 mg daily; however, it should be avoided by those who are taking a boosted PI. No interactions were found between Intelence and proton pump inhibitors Prilosec, or the acid reducer Zantac. Intelence can be safely combined with methadone with additional monitoring for potential signs of withdrawal. Intelence can also be safely combined with Viagra, Cialis, and Levitra, though a dosage adjustment may be necessary. Can be taken with Sovaldi. Taking with Harvoni or Olysio is not recommended. Cannot be used with Viekira Pak.

MORE INFORMATION

This second-generation drug was developed to have a higher (more than one virus mutation) genetic barrier to drug resistance. It has shown significant viral load reduction in people with drug resistance to Sustiva or Viramune. The older NNRTIs can develop resistance quickly, requiring only one viral mutation. For patients who have had virologic failure on an NNRTI-containing regimen, do not use Intelence in combination with a nucleoside backbone alone. Although not FDA approved, some providers are prescribing Intelence once daily (2 of the 200 mg tablets) based on clinical trials that showed that once-daily Intelence was not inferior to Sustiva-based regimens. The once-daily dosing is likely to increase patient adherence. Some patients complain of hard-to-swallow, large chalky pills; see dissolving instructions in dose section.

Refer to package insert for complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Intelence (etravirine) was approved for treatment-experienced patients but was not studied for initial therapy, thus limiting its use. It offers a higher barrier to resistance than Sustiva (efavirenz) and Viramune (nevirapine), and it retains activity against single NNRTI mutations that impair efavirenz (and to a lesser extent, nevirapine). Etravirine was especially popular when it was approved in proximity to Isentress (raltegravir) and Prezista (darunavir). The combination of these three drugs rescued many patients whose virus had become resistant to NNRTIs, nukes, and protease inhibitors. However, it is given twice daily and at this point offers no additional advantage over its younger sibling, Edurant (rilpivirine). It does dissolve in water and could be easier to take for people who can't swallow pills. Drug interactions must be carefully considered, including with common drugs such as atorvastatin (Lipitor) and clopidogrel (Plavix). It should not be given with dolutegravir [Tivicay] unless co-administered with boosted darunavir. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Intelence has helped fill an important gap in HIV treatment. Because it is at least partially active against HIV that has become resistant to efavirenz (less so for HIV resistant to nevirapine), Intelence continues to be a useful second-line non-nuke option for treatment-experienced individuals. That said, the fewer non-nuke resistance mutations in the reverse transcriptase gene the better and we know Intelence works best when combined with other drugs to which HIV is fully sensitive. So here's where drug-resistance testing and quick decision-making with a provider can make a big difference. Intelence is one tablet twice a day and can be swallowed whole—the tablets can leave a chalky taste in the mouth—or dissolved in water. —TIM HORN

Viramune XR

NOT DHHS RECOMMENDED FOR FIRST-LINE USE

nevirapine, or NVP

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects include headache, nausea, vomiting, fever, and rash (reduced with 14-day lead-in dosing). Rarely, severe and life-threatening liver damage, sometimes fatal, has occurred. Women with CD4 T-cell counts greater than 250, including pregnant women, have the highest risk of serious liver damage, though men with more than 400 T-cells are also at risk. 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. 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 rash, blistering, mouth sores, conjunctivitis (inflammation of the eye, which if untreated may result in blindness), swelling, muscle or joint aches, fever, or general ill feeling. Do not increase dose if rash develops during dose escalation or if it is accompanied by the above conditions. During the first six weeks of therapy, avoid prednisone due to increased severity and incidence of rash. Liver enzyme levels may increase and in rare instances hepatitis has developed (do not ignore yellowing of eyes or skin). 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. See page 64 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbs, supplements, and over-the-counter (OTC) products you are taking or plan to take. Viramune should not be taken with other NNRTIs or medications that contain them (Atripla and Complera). Do not take with Stribild or Tivicay. Never take St. John's wort. Rifampin or Priftin should not be used with Viramune; Mycobutin is the recommended alternative to rifampin. Use with caution with midazolam, triazolam, fluconazole, itraconazole, voriconazole, Cordarone, lidocaine or disopyramide, ethosuximide, clonazepam, calcium channel blockers (Procardia and others), immunosuppressants (including transplant drugs), and warfarin. Viramune decreases methadone levels; dose adjustment may be necessary to avoid withdrawal. Can reduce levels of protease inhibitors; a 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: carbamazepine, phenobarbital, and phenytoin. Effectiveness of birth control pills may be decreased; consider the use of other contraceptives. Do not take with Olysio, but may take with Sovaldi or Harvoni.

MORE INFORMATION

The once-daily Viramune XR was FDA approved in 2011, but many providers already prescribed off-label once-daily dosing with the old formulation. The regular Viramune (IR) formulation is now available as generic nevirapine. Viramune XR is an alternative drug under U.S. HIV treatment guidelines, and Sustiva is the recommended NNRTI. There is known data that confirms that Sustiva is better than Viramune for most patients. When taken around the time of labor, Viramune has been effective in preventing mother-to-child transmission, but drug resistance increased when taken alone—use at least one other (ideally two) HIV drug(s) to prevent resistance. Viramune may be used for babies born to HIV-positive mothers; in the first week of life, Viramune is usually given with zidovudine.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

The extended release version of Viramune (nevirapine) allows once-daily dosing and was introduced shortly before the patent expired on the original twice-daily formulation, which is now generic. Nevirapine has fallen out of favor due to liver toxicity, especially notable at higher CD4 counts, and in women more than men. It also causes rash more frequently than other NNRTIs. While IAS-USA guidelines continued to list nevirapine as an alternate regimen in 2014, the DHHS panel has now dropped nevirapine as a recommended drug due to this potentially dangerous toxicity. For persons who are now on nevirapine with good result, there is no reason to switch, but we should be careful not to drift back toward nevirapine for first-line therapy simply because it is now generic and perhaps cheaper. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

The original and extended release (XR) versions of Viramune have served many people living with HIV well over the years. It doesn't cause central nervous system side effects, unlike efavirenz, and can be used once a day (twice-daily dosing was said to be necessary when it was first approved). The thing is, it can cause serious liver toxicity soon after it's started, notably in those with healthier immune systems. In turn, it's not recommended for women and men with CD4 counts above 250 and 400, respectively. And with U.S. treatment guidelines now pretty much recommending HIV treatment as soon as possible following diagnosis, a drug that comes with CD4 cell-dependent warnings, the need for reduced dosing for the first two weeks, and data suggesting it may not be the most effective of available options has understandably lost its luster. Many people living with HIV are continuing to do well on nevirapine, which is great. For those starting therapy for the first time, however, there are better options to choose from. —TIM HORN

STANDARD DOSE

One 200 mg IR (immediate release) tablet once daily for two weeks, then full dose of one 400 mg tablet once daily of Viramune XR or one 200 mg IR tablet twice daily, with or without food, with no dietary restrictions.

Take a 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 you interrupt therapy for more than seven days, you will need to restart with lead-in dose above. Pediatric 100 mg XR tablets approved for children 6 to 18 years of age. Viramune IR frequently prescribed as two 200 mg tablets once daily, although that is not FDA approved. Viramune XR once daily is approved only for adults and children aged 6 to 18 years old. Dose for children 15 days or older is 150 mg/m^2 once daily for 14 days, then 150 mg/m^2 twice daily thereafter, not to exceed 400 mg daily. For dialysis patients, an additional 200 mg IR is required after each dialysis. 50 mg/5 mL oral suspension also available. Generic available for immediate release formulation.

MANUFACTURER

Boehringer Ingelheim
boehringer-ingelheim.com
(800) 542–6257

AWP

$798.73 / month;
$706.42 / for generic IR

Truvada

DHHS RECOMMENDED FOR FIRST-LINE USE

emtricitabine / tenofovir, or FTC / TDF

STANDARD DOSE

For adults and children 12 years or older weighing more than 77 pounds (35 kg), one tablet (200 mg emtricitabine / 300 mg tenofovir DF) once daily, with or without food, with no dietary restrictions.

Take a 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. The dosing frequency needs to be adjusted for people with decreased kidney function. Truvada should not be used if kidney function is less than 30 mL/min or if you are on dialysis, but the individual components can still be used, with the doses adjusted based on kidney function. Truvada once daily is also approved for prevention (pre-exposure prophylaxis, or PrEP) in confirmed HIV-negative adults at high risk for HIV; go to positivelyaware.com/truvada-for-prep.

MANUFACTURER

Gilead Sciences, Inc.
gilead.com
(800) GILEAD-5
(445–3235)

AWP

$1,539.90 / month

POTENTIAL SIDE EFFECTS AND TOXICITY

See the pages for the individual drugs contained in Truvada—Viread and Emtriva. Overall, it is fairly well tolerated, but some may experience diarrhea, dizziness, nausea, depression, fatigue, insomnia, abnormal dreams, and rash. Skin discoloration on palms and soles may also occur. The tenofovir (Viread) in Truvada is associated with decreases in bone mineral density (BMD). BMD monitoring should be considered in people who have a history of bone fracture due to disease or are at risk for osteopenia or osteoporosis. It is unknown if calcium supplements with or without vitamin D would be beneficial. While calcium and vitamin D levels can be checked to assess the need for these supplements, talk with your provider before starting since many calcium supplements can affect your stomach's acid level. Less common side effects include kidney toxicities and low blood phosphate. Tell your provider about persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as these could be signs of kidney problems. If Emtriva, Viread, or Truvada are discontinued abruptly in HBV-co-infected patients, exacerbation of hepatitis may occur. See Emtriva for hepatitis B information. See page 63 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See the pages for the individual drugs contained in Truvada—Viread and Emtriva. Do not take with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Hepsera, Stribild, Triumeq, Trizivir, or Viread since all or part of these medications are already in Truvada or it contains equivalent medications. Tenofovir decreases the concentration levels of Reyataz, therefore when Reyataz is taken with Truvada or Viread, it is recommended that Reyataz 300 mg is taken with Norvir 100 mg or Tybost 150 mg (all as a single daily dose with food). In addition, Reyataz and Kaletra increase tenofovir concentrations for unknown reasons. It is recommended that patients taking Reyataz or Kaletra with Truvada should be monitored for Truvada-associated adverse events, particularly decreases in kidney function. No dose adjustment is needed when used with Kaletra. Avoid taking Truvada with drugs that negatively affect the kidneys, including Zovirax, Valtrex, and high doses of drugs like Advil, Aleve, and Motrin. Tenofovir increases levels of didanosine (Videx EC), so use with caution and make sure your dose of didanosine is adjusted accordingly and monitored for toxicities. Can be taken with Olysio. Monitor kidney function when using Harvoni or Viekira Pak.

MORE INFORMATION

Currently, Department of Health and Human Services (DHHS) HIV treatment guidelines recommend Truvada over Epzicom as the NRTI component for first-time therapy (unless taking Tivicay). Studies 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 "less effective at controlling HIV" in the regimens tested. Moreover, time to a serious adverse event was sooner in the people taking Epzicom. 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. The components of Truvada are also contained in three once-daily single-tablet regimens: Atripla, Complera, and Stribild. Supplementation with calcium and vitamin D has not been clearly shown to prevent bone issues in HIV patients. The FDA recommends calcium and vitamin D supplementation for all patients who need it, regardless of HIV status. Truvada as one tablet once a day was also FDA approved in July 2012 for PrEP (prevention) in HIV-negative individuals at risk. Go to positivelyaware.com/truvada-for-prep for the use of Truvada in PrEP.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Truvada (TDF/FTC) is recommended for initial therapy by all guidelines in highly resourced countries, and, although expensive, is working its way into less resourced settings. Because both drugs have long half-lives, it can be taken once daily. The primary toxicity is due to kidney and bone effects of TDF (see Viread). The FDA has approved Truvada for prevention of the sexual transmission of HIV in HIV-negative individuals (see CDC guidelines). Both TDF and FTC also have activity against hepatitis B (HBV), so stopping the drug can lead to a flare-up of hepatitis in those who have HBV infection. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Talk about a blockbuster drug. More than 10 years following its approval as a component of HIV treatment (and more than two years after its approval as PrEP), global sales of this once-daily fixed-dose combination tablet are in the ballpark of $500 million… every quarter. For people not using Atripla, Stribild, or Complera—all three contain emtricitabine and tenofovir—Truvada is the most commonly prescribed nuke backbone for use with other recommended drugs. But the tenofovir in Truvada isn't for everyone, particularly for those with kidney problems. It has also been linked to accelerated bone loss and increased fracture risk. Gilead is currently developing a combination tablet containing emtricitabine and a new version of tenofovir (tenofovir alafenamide fumarate—see Viread), which may be easier on kidneys and bones—good news, particularly for those of us entering our "mature" years and already at a greater risk for these problems. —TIM HORN

Epzicom

DHHS RECOMMENDED FOR FIRST-LINE USE (WITH LIMITATIONS)

abacavir sulfate (abacavir) / lamivudine, or ABC / 3TC

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 Ziagen for details of symptoms). To avoid HSR, a blood test for HLA-B*5701 (a genetic marker) can identify patients at risk for this reaction. This test is covered by most insurance and also by LabCorp/ViiV (see co-pay chart). 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, Triumeq, Trizivir, or Ziagen, 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.) Check with your doctor if you have any side effects after taking this medicine—don't just stop! 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. Some observational studies have 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, older age, high cholesterol, and drug use), though other studies have found no increased risk. Department of Health and Human Services (DHHS) HIV treatment guidelines state, "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; the decision to stop or never start a regimen containing abacavir is up to you and your provider. See page 63 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See the individual drugs contained in Epzicom, Epivir and Ziagen. Do not take with Atripla, Combivir, Complera, Emtriva, Epivir, Epivir-HBV, Hepsera, Stribild, Triumeq, Trizivir, Truvada, or Ziagen, since all or part of these medications are already in Epzicom or contain medications equivalent to it. Other medications with major interactions include Copegus and Intron A, which can lead to side effects such as lactic acidosis and liver impairment. Tell your provider or pharmacist about all medications, herbal products, and supplements you are taking or thinking of taking, whether they are prescribed or not. Avoid use of alcohol, as it can increase the levels of abacavir and therefore increase the possibility of side effects. Should be okay to take with Harvoni and Viekira Pak.

MORE INFORMATION

Triumeq, a single-tablet regimen (STR) containing Tivicay and Epzicom, was FDA approved on August 22nd, 2014, and is a recommended therapy under Department of Health and Human Services (DHHS) HIV guidelines. In October 2013, an update from the guidelines listed Epzicom as the backbone when paired with the recommended Tivicay. Otherwise, DHHS guidelines recommend Truvada over Epzicom as the backbone for the NRTI component of an HIV drug combination for first-time therapy, with Epzicom listed as an alternative NRTI backbone. The DHHS guidelines state, "Pending additional data, [Epzicom] should be used with caution in individuals who have plasma HIV RNA [viral load] greater than 100,000 copies/mL, as well as in persons at higher risk for cardiovascular disease. However, Epzicom remains a good alternative dual-NRTI option for some treatment-naïve patients." The lamivudine portion of Epzicom is also used to treat the hepatitis B virus (HBV); see Epivir. See information about generics on the Epivir page.

See package insert for more complete information on potential side effects and interactions.

STANDARD DOSE

One tablet (600 mg abacavir / 300 mg lamivudine), once a day, with or without food, with no dietary restrictions.

Take a missed dose as soon as possible, unless it is within 12 hours of the time of your next dose. Do not double up on your next dose. Not indicated for patients younger than 18 years old, those with kidney function less than 50 mL/min, or those with liver problems, because dose adjustments are not possible with this fixed-dose combination.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$1,324.93 / month

DOCTOR'S COMMENTS

Abacavir/lamivudine (ABC/3TC) is a useful option for people who have some kidney or bone density problems and a relatively low viral load (less than 100,000 c/mL). And, of course, they must have a negative HLA-B*5701 screen, a marker for abacavir hypersensitivity. (See Ziagen for more information about abacavir hypersensitivity and cardiovascular controversies.)

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Epzicom, ViiV's fixed-dose combination tablet containing abacavir and lamivudine, has something of a checkered history. Though it has long been used as an alternative to Truvada—especially for those who experience, or are more likely to experience, kidney toxicity associated with the use of tenofovir—a few studies have connected abacavir to an increased risk of heart attacks (other studies failed to confirm this finding) and may be less effective than Truvada for those with pre-treatment viral loads above 100,000. However, paired with ViiV's integrase inhibitor Tivicay (dolutegravir), its efficacy and safety has been established. So much so that Epzicom and Tivicay are among the recommended combinations for first-time treatment takers in U.S. treatment guidelines, though most people will likely opt to take Triumeq, a single-tablet regimen containing dolutegravir, abacavir, and lamivudine. —TIM HORN

Emtriva

DHHS RECOMMENDED FOR FIRST-LINE USE (A COMPONENT OF TRUVADA)

emtricitabine, or FTC

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.

Take a 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. It is also available as an oral solution for children from birth and older and adults who are not able to swallow the capsules.

MANUFACTURER

Gilead Sciences, Inc.
gilead.com
(800) GILEAD-5
(445–3235)

AWP

$602.27 / month
for 200 mg capsules

POTENTIAL SIDE EFFECTS AND TOXICITY

Emtriva (emtricitabine) is very well tolerated. The most common side effects (rarely seen) may include headache, diarrhea, and nausea. Emtriva also treats hepatitis B virus (HBV), therefore, a person co-infected with HIV and HBV may experience a flare-up of HBV when stopping Emtriva (see "More information"). Skin discoloration (darkening of the skin on the palms and the soles) can occur, but is generally mild and otherwise harmless. See page 63 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, Hepsera, Stribild, Triumeq, Trizivir, or Truvada, since they contain emtricitabine or medication equivalent to it. No dose adjustment with hepatitis C medications Olysio (simeprevir), Sovaldi (sofosbuvir), or Harvoni (ledipasvir/sofosbuvir).

MORE INFORMATION

Emtriva (emtricitabine) is similar to Epivir (lamivudine); both treat HIV and HBV and have the same resistance profile, meaning that if your virus is resistant to one drug, it will be resistant to the other. However, emtricitabine remains in blood cells longer than lamivudine. Emtriva is active against chronic hepatitis B (though it is not FDA approved for this indication). You should never be treated only for HBV without treatment for HIV. If you have HIV and HBV and your HBV needs treatment, guidelines recommend treatment for both viruses. Emtriva and tenofovir (available as one tablet, Truvada) can be used as the NRTI backbone to treat HIV and HBV simultaneously. However, there are also other HBV treatments 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 provider. If your HIV develops resistance to Epivir or Emtriva, it does not mean that your HBV is also resistant to them. Truvada is approved for HIV treatment and for HIV prevention as PrEP (pre-exposure prophylaxis; go to positivelyaware.com/truvada-for-prep). Truvada is a recommended NRTI combination in the Department of Health and Human Services (DHHS) HIV treatment guidelines for the NRTI component of first-time therapy. Sometimes, drug resistance that the virus develops against emtricitabine makes the virus less able to reproduce, meaning that it multiplies at a slower rate. It also improves the antiviral activity of Retrovir (zidovudine) and Viread (tenofovir), and for that reason, some providers continue Emtriva treatment in combination with other NRTIs after resistance develops. Emtriva oral solution should be kept in the refrigerator. If kept at room temperature, the oral solution should be used within three months. Emtriva is part of the single-tablet regimens Atripla, Complera, and Stribild.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Although available as a single drug, FTC, like its older sister 3TC, is mostly used in combination with other nucleosides as a backbone regimen due to its relatively long half-life and low toxicity. Combinations containing FTC include Truvada, Atripla, Complera, Stribild, and at least five new combinations in development that substitute tenofovir alafenamide fumarate (TAF) for tenofovir disoproxil fumarate (TDF) (see discussion under Viread). FTC is slightly more potent than 3TC, its half-life is slightly longer, the potential for selection of resistance is thought to be slightly lower, and a few studies have documented a clinical benefit above that of 3TC. But mostly FTC and 3TC are viewed as interchangeable, and both select the M184V resistance mutation. FTC also has hepatitis B activity and discontinuation can cause a flare-up of hep B. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Approved in 2003, Emtriva initially raised eyebrows as a "me too" drug, in that its chemical structure, safety, and effectiveness is very similar to that of lamivudine, approved eight years earlier. The drug was developed by North Carolina-based Triangle Pharmaceuticals, which was bought by Gilead Sciences the year the drug was approved. This allowed Gilead to pair emtricitabine with its signature drug tenofovir—a potent and relatively safe nuke in its own right—and helped pave the way for the blockbuster combination tablets Truvada, Atripla, Complera, and Stribild. Does emtricitabine have an edge over lamivudine? Research suggests it's a bit more powerful and lasts longer in the blood. However, a 2012 World Health Organization analysis concluded that both drugs are largely equivalent, particularly when used with other potent ARVs. —TIM HORN

Epivir

DHHS RECOMMENDED
(A COMPONENT OF EPZICOM)

lamivudine, or 3TC

POTENTIAL SIDE EFFECTS AND TOXICITY

Epivir is 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. Flare-up of hepatitis B (HBV) in people co-infected with HBV has occurred when Epivir (lamivudine) was discontinued because it also treats HBV (see "More information"). See page 63 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, Hepsera, Stribild, Triumeq, Trizivir, or Truvada, since they contain Epivir or medication equivalent to it.

MORE INFORMATION

One benefit is that the drug resistance the virus develops against lamivudine (Epivir) makes the virus less able to reproduce. This mutation also slightly improves the antiviral activity of Retrovir (zidovudine or AZT) and Viread (tenofovir), and for that reason, some doctors will continue to use lamivudine after resistance develops. Lamivudine is also approved for the treatment of hepatitis B virus (HBV), under the brand name Epivir-HBV, which has a lower dose than traditional Epivir. Epivir-HBV is used only in people without HIV. It is important to note that if you have HIV and HBV, you will need to take full-dose Epivir along with a complete HIV regimen to treat both infections. 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 decrease the risk of HBV drug resistance, but there are other HBV treatments available that can be combined with HIV meds. Truvada, for example, contains tenofovir and a medication very similar to lamivudine, formulated in one pill. If you are co-infected with HIV and HBV and you stop taking lamivudine, 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 lamivudine, it doesn't mean that your HBV is also resistant to it. Lamivudine is also available in four combination products: Combivir (with zidovudine); Epzicom (with abacavir); Trizivir (with zidovudine and abacavir); and Triumeq (with dolutegravir and abacavir).

Lamivudine is available as a generic, which should be as effective and tolerable as the brand name drug Epivir. Some insurers may require patients to take regimens containing generics rather than brand name drugs, including simpler co-formulated products. For example, since both zidovudine (Retrovir) and lamivudine are available in generic form, a person might have to take these two generic pills instead of the fixed-dose combination tablet Combivir. The availability of generics might also limit choices of therapy. For example, newer brand name drugs and co-formulations, such as Stribild or Triumeq, might be restricted to patients who can't physically tolerate generic regimens.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Lamivudine (3TC), initially developed by Glaxo, Inc., is the oldest nucleoside in common use. It remains valuable not only for its innate potency and high tolerability, but also because the emergence of its signature M184V mutation actually increases sensitivity to other drugs such as tenofovir and zidovudine, and decreases viral fitness. Lamivudine also is active against hepatitis B and discontinuation can cause a flare-up of the disease. Some experts believe that 3TC should be continued in the setting of multidrug resistant virus, even in a regimen without other nukes, because of its beneficial effect on viral fitness, although the data are sparse. The availability of generic 3TC has opened the door for new combination regimens at decreased cost.

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Lamivudine, approved as Epivir in 1995, has withstood the test of time. It is the oldest antiretroviral in use today as a trusted component of HIV treatment regimens. Its potency, once-daily dosing, and favorable side effect profile are well established, though it is now most often used in the fixed-dose combination tablets Epzicom (with abacavir) and Triumeq (with abacavir and dolutegravir). Lamivudine's Achilles heel is its resistance profile; just one mutation (M184V) in HIV's reverse transcriptase gene drastically reduces the effectiveness of the drug. But all is not lost, as this mutation actually makes the virus more sensitive to two other nukes: tenofovir or zidovudine. Generic versions of lamivudine are now available in the U.S., though not yet as a component of fixed-dose combination tablets with other antiretrovirals. The good news is that companies developing new drugs are looking to incorporate generic lamivudine into fixed-dose combinations. Merck, for example, is developing a tablet containing its novel non-nucleoside doravirine with generic versions of lamivudine and tenofovir (which goes off patent in 2017). —TIM HORN

STANDARD DOSE

One 300 mg tablet once a day (or one 150 mg tablet twice daily), with or without food, with no dietary restrictions.

Take a 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 is lowered for people with kidney impairment. Dose for children 3 months to 16 years of age is 4 mg per 2.2 pounds (1 kg) twice daily to a maximum of 150 mg twice daily. A strawberry/banana-flavored liquid (10 mg/1 mL) is available. Generic is available.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$498.90 / month for 300 mg tablets; $429.19 for generic

Viread

DHHS RECOMMENDED
(A COMPONENT OF TRUVADA)

tenofovir disoproxil fumarate (tenofovir), or TDF

STANDARD DOSE

One 300 mg tablet once a day, with or without food, with no dietary restrictions.

Take a 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. Dosing frequency needs to be adjusted for people with decreased kidney function. One 150 mg, 200 mg, or 250 mg tablet once a day for children ages 2 or older weighing at least 37 pounds. Oral powder formulation available for children ages 2 and up. FDA approved for chronic HBV in patients 12 years and older.

MANUFACTURER

Gilead Sciences, Inc.
viread.com
(800) GILEAD-5
(445–3235)

AWP

$1,120.04 / month

POTENTIAL SIDE EFFECTS AND TOXICITY

Well tolerated, but may include headache, diarrhea, pain, depression, nausea, weakness, and gas. Decreases in bone mineral density (BMD) have been observed. BMD monitoring should be considered in people who have a history of bone fracture due to bone disease or are at risk for osteopenia or osteoporosis. Estimated creatinine clearance (eCrCl) should be assessed before initiating treatment. In addition to eCrCl, glucose and protein in the urine and serum phosphorus should be monitored more often in patients at risk for kidney problems. Less common side effects of Viread include kidney toxicities. Tell your provider about persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as these could be signs of kidney problems. 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 there should be minimal impact on individuals with liver disease. See page 63 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

Do not take Viread (TDF) with Atripla, Complera, Hepsera (adefovir), Stribild, or Truvada, since TDF is in these drugs or they contain a similar medication. Viread decreases the concentration levels of Reyataz, therefore, Reyataz 300 mg must be boosted with Norvir 100 mg or Tybost 150 mg (taken together with food) when used in combination with TDF. Kaletra, Prezista, and Reyataz increase Viread levels, but there is no dose adjustment needed when Viread is used with Kaletra or Prezista. Patients taking Kaletra, Prezista, or Reyataz with TDF should be monitored for Viread side effects (including kidney disorders) due to the higher TDF levels. Didanosine EC (Videx EC) levels are increased with Viread; therefore, use with caution and make sure your didanosine dose is adjusted accordingly and monitored for toxicities. Didanosine EC dose should be decreased to 250 mg daily for patients who weigh 132 pounds (60 kg) or more and 200 mg daily for those weighing less. Avoid taking Viread with drugs that negatively affect the kidneys, including Zovirax, Valtrex, and high-dose or multiple NSAIDS (non-steroidal anti-inflammatory drugs, such as Advil, Aleve, or Motrin). No dose adjustment with Olysio, Sovaldi, or Harvoni; however, if taking Harvoni and a boosted PI, Viread levels may be increased and risk vs. benefits should be discussed with your provider.

MORE INFORMATION

TDF with emtricitabine, as Truvada, is the recommended NRTI combination by DHHS HIV treatment guidelines for first-time therapy. The body clears most of tenofovir through the kidneys and the dosing interval needs to be adjusted for those with impaired kidney function. Two large observational studies found a greater risk of kidney toxicity with TDF than with other HIV meds. It is recommended that individuals with impaired kidney function be monitored closely. Remember that HIV itself has a negative effect on kidneys and bones. TDF is FDA approved for hepatitis B treatment, but should not be used alone by people with both hep B and HIV. If you have HIV and HBV coinfection, you should never be treated for HBV only since guidelines recommend treatment for both viruses to avoid losing HIV treatment options. If your HIV develops resistance to tenofovir or emtricitabine, it doesn't mean that your HBV is also resistant to them. If you have HIV and HBV and you stop TDF, you may experience symptoms of acute HBV. You should be closely monitored by your provider. The FDA recommends calcium and vitamin D supplementation for all patients who need it. See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

What we call "tenofovir" is actually a pro-drug of tenofovir called tenofovir disoproxil fumarate (TDF). This is important because a new pro-drug, tenofovir alafenamide fumarate (TAF), is in development and will soon replace TDF. TDF is usually co-formulated with FTC as the most commonly used backbone of the last decade, Truvada. TDF is a component of Truvada, Atripla, Complera, and Stribild. Short-term toxicities of tenofovir are few and the drug is potent, well tolerated, and has a long half-life. Although uncommon in people with normal kidney function, tenofovir can cause renal tubular disease that is occasionally serious. This toxicity may be more common when taken in combination with protease inhibitors (and perhaps when combined with cobicistat, according to the COBI package insert). Kidney function should be assessed before and during tenofovir use. Bone density typically declines over the first year of tenofovir use but then tends to plateau, and fractures are uncommon, although secondary hyperparathyroidism and osteomalacia have been sporadically reported. The end of TDF's patent will be celebrated by the advent of TAF, which promises lower rates of renal and bone disease. TAF will quickly replace TDF in combination with every possible drug. Both TDF and TAF are also active against hepatitis B. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Though Viread tablets aren't frequently prescribed, the active ingredient (tenofovir disoproxil fumarate) is commonplace in HIV treatment—it's a key component of Atripla, Stribild, Complera, and Truvada. It's very effective and well tolerated, aside from an increased risk of kidney toxicity and bone mineral decreases. The good news: Gilead is developing what is expected to be a more kidney- and bone-friendly formulation of tenofovir for use in co-formulations and single-tablet regimens. The new version, tenofovir alafenamide fumarate (TAF), may also be at least somewhat active against tenofovir-resistant HIV. The curious news: Despite the fact that Gilead has known about TAF since at least 2001, its likely approval comes about just as the original version of tenofovir enters the twilight of its patent protection. Coincidentally, I'm sure; just as we begin thinking about the cost-saving potential of generic tenofovir, a new and improved version comes along to take its place. —TIM HORN

Ziagen

DHHS RECOMMENDED
(A COMPONENT OF EPZICOM)

abacavir sulfate (abacavir), or ABC

POTENTIAL SIDE EFFECTS AND TOXICITY

Approximately 5–8% of people who took abacavir experienced hypersensitivity reaction (HSR), an allergic-like reaction. To avoid HSR, a blood test for HLA-B*5701 (a genetic marker) can identify patients at risk for this reaction. This test is covered by most insurance and also by LabCorp/ViiV (see co-pay chart, page 63). If the HLA-B*5701 test is positive, you would likely have HSR if you started taking abacavir. An allergy to it should be entered in your medical record. If you start abacavir without having the HLA-B*5701 test done, you should be monitored closely the first six weeks or so (HSR usually occurs within that time). Symptoms of HSR usually include some combination of the following: fever, skin rash, malaise (general ill feeling), severe nausea, headache, muscle ache, chills, diarrhea, vomiting, abdominal pain, respiratory symptoms (cough, difficulty breathing, sore throat), and/or joint pain. 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, but 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. Do not use a skin patch test to confirm HSR. Symptoms resolve quickly (24–48 hours) after permanent discontinuation. If you develop HSR, abacavir should be stopped and you can never take abacavir or any product containing abacavir (Epzicom, Trizivir, or Triumeq) again (called re-challenging). Re-challenging can cause a rare life-threatening reaction. This does not apply to missed doses when there is no HSR, but watch for symptoms if you've stopped the drug for a few days.

Check with your doctor if you have any side effects after taking this medicine—don't just stop! 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 seem to suggest that abacavir may increase the risk of cardiovascular events, including heart attacks, in people with risk factors (such as older age, smoking, diabetes, high blood pressure, high cholesterol, and drug use). Multiple studies have looked at the association between abacavir use and the risk for heart attack, but to date no consensus has been reached on the association of abacavir with cardiac 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 of course up to you and your provider.

POTENTIAL DRUG INTERACTIONS

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

MORE INFORMATION

It is recommended that people with symptoms of acute respiratory disease consider HSR even if another diagnosis such as pneumonia, bronchitis, or flu is possible. FDA researchers reported finding a mechanism for autoimmune drug reactions, including abacavir HSR, and hope it helps improve drug safety in the future. Abacavir is part of Epzicom, Trizivir, and Triumeq; see those pages.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Abacavir has stayed the course as a useful nucleoside since 1998, in spite of the early discovery that it could cause a life-threatening hypersensitivity reaction (HSR), particularly in persons of Western European descent. Rechallenge (starting up again after stopping) with the drug after the onset of HSR caused several deaths and brought the syndrome to light. The manufacturer reacted swiftly to define the symptoms and epidemiology of abacavir HSR and to educate prescribers about early recognition and management. This allowed early detection of HSR and higher confidence that the drug could be safely administered by educated providers. The discovery that the genetic marker HLA B*5701 was highly predictive of HSR led to this test being recommended prior to abacavir initiation. Except when used with Tivicay (dolutegravir), abacavir is not recommended for initial therapy when baseline HIV RNA is above 100,000 copies/mL. The D:A:D study (among others) raised concerns about the association of abacavir with cardiovascular events, but data have been mixed, including an FDA meta-analysis (and others) that showed no association. Abacavir also has limited activity against hepatitis B and has been known to cause hep B flares in persons with HBV who stop abacavir. Abacavir is now generic in the U.S., although not yet as a combination with 3TC. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Ziagen's approval in 1998 was met with high hopes, given its once-daily dosing, potency, and activity against HIV resistant to AZT or lamivudine (but not both). As with many other drugs in the nuke class, however, problems emerged. For starters, abacavir is associated with hypersensitivity reactions in approximately 5% of people living with HIV, which necessitated the development of a blood test to screen for the genetic variation (HLA-B*5701) that facilitates this potentially serious adverse effect. Though it appears effective when combined with sister ViiV Healthcare drugs dolutegravir and lamivudine, there are concerns that other abacavir-inclusive regimens work less well for those starting treatment with high viral loads (greater than 100,000) compared with tenofovir-inclusive regimens. And while there are also lingering concerns in the wake of study results which suggested that abacavir can increase the risk of heart attacks, not all data reported to date confirm this link. The take-home message: abacavir is still a decent option to choose from, though there's certainly no faulting health care providers choosing to limit its use to those with kidney problems (and potentially unsuitable candidates for tenofovir-inclusive treatment), a low risk of cardiovascular disease, and treatment-experienced patients. —TIM HORN

STANDARD DOSE

Adults: two 300 mg tablets once a day (or one 300 mg tablet twice a day), with or without food, with no dietary restrictions. **Children's dose** varies with age and weight. Scored tablets and strawberry-banana flavored liquid available (may be used for children as young as 3 months).

Dose adjustment is not needed for people with kidney impairment. Dose adjustment is needed for people with mild liver disease. Abacavir should not be used for people with moderate or severe liver disease.

Take a 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.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$670.37 for 60 tablets;
$602.66 for generic;
$176.23 for 240 mL solution (20 mg/mL)

Combivir

NOT DHHS RECOMMENDED FOR FIRST-LINE USE; OTHERWISE USED IN ONLY SPECIAL SITUATIONS

lamivudine / zidovudine, or 3TC / AZT

STANDARD DOSE

One tablet (150 mg lamivudine / 300 mg zidovudine) twice a day (12 hours apart), with or without food, with no dietary restrictions.

Take a 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. Should not be used for children weighing less than 66 pounds, nor for people with kidney function less than 50 mL/min or liver disease (because the dose cannot be adjusted appropriately with this fixed-dose combination). Generic lamivudine and zidovudine are available.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$1,081.70 / month;
$931.61 for generic

POTENTIAL SIDE EFFECTS AND TOXICITY

See the individual drugs contained in Combivir, Epivir (lamivudine) and Retrovir (zidovudine or AZT), for more details. Side effects include nausea, fatigue, and myopathy (muscle damage). Taking with food may help decrease nausea. Flare-up of hepatitis B upon stopping may occur (due to the withdrawal of lamivudine; see Epivir). The Retrovir 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. Retrovir 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 your regimen is changed. See page 63 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

Also see the individual drugs contained in Combivir, Epivir (lamivudine) and Retrovir (zidovudine or AZT), for more information. Do not take Combivir with Atripla, Complera, Emtriva, Epivir, Epivir-HBV, Epzicom, Hepsera, Retrovir, Stribild, Triumeq, Trizivir, or Truvada, since all or part of these medications are already in Combivir or contain medications equivalent to it. Zerit (stavudine) cannot be taken with Combivir, as it can limit effectiveness of the Retrovir part of Combivir. Taking with ribavirin is not recommended.

MORE INFORMATION

One head-to-head study against Truvada (emtricitabine and tenofovir) found greater toxicity with Combivir, due to anemia (see Retrovir). Under HIV treatment guidelines (DHHS), Combivir is not a recommended or alternate drug for adult men, and women who aren't pregnant. Combivir continues to be recommended for pregnant women who are taking therapy for the first time. Anyone taking zidovudine (Retrovir) might consider taking Combivir instead, even if they are already resistant to the Epivir (lamivudine) component. Resistance to Epivir makes HIV less fit to reproduce. It also slightly improves the antiviral activity of zidovudine and Viread (tenofovir), and for that reason, some doctors keep lamivudine onboard in combination with those drugs after resistance develops.

The drugs in Combivir, zidovudine and lamivudine, are available as generics, which should be as effective and tolerable as their brand name medications. Some insurers may require patients to take regimens containing generics rather than brand-name drugs, including simpler co-formulated products. For example, zidovudine and lamivudine might have to be taken as two generic pills instead of fixed-dose Combivir. The availability of generics might also limit choices of therapy. For example, newer brand-name drugs and co-formulations, such as Stribild or Triumeq, might be restricted to patients who can't physically tolerate generic regimens.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Combivir ushered in the era of dosing simplification as the first co-formulated antiretroviral, and now, co-formulated zidovudine/lamivudine (AZT/3TC) is the first combination antiretroviral to become generic in the US. Unfortunately, this combination is now obsolete and is not recommended due to the toxicity and short half-life of AZT. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

During the early years of combination antiretroviral therapy, multiple pills taken at least twice a day were the norm and a real challenge for many. To help alleviate this pill burden, a fixed-dose combination tablet containing two drugs was developed by GlaxoSmithKline and approved by the FDA in 1997—the first of its kind in the HIV treatment toolbox. Despite the fact that it contained toxicity-inducing zidovudine and had to be taken twice a day, Combivir was widely prescribed for use in combination with a third drug and was utilized in numerous clinical trials as the nucleoside reverse transcriptase inhibitor duo to beat. Fortunately, kinder and gentler fixed-dose combinations ultimately prevailed. —TIM HORN

Retrovir

NOT DHHS RECOMMENDED FOR FIRST-LINE USE; OTHERWISE USED ONLY IN SPECIAL SITUATIONS

zidovudine, ZDV, or AZT

POTENTIAL SIDE EFFECTS AND TOXICITY

May include headache, fever and chills (more common in children), muscle pain, fatigue, nausea, and fingernail discoloration. Zidovudine has been associated with alteration of various blood cells through bone marrow suppression, resulting in anemia (low red blood cell counts), which can cause shortness of breath and tiredness; and/or neutropenia (low white blood cell counts), which can increase risk for getting 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. Your provider may check your blood in the first 4–6 weeks after you start zidovudine. Zidovudine is 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 your HIV regimen is changed. See page 63 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

Do not take with Combivir or Trizivir, since zidovudine is already in these medications. Zidovudine and stavudine (Zerit) should never be used together. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. Clarithromycin and rifampin may decrease zidovudine blood levels. Do not take with the cancer treatment doxorubicin. Probenecid, phenytoin, and valproic acid may increase blood levels and decrease clearance of zidovudine, but no dosing adjustments are recommended. Bone marrow suppression should be monitored with use of ganciclovir, Valcyte, amphotericin B, pentamidine, dapsone, flucytosine, sulfadiazine, interferon-alpha, and ribavirin. Do not use ribavirin and zidovudine together, as ribavirin may decrease the effectiveness of zidovudine and increase the risk of lactic acidosis and anemia. Measure hemoglobin once a week after starting other medications that can cause anemia until hemoglobin has stabilized. Notify your health care provider if you experience 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—no dose adjustments are recommended, but 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. Thanks to extensive data, zidovudine is also a recommended drug for pregnant women who are taking therapy for the first time, according to Department of Health and Human Services (DHHS) HIV treatment guidelines. Typically, zidovudine use in non-pregnant patients is rare and is mostly limited to people who have been stable on it for a long time or in salvage situations (where they have gone through other regimens and are running out of options). You can take erythropoietin for some anemias, but it's an expensive weekly injectable. Most doctors would prefer switching out the zidovudine for another drug. Taking with food may decrease upset stomach. Zidovudine crosses the blood-brain barrier to a useful degree, which may be beneficial for those at risk for neurological damage (such as dementia) from HIV.

Zidovudine is available as a generic, which should be as effective and tolerable as the brand name drug Retrovir. Some insurers may require patients to take regimens containing generics rather than brand name drugs, including simpler co-formulated products. For example, since both zidovudine and lamivudine (Epivir) are available in generic form, a person might have to take these two generic pills instead of the fixed-dose combination tablet Combivir. The availability of generics might also limit choices of therapy. For example, newer brand name drugs and co-formulations, such as Stribild or Triumeq, might be restricted to patients who can't physically tolerate generic regimens.

See package insert for more complete information on potential side effects and interactions.

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.

Take a 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. Clear, strawberry-flavored liquid available for infants four weeks of age and up; dose is weight-based. 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.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$582.94 / month for 300 mg tablets; $360.97 for generic. $77.71 for 240 mL of 10 mg/mL syrup; $56.42 for generic

DOCTOR'S COMMENTS

This is the drug that started it all. The team of Nobel prize winner Gertrude Elion, PhD, at Burroughs Wellcome collaborated with the National Cancer Institute to test the drug against HIV. The first randomized, placebo controlled, clinical endpoint trial of a potential HIV therapy ended abruptly when many more people died in the placebo arm than in the AZT arm. Approval by the FDA followed in record time and AZT was the first ray of hope for people with HIV. It should be noted that AZT also was the first drug to have an HIV prevention indication (mother-to-child transmission). Toxicities of AZT include nausea, headaches, low red and white blood cell counts (sometimes severe), lipoatrophy, myopathy, cardiomyopathy, and occasionally lactic acidosis. DHHS and IAS-USA guidelines panels no longer recommend AZT due to its toxicity and the availability of better drugs. Thanks, AZT, you played a very important role—now it is time to take a rest. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

We had to start somewhere. After being pulled from dusty shelves where it had languished since the mid-1960s as a failed therapy for cancer, Retrovir—universally known as AZT—was put into trials for HIV and ultimately approved as the first antiretroviral in 1987. Whatever benefit it offered, tolerability was a serious issue for many, particularly in its early years when the dose was double what it is now. At the same time, our modern-day treatment and prevention approaches are all built on AZT-based science: prevention of mother-to-child HIV transmission and, ultimately, pre-exposure prophylaxis (PrEP); post-exposure prophylaxis (PEP); the need for combination therapy to prevent the emergence of drug-resistant virus; and the potential value of using brain-penetrating drugs. —TIM HORN

Selzentry ▼

NOT DHHS RECOMMENDED FOR FIRST-LINE USE

maraviroc, or MVC

STANDARD DOSE

The recommended dose varies, depending on other medications being taken, but will be either 150, 300, or 600 mg twice daily (available in 150 mg and 300 mg tablets). Can be taken with or without food, with no dietary restrictions. Your provider or pharmacist can determine which medications will affect Selzentry levels and recommend the appropriate dose for you.

Take a missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose. Before you start Selzentry, you will need a specific blood test (a tropism assay: Trofile, Trofile DNA, or HIV-1 Coreceptor Tropism with Reflex to UDS) to determine if this medication will work for you. Results of a phenotypic tropism test (Trofile or Trofile DNA) may take up to a month. Genotypic tests are also available and may provide a faster and less expensive alternative. Selzentry only works for those people with CCR5-tropic virus.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AWP

$1,361.21 / month for 150 mg or 300 mg tablets

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects include cough, fever, cold, rash, muscle and joint pain, stomach pain, dizziness, and trouble sleeping. Other potential side effects may include allergic reactions, liver toxicity, and heart problems in those with a history of heart disease. Rarely, Selzentry can cause dizziness or fainting when standing up due to low blood pressure. In March 2014, the FDA updated the Selzentry label stating, "Caution should be used when administering Selzentry in patients with a history of or risk factors for postural hypotension, cardiovascular comorbidities, or on concomitant medication known to lower blood pressure. Patients with cardiovascular comorbidities could be at increased risk of cardiovascular adverse events triggered by postural hypotension." Stop taking Selzentry and contact your provider right away if you develop a rash, yellowing of your eyes or skin, dark urine, vomiting, or upper stomach pain. Selzentry should not be used in people with severe or end-stage kidney disease who are taking medications that can affect the levels of Selzentry (check with your provider). Selzentry affects immune system cells and could possibly increase the risk of infections and cancer, although this has not been observed in studies with up to five years of follow-up, and some data indicates it may be beneficial in cancer or for preventing metastasis (the spread of cancer to other parts of the body). See page 67 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

See package insert for the most complete list. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not. Dose adjustments with other medications and anti-HIV drugs include 150 mg twice daily if taken with medications that increase the levels of Selzentry such as protease inhibitors (except for Aptivus), Rescriptor, clarithromycin, and itraconazole; 300 mg twice daily if taken with Aptivus, Viramune, Isentress, Fuzeon, and all of the NRTIs and medications that do not affect the levels of Selzentry; and 600 mg twice daily if taken with medications that decrease the levels of Selzentry such as Sustiva, Intelence, rifampin, and some anti-convulsants such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin). Dose change may be required if kidney function is less than 30 mL/min. Likely dose with rifapentine is 600 mg twice daily, but use with caution. Not recommended with St. John's wort. There are data supporting Vitekta 150 mg plus Norvir 100 mg and co-administering Selzentry 150 mg twice daily. U.S. HIV treatment guidelines do not recommend concurrent use of Stribild and Selzentry, because of limited or no data. If Tybost (found in Stribild) is used with Selzentry, as with Norvir, the Selzentry dose should be 150 mg twice daily. The pharmacokinetics (PK) of maraviroc has not been evaluated with dolutegravir. However, based on the PK properties of both drugs, no dosage adjustment would be anticipated and the corresponding maraviroc dose would be 300 mg twice daily. Selzentry may be co-administered with newer hepatitis C medications including Sovaldi, Olysio, and Harvoni at a dose of 300 mg twice daily; however, ledipasvir (in Harvoni) may have potential to increase Selzentry levels.

MORE INFORMATION

Selzentry is now generally recommended only when anti-HIV medications from other classes cannot be used. Complex dosing, the need for a tropism test, and competition from newer drugs have dimmed some of the initial enthusiasm for this drug. Viral tropism refers to the types of HIV that a person can have: CCR5 (R5), CXCR4 (X4), or dual-mixed tropic (R5 and X4). Selzentry blocks CCR5, a receptor on the outside of a cell, and shuts down this point of entry for the virus. Most people are infected with R5 virus, and then over time, X4 and mixed viruses may accumulate. Blocking R5 with Selzentry does not cause a shift to X4 or negatively affect disease progression or CD4 count in people whose virus is dual-mixed. ViiV may cover the payment for the Trofile test if someone is ADAP-eligible and insurance doesn't cover the test.

See package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

Selzentry (maraviroc) blocks a cellular receptor called CCR5 that is needed by HIV to enter the cell. CCR5 inhibitors do not block viruses that use the CXCR4 receptor for cell entry. Its modest potency, twice-daily dosing, and requirement for expensive tropism testing have led to low usage. Maraviroc recently failed the test of once-daily administration when given with darunavir/ritonavir in a nuke-sparing regimen in the MODERN trial. It seems that maraviroc should be useful in the setting of resistance, but finding a niche somewhere after first-line therapy and before the emergence of X4 virus is challenging. A pre-exposure prophylaxis trial using maraviroc is in progress, as most transmitted viruses use CCR5.

—MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

The 1990s discovery of CCR5 as one of two co-receptors used by HIV to gain CD4 cell entry proved interesting and enlightening. Unfortunately, it hasn't proved to be a boon on the therapeutic front (though there's some exciting cure work underway). Selzentry helps block the HIV-CCR5 interaction. However, maraviroc-based regimens don't work as well as others in first-time treatment takers. And while it can be a valuable option for treatment-experienced patients, many of these folks have HIV that has adapted over time to target CXCR4, another co-receptor on CD4 cells, rendering the benefits of maraviroc short-lived. Plus, costly and time-consuming laboratory testing is needed to determine if maraviroc will work (though there are assistance programs to help pay for the test). Selzentry, therefore, remains a niche—but potentially important—antiretroviral. —TIM HORN

Fuzeon

ADVANCED MULTIDRUG RESISTANCE ONLY

enfuvirtide, T-20, or ENF

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; however, it may be worthwhile to massage the injection site after the dose has been given to help prevent these nodules from forming. 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 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 page 67 for potential drug class side effects.

POTENTIAL DRUG INTERACTIONS

To date, no interactions that are clinically significant have been found. However, if Fuzeon is used with Aptivus (tipranavir) and Norvir, there may be increased levels of Aptivus and Norvir which could lead to increased rates of nausea, vomiting, and diarrhea; monitoring of liver function tests may be necessary. Aptivus is rarely used, thus this is an unlikely combination.

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, or 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 anti-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 package insert for more complete information on potential side effects and interactions.

DOCTOR'S COMMENTS

While potent, enfuvirtide (T-20) is a drug that is reserved for use when there are not enough options available to make an effective regimen without it. It is given twice daily by subcutaneous injection and it typically causes tender red nodules at the injection site, so injection rotation is a must. Resistance easily develops to enfuvirtide if a strong background regimen is not available, thus limiting its use with multidrug resistant virus. It is expensive and usually kept in the back pocket to be used only as a last alternative while waiting for new therapies to emerge from the pipeline. —MELANIE THOMPSON, MD

ACTIVIST'S COMMENTS

Fuzeon became available in 2003 when we needed it most. For the many people at the end of their treatment rope, Fuzeon's unique mechanism of action meant that it could be used against HIV resistant to drugs in other classes. However, because it had to be injected twice daily and is very expensive, compounded by the eventual arrival of oral drugs with activity against drug-resistant HIV, Fuzeon was remanded to the sidelines. It's still available, but generally reserved for those with hard-to-treat HIV. —TIM HORN

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. Take with or without food, with no dietary restrictions.

Take a 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. Each injection should be given in a different location (or site) from the previous one and at a site where there is no current injection site reaction, scar tissue, mole/birthmark, bruise, nodule, and avoid the belly button. It is also approved for children 6 years or older. The dose for children is based on weight.

MANUFACTURER

Genentech
genentech.com,
fuzeon.com
(877) 4–FUZEON
(438–9366)

AWP

$3,759.43 / month
for 90 mg kit

NON-HIV: FOR HIV-RELATED EXCESS BELLY FAT

Egrifta

tesamorelin for injection

STANDARD DOSE
2 mg via subcutaneous (under the skin) injection once daily in the abdomen, rotating injection sites and avoiding scar tissue, bruises, and the navel (see step-by-step video at egrifta.com).

MANUFACTURER
Theratechnologies Inc.
egrifta.com
(844) EGRIFTA
(347-4382)

AWP
$3,531.73 for 30 days

Each dose necessitates mixing 1-mg vials (requiring refrigeration) of Egrifta with 2.2 mL of sterile water for injection (vial stored at room temperature). Do not use an unopened vial if the solution is colored, cloudy, or contains visible particles. Once mixed, the vial should be rolled gently, not shaken, between the hands for 30 seconds to ensure reconstitution into a clear, colorless solution and administered right away. If not used immediately, the reconstituted Egrifta should be discarded.

A potential complication of HIV, antiretroviral therapy, or both may be changes in the distribution of adipose tissue (fat), otherwise known as lipodystrophy; reports of prevalence in the U.S. vary widely, anywhere from 2–60% of all HIV-positive patients. Abdominal lipohypertrophy (a form of lipodystrophy) is the accumulation of excess visceral adipose tissue (VAT)—deep belly fat surrounding the liver, stomach, and other abdominal organs. Egrifta is the first, and only, FDA approved medication to reduce VAT. Unlike growth hormone products, Egrifta is an analogue of human growth hormone-releasing factor (GRF), which stimulates the pituitary gland to produce and secrete the body's own growth hormone. The effect of this agent appears to be greatest within the first three to six months of initiation.

Two Phase 3 clinical trials found that Egrifta significantly lowered VAT (up to 15–20% on average) at both 26 and 52 weeks. Egrifta may also lower triglycerides (a type of cholesterol). Adverse events were more commonly seen in the groups given Egrifta than in those receiving placebos. It is important to note that excess VAT returns once Egrifta is discontinued. Egrifta should not be administered to patients who have pituitary gland tumor(s), pituitary gland surgery, or other pituitary gland problems; active cancer; hypersensitivity to either tesamorelin and/or mannitol; or who are pregnant. Egrifta should be used with caution in patients who have a history of non-malignant neoplasms (abnormal growth of tissue such as a tumor), a history of treated and stable malignancies, elevated insulin-like growth factor 1 (IGF-1), fluid retention, diabetes, or pre-diabetes.

The most common side effects include joint pain, injection site reactions (including redness, pain, and itching), pain in legs and arms, swelling in legs, muscle soreness, tingling, numbness and prickling, nausea, vomiting, rash, and itchiness. Other warnings include hypersensitivity reactions and acute critical illness. Patients receiving Egrifta had a higher risk of developing diabetes compared to those on placebo. Despite initial thoughts that Egrifta may have significant drug-drug interactions with medications that use CYP450 (an enzyme in the liver) for metabolism, a study in healthy volunteers proved otherwise. However, it has not been studied with medications that use other enzymes in the liver; therefore, response to medications that are metabolized through the liver should be monitored for response and adverse reactions. Long-term safety data is unknown. There have been previous reports of a theoretical increased risk of cancer with elevated IGF-1 levels. Other long-term concerns include potential development of retinopathy in patients with diabetes.

NON-HIV: FOR HIV/AIDS TREATMENT-ASSOCIATED DIARRHEA

Fulyzaq

crofelemer

STANDARD DOSE
One 125 mg delayed-release tablet taken twice a day, with or without food. The tablet should be swallowed whole and not crushed or chewed.

MANUFACTURER
Salix Pharmaceuticals
fulyzaq.com
(919) 862-1000

AWP
$648.00 / month

Fulyzaq (crofelemer) is the first, and only, anti-diarrheal indicated for the symptomatic relief of non-infectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy. Currently, what is typically recommended is for the patient to take medication(s) with food and/or use Imodium (loperamide) for symptomatic diarrhea.

Fulyzaq approval was based on a randomized, placebo-controlled study of 374 HIV-positive patients who had about 3 watery stools per day and on anti-HIV medicines. At study entry, patients experienced an average of approximately 20 watery stools per week. To be considered a responder, watery stools had to be decreased to two or fewer per week, which occurred in 18% of Fulyzaq-treated patients vs. 8% of placebo-treated patients at 4 weeks. In an open label extension phase of the study, about 50% of the patients reported two or fewer watery stools per week at 3 months, an effect which was maintained until study end at 6 months. These findings suggest that it may take some time to achieve the optimal effect. Fulyzaq appears to work best in those who have tried and failed non-prescription anti-diarrheals, have had diarrhea for more than two years, have more than two watery bowel movements per day, and whose bowel movements tend to be "pourable" (not clumpy). Fulyzaq was less effective in African Americans in this clinical study.

An infectious cause should be ruled out prior to initiating Fulyzaq. In the placebo-controlled part of the study, side effects were comparable to placebo. The most commonly reported side effect was upper respiratory tract infection (Fulyzaq, 3.8% of patients vs. placebo, 2.9%). Other reported side effects included bronchitis, cough, flatulence (gas) and increased bilirubin. Based on animal data, Fulyzaq may cause fetal harm. Fulyzaq has not been studied in patients younger than 18 years old. Its usefulness in pediatrics is unknown and use in this population cannot be recommended at this time.

There were no significant drug interactions in participants in the clinical study. There was little or no change in CD4 counts and viral load throughout the study.

In a review article to be published in 2015 by Patrick Clay et al, it appears Fulyzaq's use is considered last line after unsuccessful attempts with diet modifications and/or over-the-counter anti-diarrheals (such as Immodium). It may require some time to observe optimal effects.

An out-of-pocket expense savings program is offered at fulyzaq.com/patient-assistance-copay-program.

Serostim

somatropin (rDNA origin) for injection

Serostim is recombinant (made in a lab) human growth hormone for treatment of HIV wasting (unintentional loss of weight) or cachexia (general ill health resulting from emaciation), decreased lean body mass (muscle), and loss of physical endurance. Loss of muscle can be difficult to notice or diagnose. Serostim has been shown to increase HIV replication in the test tube; therefore, patients must be taking anti-HIV therapy, known as HAART (or cART), in order to be prescribed Serostim.

Most common potential side effects include swelling (especially of the hands and feet), muscle pain, joint pain, numbness, and pain in extremities (the ends of limbs, especially the hands and feet), carpal tunnel syndrome (requiring discontinuation if unresolved by decreasing the number of doses), injection site reactions (pain, numbness, redness, or swelling), increased blood fat (triglycerides) and blood sugar, including new or worsening cases of diabetes (sometimes reversible upon stopping Serostim), nausea, and fatigue. More rarely, potential side effects include pancreatitis (watch for persistent severe abdominal pain) and intracranial hypertension (rise in pressure in the skull, with visual changes, headache, nausea, or vomiting). Serostim should be avoided in patients who are acutely ill, have an active cancer, or have diabetic retinopathy (damage to one or both retinas). Since HIV-positive patients may have an increased risk of developing new tumors, including from birth marks or other moles, risks versus benefits of starting Serostim should always be discussed with your provider. Additionally, patients with known malignancies should be carefully monitored, because Serostim may cause increased growth or malignant changes.

Rotate injection sites to avoid injection site reactions. Do not use while experiencing cancer or cancer treatment; serious injuries; severe breathing problems; certain eye diseases related to diabetes; or after critical illness due to complications of abdominal or open heart surgery.

Based on how the drug is broken down in your body, there are some potential drug-drug interactions, though no formal drug studies have been conducted. These theoretically potential interactions include patients on glucocorticoid (such as prednisone) therapy and may require an increased prednisone dose. Others may include medications that are metabolized through the CYP450 enzyme in your liver (like some antiretrovirals, cholesterol medications, or anticonvulsants); or medications like oral estrogen, insulin, or oral diabetes drugs. Be sure to tell your provider, pharmacist, and/or other providers about all of the medications you are taking, including herbs, supplements, and over-the-counter (OTC) products, prescribed or not.

If someone is having difficulty paying for Serostim, there are several programs that may be able to assist the patient with acquiring it. These programs include EMD Serono Secured Distribution Program, the AXIS Center, the Serostim Patient Assistance Program (PAP), or a co-pay assistance program. To find out more about these programs, call (877) 714-AXIS (2947).

Go to serostim.com for additional information. Also go to powerusa.org (Program for Wellness Restoration), a community-based resource for information about growth hormone and other HIV-related therapies.

STANDARD DOSE

0.1 mg/kg via subcutaneous (under the skin) injection, which may be in the thigh, upper arm, abdomen, or buttock once daily at bedtime (up to 6 mg), rotating injection sites and avoiding scar tissue, bruises, and the navel. It is available in 4 mg, 5 mg, and 6 mg vials. The multi-use 4 mg vial is reconstituted with bacteriostatic (containing a biological or chemical agent that stops bacteria from reproducing) water for injection and may be refrigerated for up to 14 days after reconstitution. The single-use 5 mg and 6 mg vials are reconstituted with sterile water for injection and must be used immediately; after administering the dose, any unused portion should be discarded. Some loss of the dose can be expected (approximately 10%). Inject the water into the vial aiming for the glass wall. The vial should be swirled gently in a circular motion until solution is completely dissolved; it must be clear and colorless. Do not shake. Do not inject if solution is cloudy or contains particles.

MANUFACTURER

EMD Serono, Inc.
serostim.com
(877) 714-AXIS (2947)

AWP

$2,268.67 / week for 4 mg;
$2,835.84 / week for 5 mg;
$3,403.01 / week for 6 mg

DRUG SIDE EFFECTS

THE MOST COMMON SIDE EFFECTS FOR ANTIRETROVIRAL THERAPY FOR EACH DRUG AND BY DRUG CLASS

REMEMBER THAT some side effects are more common than others, and each person may react differently to the same medicine. For this reason, a drug regimen can't be based solely on possible side effects. While taking medications, discuss any physical changes or new symptoms with your doctor and pharmacist. Some side effects can be managed or controlled, while others require intervention or medication changes. Although not always stated here, some side effects may be rare. See drug page or package insert for more information.

ART

There are both benefits and potential side effects associated with HIV medications, known as antiretroviral therapy (ART). Benefits of ART include restoration of the immune system and reduction in risk of HIV transmission, especially if the viral load is undetectable (less than 50 copies/mL). Safer sex methods should be practiced, and additional information regarding HIV transmission can be found at aidsinfo.nih.gov. One potential side effect of ART is known as immune reconstitution inflammatory syndrome (IRIS), which may occur as the immune system regains strength following initiation of therapy. Symptoms of illnesses such as shingles and tuberculosis should be reported to a health care provider immediately.

NRTIs NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

POTENTIAL DRUG CLASS SIDE EFFECTS: Rare but potentially serious side effects with all NRTIs are enlarged, fatty liver 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, and difficulty breathing. These conditions are seen even less with newer and now commonly used NRTIs (specifically Epzicom and Truvada).

Combivir

lamivudine / zidovudine—fixed-dose combination

See Epivir and Retrovir.

Emtriva

emtricitabine, or FTC

A very tolerable drug, but side effects may include headache, diarrhea, and nausea. A flare-up of existing hepatitis B may occur when stopping Emtriva. Darkening of the skin on the palms and the soles of the feet has also been reported.

Epivir

lamivudine, or 3TC

A very tolerable drug, but side effects may include headache, nausea, vomiting, diarrhea, fever, fatigue, hair loss, insomnia, malaise (general ill feeling), nasal symptoms, and cough. A flare-up of existing hepatitis B may occur when stopping Epivir.

Epzicom

abacavir / lamivudine—fixed-dose combination

See Ziagen and Epivir.

Retrovir

zidovudine, AZT, or ZDV

Headaches, fever, chills, muscle soreness and/or damage, fatigue, nausea, lipoatrophy (fat loss in the arms, legs, face, and/or buttocks—sometimes called "AZT butt"), blue/black nail discoloration, anemia (low red blood cell count), and neutropenia (low white blood cell count).

Trizivir

abacavir / lamivudine / zidovudine—fixed-dose combination

See Ziagen, Epivir, and Retrovir.

Truvada

emtricitabine / tenofovir

See Emtriva and Viread.

Abdominal distension/pain.

Videx EC

didanosine, or ddI

Peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet), upset stomach, diarrhea, vomiting, rash, pruritis (itchiness), and headache. Pancreatitis and lactic acidosis. Eye changes and optic neuritis. Increased uric acid levels, alkaline phosphatase, and amylase levels. Body fat redistribution, insulin resistance, and diabetes. Non-cirrhotic portal hypertension.

Viread

tenofovir, or TDF

A very tolerable drug, but side effects may include headache, diarrhea, pain, depression, nausea, weakness, and gas. Kidney toxicities and decreased bone mineral density. A flare-up of existing hepatitis B may occur when stopping tenofovir.

Zerit

stavudine, or d4T

Headache, diarrhea, nausea, vomiting, rash, peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet), pancreatitis, lipoatrophy (fat loss in the arms, legs, face, and/or buttocks), mitochondrial toxicities (a variety of symptoms caused by cell damage), and elevated cholesterol levels.

Ziagen

abacavir, or ABC

Hypersensitivity reaction, nausea, vomiting, diarrhea, fatigue, headache, fever, rash, trouble sleeping, unusual dreams, anorexia (loss of appetite), and potential for increased cardiovascular event, especially in patients with risk factors.

NNRTIs
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

POTENTIAL DRUG CLASS SIDE EFFECTS: Common with NNRTIs is rash, and rarely, severe rash which may require immediate medical attention.

Edurant
rilpivirine, or RPV
Insomnia, headache, rash, and depressive disorders. Liver problems may occur. Nephrotic syndrome (kidney disorder, which may not be related to rilpivirine).

Intelence
etravirine, or ETR
Rash and increased cholesterol. Skin or hypersensitivity reactions. Rarely, peripheral neuropathy.

Rescriptor
delavirdine, or DLV
Increased liver enzyme levels and itchy skin or rash.

Sustiva
efavirenz, or EFV
Central nervous system (CNS) and psychiatric symptoms. Rash, nausea, vomiting, diarrhea, fever, and increases in triglycerides, cholesterol, and liver enzyme levels. False positive tests for marijuana. Birth defects.

Viramune XR
nevirapine, or NVP
Headache, nausea, vomiting, fever, rash, Stevens-Johnson syndrome, increased liver enzyme levels, liver damage, and drug-induced hepatitis.

PIs PROTEASE INHIBITORS
POTENTIAL DRUG CLASS SIDE EFFECTS: The most common class side effects of protease inhibitors include gastrointestinal (GI) side effects such as nausea, vomiting, and diarrhea. These occur most frequently only at the beginning of therapy. Additional side effects seen with most PIs (except for unboosted Reyataz) include increased levels of total cholesterol, triglycerides, and blood sugar, which may be associated with an increased risk of heart disease. Other possible side effects include lipodystrophy (body fat changes), liver toxicity, osteoporosis, increased bleeding in hemophiliacs, and rash (especially with sulfa allergies). Medical attention needed for severe rash.

Aptivus
tipranavir, or TPV
(must be taken with Norvir)
Use with caution in patients allergic to sulfa drugs. Most common are mild diarrhea, nausea, vomiting, abdominal pain, and fatigue. Other side effects may include headache, fever, dry mouth, dizziness, rash (including sensitivity to the sun), liver abnormalities, and bleeding in the brain. May also increase blood sugar, cholesterol, and triglycerides. Also see Norvir.

Crixivan
indinavir sulfate, or IDV
Kidney stones, itchy/dry skin, ingrown toe nails, hair loss, headache, fatigue, 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, liver toxicity, Stevens-Johnson syndrome, hemolytic anemia, diabetic ketoacidosis, increase in bilirubin, insulin resistance, diabetes, body fat changes, and increased cholesterol levels. Kidney stones and jaundice can be minimized or avoided by drinking at least 1.5 liters of water per day.

Invirase
saquinavir, or SQV
(must be taken with Norvir)
Most common side effects are diarrhea, abdominal discomfort, vomiting, and nausea. Other side effects may include lipodystrophy and potential heart problems when given with certain other medications. Also see Norvir.

Kaletra
lopinavir / ritonavir, or LPV / r
Diarrhea is the most common side effect. Other side effects may include elevated cholesterol and triglycerides (fat in the blood), insulin resistance, rash, nausea, vomiting, stomach pain, headache, muscle weakness, and lipodystrophy. Also see Norvir.

Lexiva
fosamprenavir calcium, or FPV
Use with caution in patients allergic to sulfa drugs. Nausea, rash, diarrhea, headache, vomiting, and elevated liver enzymes.

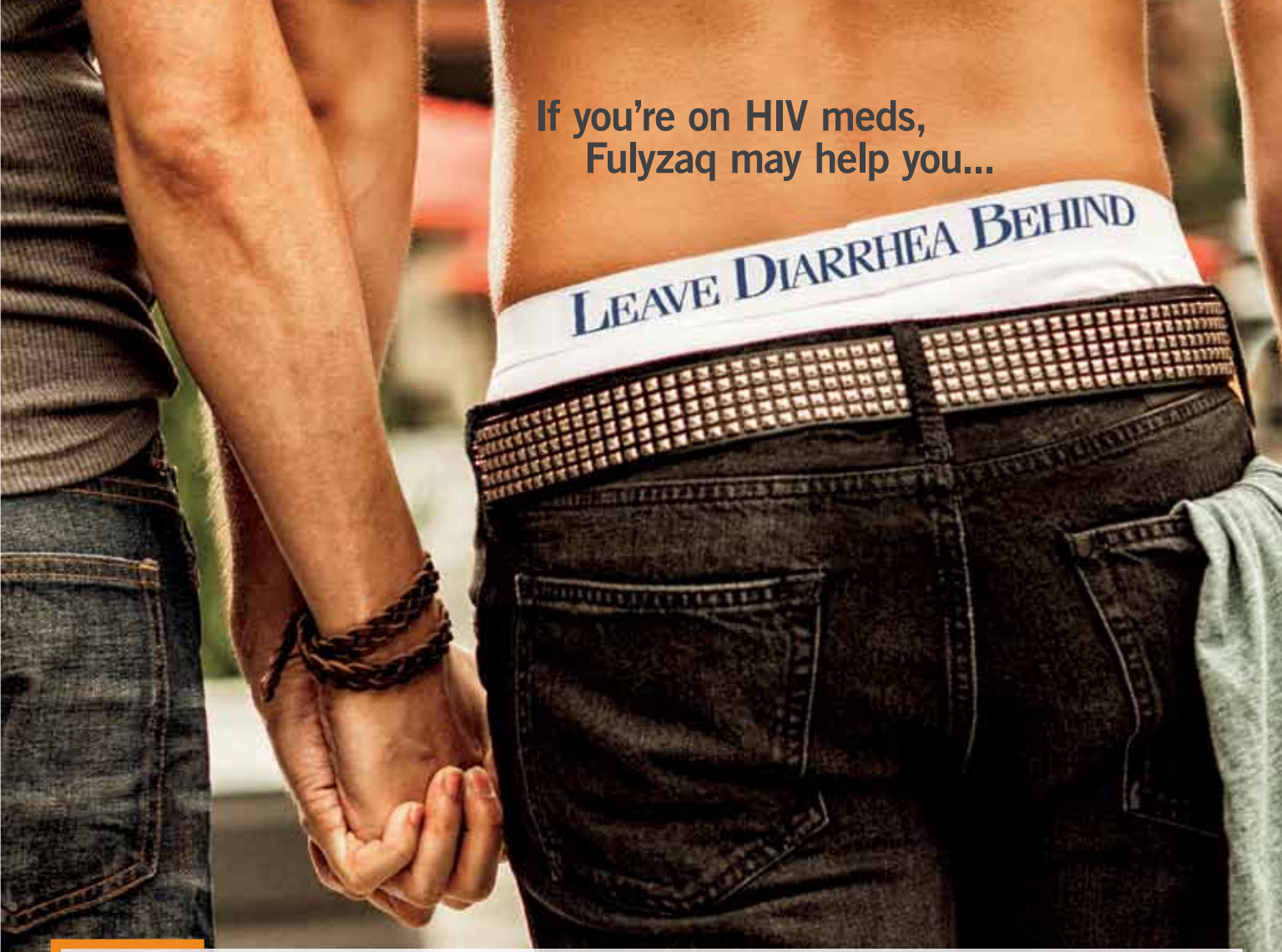
Norvir
ritonavir, or RTV
Weakness; stomach pain; nausea; diarrhea; vomiting; tingling/numbness around the mouth, hands, or feet; loss of appetite; taste disturbance; weight loss; headache; dizziness; pancreatitis; alcohol intolerance; increased liver enzyme levels; hepatitis (liver inflammation); jaundice (yellowing of skin or eyes); increased muscle enzyme (CPK); and uric acid.

Prezista
darunavir, or DRV
(must be taken with Norvir)
Use with caution in patients allergic to sulfa drugs. Side effects may include: diarrhea, nausea, headache, rash, vomiting, and abdominal pain. Also see Norvir.

Reyataz
atazanavir sulfate, or ATV
Dizziness, nausea, possible jaundice (yellowing of the skin or eyes), rash, kidney stones, gall stones, abnormal heart rhythm, and elevated liver enzymes

Viracept
nelfinavir, or NFV
Diarrhea, stomach discomfort, nausea, gas, weakness, and rash.

CONTINUES ON PAGE 67



Is diarrhea holding you back? If you are on HIV medications, Fulyzaq is a plant-based, FDA-approved prescription medication that may help manage your diarrhea.

Fulyzaq may help manage your diarrhea over time by making your bowel movements less frequent and loose. Fulyzaq works by normalizing the flow of water in your gut. Fulyzaq did not interfere with commonly used HIV medications, and did not affect CD4 count or viral load in a 4-week study.

It's time to stop dealing with diarrhea and 'Start the Conversation' about Fulyzaq today.

Indication
FULYZAQ® (crofelemer) is an antidiarrheal indicated for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on antiretroviral therapy.

Important Safety Information about FULYZAQ
FULYZAQ® (crofelemer) delayed-release tablets should not be used for the treatment of infectious diarrhea. It is important that your healthcare provider considers infectious causes of diarrhea before you start taking FULYZAQ. If infectious causes are not considered, and you begin taking FULYZAQ based on a probable diagnosis of noninfectious diarrhea, there is a risk that you will not receive the appropriate treatments, and your disease may worsen. • FULYZAQ tablets should be swallowed whole. FULYZAQ tablets should not be crushed or chewed. You may take FULYZAQ with or without food. You should follow the instructions of your healthcare provider. • If you are pregnant, or planning to become pregnant, talk to your healthcare provider before taking FULYZAQ. The safety and effectiveness of FULYZAQ have not been established in people younger than 18 years of age. • In clinical studies, the most common adverse reactions associated with FULYZAQ – occurring in at least 3% of patients taking FULYZAQ – were upper respiratory tract infection, bronchitis (inflammation of the lining of the tubes which carry air to and from your lungs), cough, flatulence (intestinal gas passed through your rectum), and increased bilirubin (a waste product of the breakdown of red blood cells). • 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 following page for brief summary of Prescribing Information for FULYZAQ.

Fulyzaq®
(crofelemer) 125 MG DELAYED-RELEASE TABLETS

Snap a picture of our logo and show your doctor to 'Start the Conversation'

Fulyzaq®

(crofelemer) 125 MG DELAYED-RELEASE TABLETS

IMPORTANT PATIENT INFORMATION

The following is a brief summary only. See complete Prescribing Information at Fulyzaq.com or request complete Prescribing Information by calling 1-800-508-0024. This information does not take the place of talking with your doctor about your medical condition or your treatment.

WHAT IS FULYZAQ?

FULYZAQ is a prescription medication used to improve symptoms of noninfectious diarrhea (diarrhea not caused by a bacterial, viral, or parasitic infection) in adult patients with HIV/AIDS who take HIV medication.

WHO SHOULD NOT TAKE FULYZAQ?

- FULYZAQ should not be taken if you have diarrhea caused by an infection
- Your doctor and you should make sure your diarrhea is not caused by an infection (such as bacteria, virus, or parasite) before you start taking FULYZAQ

WHAT ARE THE POSSIBLE SIDE EFFECTS OF FULYZAQ?

- Upper respiratory tract infection (nasal or sinus infection)
- Bronchitis (inflammation of the lining of the tubes which carry air to and from your lungs)
- Cough
- Flatulence (intestinal gas passed through your rectum)
- Increased bilirubin (a waste product of the breakdown of red blood cells)

For a full list of side effects, please talk to your doctor.

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

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.

SHOULD I TAKE FULYZAQ IF I AM:

Pregnant or Planning to Become Pregnant?

- Studies in animals show that FULYZAQ could cause harm to an unborn baby or affect the ability to become pregnant
- There are no studies in pregnant women taking FULYZAQ
- This drug should only be used during pregnancy if clearly needed

A Nursing Mother?

- It is not known whether FULYZAQ is passed through human breast milk
- If you are nursing, you should tell your doctor before starting FULYZAQ
- Your doctor will help you to make a decision whether to stop nursing or to stop taking FULYZAQ

Under 18 or Over 65 Years of Age?

- FULYZAQ has not been studied in children under 18 years of age
- FULYZAQ studies did not contain a large number of patients over the age of 65; therefore, it is unclear if this age group will respond differently

Talk to your doctor to find out if FULYZAQ is right for you.

HOW SHOULD I TAKE FULYZAQ?

- FULYZAQ should be taken orally, by mouth 2 times per day
- FULYZAQ tablets may be taken with or without food
- FULYZAQ tablets should not be crushed or chewed
- FULYZAQ tablets should be swallowed whole

WHAT SHOULD I KNOW ABOUT TAKING FULYZAQ WITH OTHER MEDICATIONS?

- If you are taking any prescription or over-the-counter (OTC) medications, or herbal supplements or vitamins, tell your doctor before starting FULYZAQ

WHAT IF I HAVE MORE QUESTIONS ABOUT FULYZAQ?

- For more information, please see the full Prescribing Information at **Fulyzaq.com** or speak to your doctor or pharmacist

To report side effects, a product complaint, or for additional information, call: 1-800-508-0024.

Rx Only

Manufactured by Patheon, Inc. for
Salix Pharmaceuticals, Inc.
8510 Colonnade Center Drive, Raleigh, NC 27615
www.salix.com

US Patent Nos. 7,341,744 and 7,323,195.
FUL-RALAB49-062014

Fulyzaq is manufactured for Salix Pharmaceuticals, Inc. by Patheon, Inc. and distributed under license from Napo Pharmaceuticals, Inc.

FUL50-0614

napo pharmaceuticals

The botanical drug substance of FULYZAQ is extracted from *Croton lechleri* (the botanical raw material) that is harvested from the wild in South America.

Salix®
Pharmaceuticals, Inc.
Advancing Treatment in Gastroenterology℠

STRs SINGLE-TABLET REGIMENS

POTENTIAL DRUG CLASS SIDE EFFECTS: Because STRs contain a combination of medications from different drug classes, you should look up each drug contained in the pill.

Atripla

efavirenz / emtricitabine / tenofovir

See Sustiva and Truvada (Emtriva and Viread). Diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, rash, and false positive test for marijuana. Risk of birth defects.

Complera

rilpivirine / emtricitabine / tenofovir

See Edurant and Truvada (Emtriva and Viread). Insomnia, headache, depressive disorders, and a slight increase in liver enzymes.

Stribild

elvitegravir / cobicistat / emtricitabine / tenofovir

See Vitekta, Tybost, and Truvada (Emtiva and Viread). Nausea, diarrhea, headache, abnormal dreams, fatigue, increases in total cholesterol, bone problems, elevated liver function tests, and changes in kidney function tests.

Triumeq

dolutegravir / lamivudine / abacavir

See Tivicay, Epivir, and Ziagen. Most common side effects are insomnia, headache, and fatigue. A small increase in serum creatinine may be seen. Hypersensitivity and possibility of heart problems.

PKE

PHARMACOKINETIC ENHANCER (NOT AN ANTIRETROVIRAL)

POTENTIAL DRUG CLASS SIDE EFFECTS: No class side effects known to date.

Tybost

cobicistat, or COBI

Side effects seen in clinical studies include diarrhea, nausea, increases in cholesterol and triglycerides, red blood cells in the urine, and modest increase in serum creatinine (SCr) and decreased estimated creatinine clearance (CrCl).

INSTIs INTEGRASE STRAND TRANSFER INHIBITORS

POTENTIAL DRUG CLASS SIDE EFFECTS: No class side effects known to date.

Isentress

raltegravir, or RAL

Very tolerable and infrequent side effects, which may include diarrhea, insomnia, nausea, headache, dizziness, and fatigue. Rare side effects may include abdominal pain; vomiting; weakness; mild to moderate rash; anxiety; anemia (low red blood cells); neutropenia (low white blood cells); lipodystrophy; elevated levels of creatine kinase; increases in ALT, AST, and total bilirubin; hypersensitivity reactions; and cerebellar ataxia. Chewable tablets contain phenylalanine.

Tivicay

dolutegravir, or DTG

A very tolerable drug, but side effects may include insomnia, headache, fatigue, and hypersensitivity.

Vitekta

elvitegravir, or EVG

Most common side effects are nausea, diarrhea, headache, and fatigue. Elevated liver enzymes.

PI-PKE BOOSTED PIs PROTEASE INHIBITORS CONTAINING COBICISTAT BOOSTER

POTENTIAL DRUG CLASS SIDE EFFECTS: Because boosted protease inhibitors contain two medicines from different drug classes, you should look up each drug contained in the pill.

EvoTaz

atazanavir / cobicistat

See Reyataz and Tybost.

Prezcobix

darunavir / cobicistat

See Prezista and Tybost.

EIs ENTRY INHIBITORS

POTENTIAL DRUG CLASS SIDE EFFECTS: No class side effects known to date.

Fuzeon (FUSION INHIBITOR)

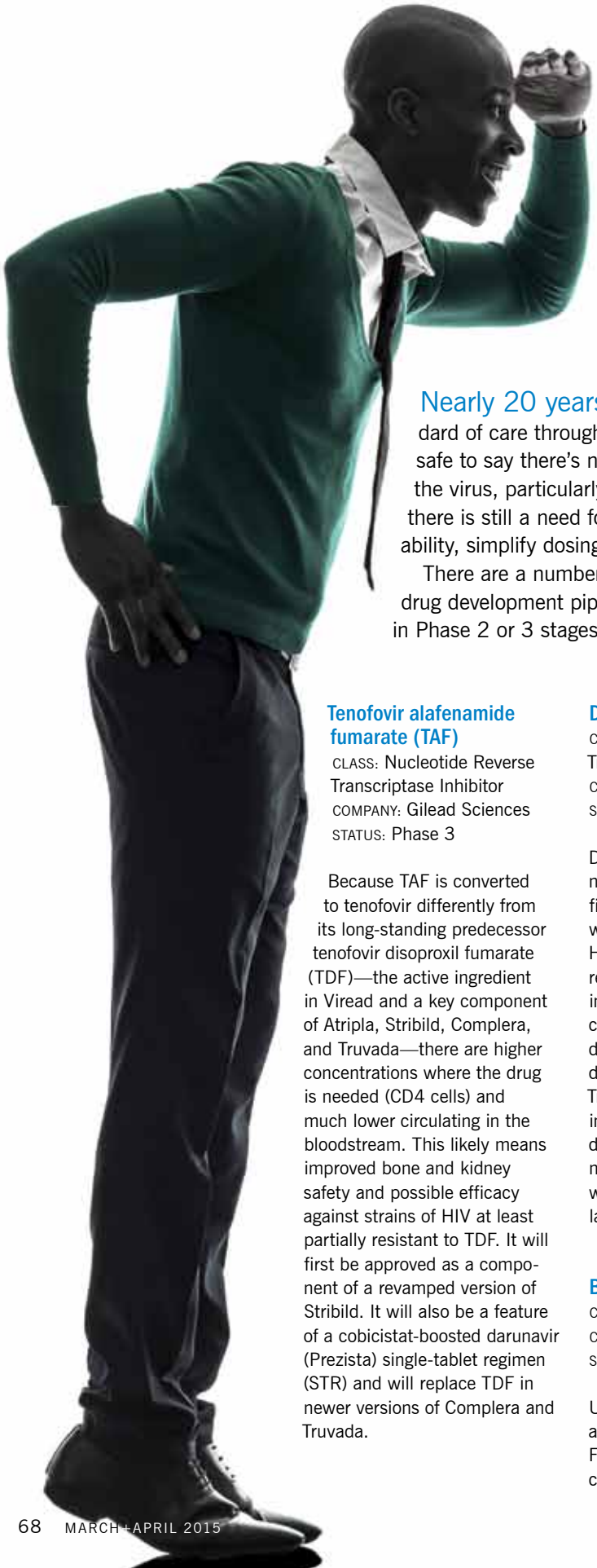
enfuvirtide, T-20, or ENF

Injection site reactions (ISRs) such as itching, pain/discomfort, or redness at site of injection; pneumonia; diarrhea; nausea; and fatigue. Hypersensitivity possible.

Selzentry (CCR5 ANTAGONIST)

maraviroc, or MVC

The most common side effects include cough, fever, cold, rash, muscle and joint pain, stomach pain, dizziness, and trouble sleeping. Other side effects may include allergic reactions, liver toxicity, and heart problems in those with a history of heart disease. Rarely, dizziness or fainting when standing up due to low blood pressure. Possible increased risk of infections and cancer.



WHAT'S ON

A LOOK AT NEW DRUGS IN DEVELOPMENT

BY **TIM HORN**

Nearly 20 years after combination antiretroviral therapy became the standard of care throughout the world for the long-term management of HIV, it's safe to say there's no shortage of highly effective options for people living with the virus, particularly those starting HIV treatment for the first time. However, there is still a need for new agents, particularly those that further improve tolerability, simplify dosing, and are active against drug-resistant strains of the virus.

There are a number of intriguing compounds making their way down the HIV drug development pipeline. Here we provide a snapshot of experimental agents, in Phase 2 or 3 stages of evaluation, to keep an eye on.

Tenofovir alafenamide fumarate (TAF)

CLASS: Nucleotide Reverse Transcriptase Inhibitor
COMPANY: Gilead Sciences
STATUS: Phase 3

Because TAF is converted to tenofovir differently from its long-standing predecessor tenofovir disoproxil fumarate (TDF)—the active ingredient in Viread and a key component of Atripla, Stribild, Complera, and Truvada—there are higher concentrations where the drug is needed (CD4 cells) and much lower circulating in the bloodstream. This likely means improved bone and kidney safety and possible efficacy against strains of HIV at least partially resistant to TDF. It will first be approved as a component of a revamped version of Stribild. It will also be a feature of a cobicistat-boosted darunavir (Prezista) single-tablet regimen (STR) and will replace TDF in newer versions of Complera and Truvada.

Doravirine

CLASS: Non-Nucleoside Reverse Transcriptase Inhibitor
COMPANY: Merck
STATUS: Phase 3

Doravirine is a once-daily non-nuke primarily being studied in first-time treatment takers, but with suggested activity against HIV with mutations that confer resistance to current options in this drug class. A Phase 3 clinical trial comparing 100 mg doravirine to ritonavir-boosted darunavir, combined with either Truvada or Epzicom, was started in late 2014. Merck is also developing a single-tablet regimen that combines doravirine with generic tenofovir DF and lamivudine.

BMS-663068

CLASS: Attachment Inhibitor
COMPANY: Bristol-Myers Squibb
STATUS: Phase 3

Unlike the cumbersome injectable attachment inhibitor Fuzeon (enfuvirtide), BMS-068 can be taken orally. Because attachment inhibitors are a very useful class of drugs for HIV-positive individuals with a lot of antiretroviral therapy experience under their belts, community activists are pleased with BMS's decision to focus on getting this drug approved for those in need of novel therapies. A Phase 3 trial is starting soon.

Cenicriviroc

CLASS: CCR5 Antagonist
COMPANY: Tobira
STATUS: Phase 2/3

Like ViiV's Selzentry (maraviroc), cenicriviroc blocks HIV targeting the CCR5 co-receptor on CD4 cells, but not HIV targeting the CXCR4 co-receptor (which tends to emerge some years after HIV first establishes infection). Unlike Selzentry, it also targets CCR2, a co-receptor believed to be associated with inflammation. Whether this translates into health benefits, such as a reduced risk of cardiovascular disease or cancer, has yet to be determined. Development of this drug has been slow, but plans

PHOTO: THINKSTOCK

THE HORIZON

for Phase 3 clinical trials have been discussed. Cenicriviroc will also be studied in a fixed-dose combination with generic lamivudine and, possibly, an STR that includes a third drug.

Once-daily raltegravir

CLASS: Integrase Inhibitor
COMPANY: Merck
STATUS: Phase 2/3

Raltegravir (Isentress) was the first approved integrase inhibitor. Though it's very effective and well tolerated, it needs to be taken twice a day—a deterrent for some people. Merck is currently developing a once-daily formulation to help broaden its acceptability and appeal.

Long-acting cabotegravir

CLASS: Integrase Inhibitor
COMPANY: ViiV Healthcare
STATUS: Phase 2

In tablet form, cabotegravir is very similar to its predecessor Tivicay (dolutegravir). It's the injectable form that is garnering a lot of attention. This long-acting formulation of the drug is being studied in combination with an injectable version of the non-nuke rilpivirine (see below) for once-monthly administration as maintenance therapy, to be initiated after a standard combination of oral drugs suppresses viral load to undetectable. It's an excitingly novel approach to long-term treatment, though there's much more to be learned about its safety, efficacy, and acceptability. Because the injections are intramuscular and will require a high volume of drug that likely needs to be administered by a health care provider every month, it's unclear for whom this will be preferable, compared with oral daily dosing. It's also being studied as pre-exposure prophylaxis (PrEP), with injections likely to be administered once every two or three months.

Long-acting rilpivirine

CLASS: Non-Nucleoside Reverse Transcriptase Inhibitor
COMPANY: Janssen Pharmaceuticals
STATUS: Phase 2

Approved for once-daily oral dosing as Edurant and as a component of the single-tablet regimen Complera, rilpivirine is back in the drug development pipeline in the form of a long-acting injectable formulation. In clinical trials, it's being paired with long-acting cabotegravir (see above) as a component of two-drug maintenance therapy. It's also being studied as long-acting PrEP.

BMS-955176

CLASS: Maturation Inhibitor
COMPANY: Bristol-Myers Squibb
STATUS: Phase 2

Maturation inhibitors act during the final stages of HIV's life cycle; they bind to a protein called gag, which helps prevent the formation of virus capable of infecting other cells. Another company's previous candidate, bevirimat, didn't get very far—it didn't work well against HIV resistant to protease inhibitors—but there are high hopes for BMS's lead contender. It is set to be evaluated in studies involving first-time treatment takers and treatment-experienced folks. Fixed-dose combinations and single-tablet regimens are also in the works.

Apricitabine

CLASS: Nucleoside Reverse Transcriptase Inhibitor
COMPANY: Avexa Ltd.
STATUS: Phase 2

This Epivir (lamivudine)-like molecule has been stalled since a Phase 3 study was halted in 2009. The drug may have a potential role for those with multiclass-resistant HIV—data supporting this hypothesis are limited—and another Phase 3 study is planned to confirm this. The company has also announced that apricitabine is available through an early access program for people in need of additional options.

Ibalizumab

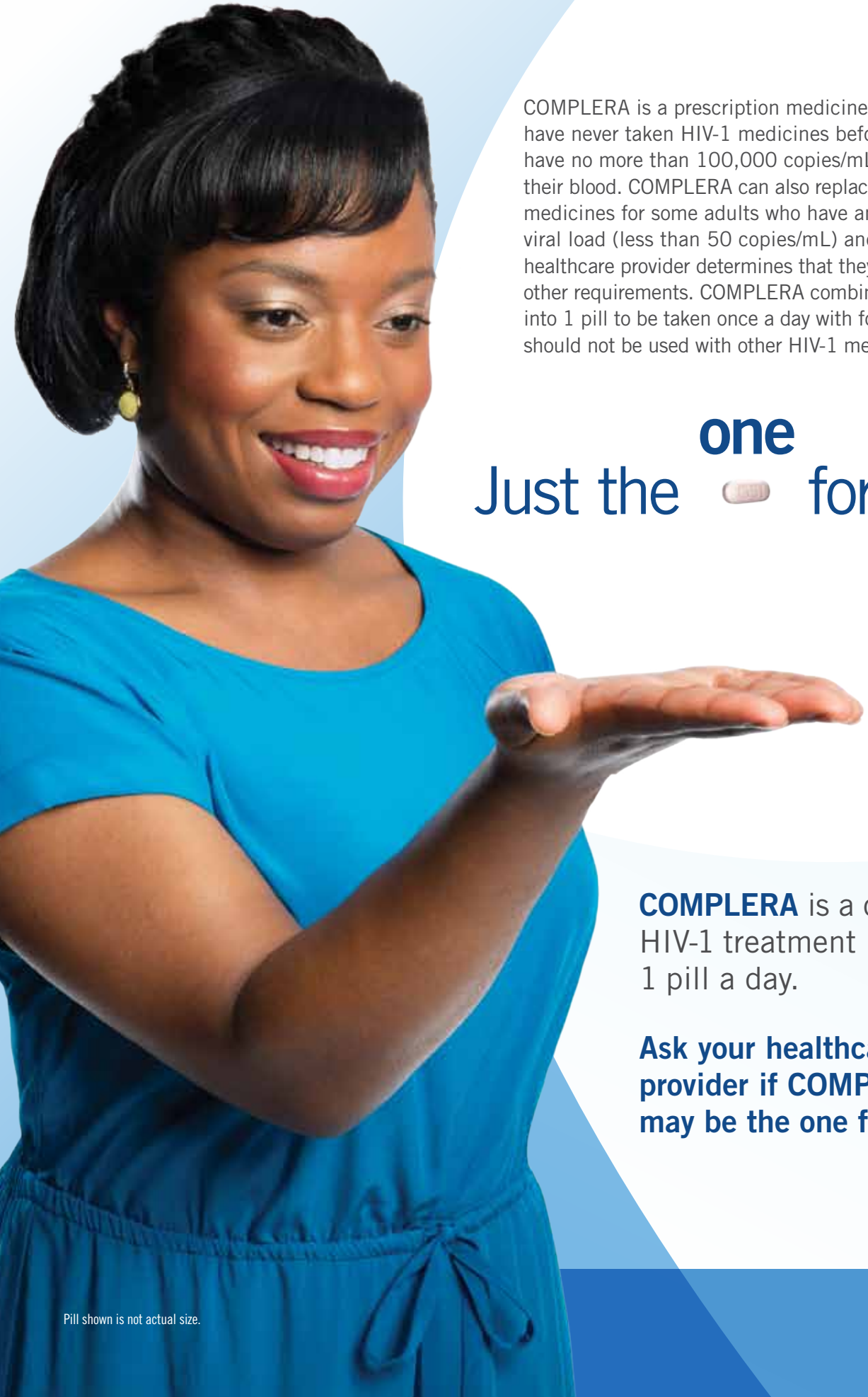
CLASS: CD4 Antagonist
COMPANY: TaiMed Biologics
STATUS: Phase 2

Ibalizumab, a monoclonal antibody that blocks HIV attachment to the CD4 receptor on T-cells, has been slow to develop and has passed through various companies over the years. Its potential for subcutaneous injections administered every few weeks is still being explored. Though no Phase 3 studies have been announced, ibalizumab is to be rapidly reviewed as an "orphan drug" by the FDA—the first HIV medication to do so—given its limited potential (people with multi-class-resistant HIV). The older intravenous formulation of the agent is available on a case-by-case basis through an FDA treatment IND (investigational new drug) approval process.

PRO 140

CLASS: CCR5 Antagonist
COMPANY: Progenics
STATUS: Phase 2

Like the monoclonal antibody ibalizumab, PRO 140 has been slow going in the HIV drug development pipeline. A dose optimization study is now underway, as is a small clinical trial evaluating once-weekly injections of the drug as maintenance therapy following viral load suppression with a standard oral combination of drugs. A third trial, evaluating the added benefit of PRO 140 when combined with approved antiretrovirals in injection drug users experiencing viral load rebounds or adherence difficulties, is planned.



COMPLERA is a prescription medicine for adults who have never taken HIV-1 medicines before and who have no more than 100,000 copies/mL of virus in their blood. COMPLERA can also replace current HIV-1 medicines for some adults who have an undetectable viral load (less than 50 copies/mL) and whose healthcare provider determines that they meet certain other requirements. COMPLERA combines 3 medicines into 1 pill to be taken once a day with food. COMPLERA should not be used with other HIV-1 medicines.

Just the **one** for me

COMPLERA is a complete HIV-1 treatment in only 1 pill a day.

Ask your healthcare provider if COMPLERA may be the one for you.

Pill shown is not actual size.

COMPLERA does not cure HIV-1 infection or AIDS.

To control HIV-1 infection and decrease HIV-related illnesses you must keep taking COMPLERA. Ask your healthcare provider if you have questions about how to reduce the risk of passing HIV-1 to others. Always practice safer sex and use condoms to lower the chance of sexual contact with body fluids. Never reuse or share needles or other items that have body fluids on them.

It is not known if COMPLERA is safe and effective in children under 18 years old.

IMPORTANT SAFETY INFORMATION

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

COMPLERA can cause serious side effects:

- **Build-up of an acid in your blood (lactic acidosis),** which is a serious medical emergency. Symptoms of lactic acidosis include feeling very weak or tired, unusual (not normal) muscle pain, trouble breathing, stomach pain with nausea or vomiting, feeling cold especially in your arms and legs, feeling dizzy or lightheaded, and/or a fast or irregular heartbeat.
- **Serious liver problems.** The liver may become large (hepatomegaly) and fatty (steatosis). Symptoms of liver problems include 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, and/or stomach pain.
- **You may be more likely to get lactic acidosis or serious liver problems** if you are female, very overweight (obese), or have been taking COMPLERA for a long time. In some cases, these serious conditions have led to death. Call your healthcare provider right away if you have any symptoms of these conditions.
- **Worsening of hepatitis B (HBV) infection.** If you also have HBV and stop taking COMPLERA, your hepatitis may suddenly get worse. Do not stop taking COMPLERA without first talking to your healthcare provider, as they will need to monitor your health. COMPLERA is not approved for the treatment of HBV.

Who should not take COMPLERA?

Do not take COMPLERA if you:

- **Take a medicine that contains:** adefovir (Hepsera), lamivudine (Epivir-HBV), carbamazepine (Carbatrol, Equetro, Tegretol, Tegretol-XR, Teril, Epitol), oxcarbazepine (Trileptal), phenobarbital (Luminal), phenytoin (Dilantin, Dilantin-125, Phenytek), rifampin (Rifater, Rifamate, Rimactane, Rifadin), rifapentine (Priftin), dexlansoprazole (Dexilant), esomeprazole (Nexium, Vimovo), lansoprazole (Prevacid), omeprazole (Prilosec, Zegerid), pantoprazole sodium (Protonix), rabeprazole (Aciphex), more than 1 dose of the steroid medicine dexamethasone or dexamethasone sodium phosphate, or the herbal supplement St. John's wort.
- **Take any other medicines to treat HIV-1 infection,** unless recommended by your healthcare provider.

What are the other possible side effects of COMPLERA?

Serious side effects of COMPLERA may also include:

- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do blood tests to check your kidneys before starting treatment with COMPLERA. If you have had kidney problems, or take other medicines that may cause kidney problems, your healthcare provider may also check your kidneys during 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.
- **Changes in liver enzymes:** People who have had hepatitis B or C, or who have had changes in their liver function tests in the past may have an increased risk for liver problems while taking COMPLERA. Some people without prior liver disease may also be at risk. Your healthcare provider may do tests to check your liver enzymes before and during treatment with COMPLERA.
- **Bone problems,** including bone pain or bones getting soft or thin, which may lead to fractures. Your healthcare provider may do tests to check your bones.
- **Changes in body fat** can happen in people taking HIV-1 medicines.
- **Changes in your immune system.** Your immune system may get stronger and begin to fight infections. Tell your healthcare provider if you have any new symptoms after you start taking COMPLERA.

The most common side effects of COMPLERA include trouble sleeping (insomnia), abnormal dreams, headache, dizziness, diarrhea, nausea, rash, tiredness, and depression. Other common side effects include vomiting, stomach pain or discomfort, skin discoloration (small spots or freckles), and pain. Tell your healthcare provider if you have any side effects that bother you or do not go away.

What should I tell my healthcare provider before taking COMPLERA?

- **All your health problems.** Be sure to tell your healthcare provider if you have or had any kidney, mental health, bone, or liver problems, including hepatitis virus infection.
- **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. Keep a list of all your medicines and show it to your healthcare provider and pharmacist. Do not start any new medicines while taking COMPLERA without first talking with your healthcare provider.
- **If you take rifabutin (Mycobutin).** Talk to your healthcare provider about the right amount of rilpivirine (Edurant) you should take.
- **If you take antacids.** Take antacids at least 2 hours before or at least 4 hours after you take COMPLERA.
- **If you take stomach acid blockers.** Take acid blockers at least 12 hours before or at least 4 hours after you take COMPLERA. Ask your healthcare provider if your acid blocker is okay to take, as some acid blockers should never be taken with COMPLERA.
- **If you are pregnant** or plan to become pregnant. It is not known if COMPLERA can harm your unborn baby. Tell your healthcare provider if you become pregnant while taking COMPLERA.
- **If you are breastfeeding** (nursing) or plan to breastfeed. Do not breastfeed. HIV-1 can be passed to the baby in breast milk. Also, some medicines in COMPLERA can pass into breast milk, and it is not known if this can harm the baby.

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 Brief Summary of full Prescribing Information with **important warnings** on the following pages.

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

GILEAD

Brief Summary of full Prescribing Information

COMPLERA® (kom-PLEH-rah)

(emtricitabine 200 mg, rilpivirine 25 mg, tenofovir disoproxil fumarate 300 mg) tablets

Brief summary of full Prescribing Information. For more information, please see the full Prescribing Information, including Patient Information.

What is COMPLERA?

- **COMPLERA** is a prescription medicine used as a complete HIV-1 treatment in one pill a day. COMPLERA is for adults who have never taken HIV-1 medicines before and who have no more than 100,000 copies/mL of virus in their blood (this is called 'viral load'). Complera can also replace current HIV-1 medicines for some adults who have an undetectable viral load (less than 50 copies/mL) and whose healthcare provider determines that they meet certain other requirements.
- COMPLERA is a complete regimen and should not be used with other HIV-1 medicines. HIV-1 is the virus that causes AIDS. When used properly, COMPLERA may reduce the amount of HIV-1 virus in your blood and increase the amount of CD4 T-cells, which may help improve your immune system. This may reduce your risk of death or getting infections that can happen when your immune system is weak.
- **COMPLERA does not cure HIV-1 or AIDS.** You must stay on continuous HIV-1 therapy to control HIV-1 infection and decrease HIV-related illnesses.
- **Ask your healthcare provider about how to prevent passing HIV-1 to others.** Do not share or reuse needles, injection equipment, or personal items that can have blood or body fluids on them. Do not have sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

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

COMPLERA can cause serious side effects, including:

- **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:**
  - feel very weak or tired
  - have unusual (not normal) muscle pain
  - have trouble breathing
  - having stomach pain with nausea or vomiting
  - feel cold, especially in your arms and legs
  - feel dizzy or lightheaded
  - have a fast or irregular heartbeat
- **Severe liver problems.** Severe liver problems can happen in people who take COMPLERA. 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). **Call your healthcare provider right away if you get 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 for a long time.**
- **Worsening of Hepatitis B infection.** If you have hepatitis B virus (HBV) infection and take COMPLERA, your HBV may get worse (flare-up) if you stop taking COMPLERA. 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 with your healthcare provider.
  - Do not run out of COMPLERA. Refill your prescription or talk to your healthcare provider before your COMPLERA is all gone.
  - 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 blood tests regularly to check your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking COMPLERA.

Who should not take COMPLERA?

Do not take COMPLERA if you also take any of the following medicines:

- **Medicines used for seizures:** carbamazepine (Carbatrol, Equetro, Tegretol, Tegretol-XR, Teril, Epitol); oxcarbazepine (Trileptal); phenobarbital (Luminal); phenytoin (Dilantin, Dilantin-125, Phenytek)
- **Medicines used for tuberculosis:** rifampin (Rifater, Rifamate, Rimactane, Rifadin); rifapentine (Priftin)
- **Certain medicines used to block stomach acid called proton pump inhibitors (PPIs):** dexlansoprazole (Dexilant); esomeprazole (Nexium, Vimovo); lansoprazole (Prevacid); omeprazole (Prilosec, Zegerid); pantoprazole sodium (Protonix); rabeprazole (Aciphex)
- **Certain steroid medicines:** More than 1 dose of dexamethasone or dexamethasone sodium phosphate
- **Certain herbal supplements:** St. John's wort
- **Certain hepatitis medicines:** adefovir (Hepsera), lamivudine (Epivir-HBV)

Do not take COMPLERA if you also take any other HIV-1 medicines, including:

- Other medicines that contain tenofovir (ATRIPLA, STRIBILD, TRUVADA, VIREAD)
- Other medicines that contain emtricitabine or lamivudine (ATRIPLA, Combivir, EMTRIVA, Epivir, Epzicom, STRIBILD, Trizivir, TRUVADA)
- rilpivirine (Edurant), unless you are also taking rifabutin (Mycobutin)

COMPLERA is not for use in people who are less than 18 years old.

What are the possible side effects of COMPLERA?

COMPLERA may cause the following serious side effects:

- **See "What is the most important information I should know about COMPLERA?"**
- **New or worse kidney problems, including kidney failure.** Your healthcare provider should do blood and urine tests to check your kidneys before you start and while you are taking COMPLERA. If you have had kidney problems in the past or need to take another medicine 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
- **Change in liver enzymes.** People with a history of hepatitis B or C virus infection or who have certain liver enzyme changes may have an

increased risk of developing new or worsening liver problems during treatment with COMPLERA. Liver problems can also happen during treatment with COMPLERA in people without a history of liver disease. Your healthcare provider may need to do tests to check your liver enzymes before and during treatment with COMPLERA.

- **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 tests to check your bones.
- **Changes in body fat** can happen in people taking HIV-1 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-1 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 any new symptoms after starting your HIV-1 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.
- Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

What should I tell my healthcare provider before taking COMPLERA?

Tell your healthcare provider about all your medical conditions, including:

- If you have or had any kidney, mental health, bone, or liver problems, including hepatitis B or C infection.
- If you are pregnant or plan to become pregnant. It is not known if COMPLERA can harm your unborn child.
  - There is a pregnancy registry for women who take antiviral medicines during pregnancy. The purpose of this registry 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.
- If you are breastfeeding (nursing) or plan to breastfeed. Do not breastfeed if you take COMPLERA.
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
  - Two of the medicines in COMPLERA can pass to your baby in your breast milk. It is not known if this could harm your baby.
  - Talk to your healthcare provider about the best way to feed your 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.
- 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-1 infection. The HIV-1 virus in your body may become resistant to COMPLERA or other HIV-1 medicines that are like it.
- Be sure to tell your healthcare provider if you take any of the following medicines:
  - Rifabutin (Mycobutin), a medicine to treat some bacterial infections. Talk to your healthcare provider about the right amount of rilpivirine (Edurant) you should take.
  - Antacid medicines that contain aluminum, magnesium hydroxide, or calcium carbonate. Take antacids **at least 2 hours before or at least 4 hours after** you take COMPLERA.
  - Certain medicines to block the acid in your stomach, including cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid), or ranitidine hydrochloride (Zantac). Take the acid blocker **at least 12 hours before or at least 4 hours after** you take COMPLERA. Some acid blocking medicines should never be taken with COMPLERA (see "Who should not take COMPLERA?" for a list of these medicines).
  - Medicines that can affect how your kidneys work, including acyclovir (Zovirax), cidofovir (Vistide), ganciclovir (Cytovene IV, Vitrasert), valacyclovir (Valtrex), and valganciclovir (Valcyte).
  - clarithromycin (Biaxin)
  - erythromycin (E-Mycin, Eryc, Ery-Tab, PCE, Pediazole, Ilosone)
  - fluconazole (Diflucan)
  - itraconazole (Sporanox)
  - ketoconazole (Nizoral)
  - methadone (Dolophine)
  - posaconazole (Noxafil)
  - telithromycin (Ketek)
  - voriconazole (Vfend)

Know the medicines you take. Keep a list of all your medicines and show it to your healthcare provider and pharmacist when you get a new medicine. Do not start any new medicines while you are taking COMPLERA without first talking with your healthcare provider.

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 food. Taking COMPLERA with food is important to help get the right amount of medicine in your body. A protein drink is not a substitute for food. If your healthcare provider decides to stop COMPLERA and you are switched to new medicines to treat HIV-1 that includes rilpivirine tablets, the rilpivirine tablets should be taken only with a meal.

Keep COMPLERA and all medicines out of reach of children.

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

Issued: June 2014

GILEAD

THE HIGH COST OF LIVING

ACCESSING EXPENSIVE MEDICATIONS IS AN ART

BY **JEFF BERRY**

TODAY'S THERAPIES are vastly improved over the first drugs used to treat HIV, but these advancements have come at a cost. The prices of HIV drugs continue to rise year after year at an average of 7–9 percent. While in the past this usually hasn't directly affected someone who has drug coverage through their health insurance plan, increasingly individuals are having to pay co-insurance (a percentage of the cost) on their medications. The good news is that help is out there. Several non-profit organizations and the pharmaceutical companies themselves have assistance programs in place to help you pay for the treatment you need.

CO-PAY AND PATIENT ASSISTANCE PROGRAMS

Most pharmaceutical companies provide some level of assistance through a patient assistance program (PAP) for people who can't afford their HIV medications for treatment or prevention. These PAPs are typically for patients without insurance 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). Patients or providers should contact the program to see if they are eligible (see charts beginning on this page).

Many companies also have co-pay assistance programs for those who have drug coverage through privately held insurance. These programs may cover all or part of the drug co-pay, co-insurance, and deductibles up to a specified amount. Certain restrictions and eligibility requirements apply (for example, recipients of ADAP, Medicare, and Medicaid may not be eligible). Individuals can get the co-pay card directly from their provider, the manufacturer's website, or by calling a toll-free number. Some programs have a reimbursement process if you have to pay the co-pay out of pocket. Some PAPs will make exceptions; for example, for a person on ADAP who has insurance but who has a high deductible, they may cover a certain percentage. Be sure to ask for an exception or review if you are at first denied.

THE AFFORDABLE CARE ACT

Commonly referred to as "Obamacare," the Affordable Care Act has already improved access to coverage for many people with HIV or at risk of HIV. Although the new law is far from perfect, the ACA's intention to provide more affordable benefits will allow many people with HIV to address their health needs. The law also provides access to pre-exposure prophalyxis (PrEP), medications to prevent HIV. Insurers can no longer deny coverage to people with HIV/AIDS or impose annual limits on coverage. Low- and middle-income earners may be eligible for tax subsidies to help them buy coverage from health insurance exchanges, or marketplaces. Medicaid eligibility has now expanded in 28 states to generally include those under 65 with incomes up to 133% of the Federal Poverty Level.

Advocates have raised concerns about the high cost of some HIV drugs available

HIV MEDICATIONS

DRUG	COMPANY
Aptivus	Boehringer Ingelheim
Atripla	Gilead Sciences
Combivir	ViiV Healthcare
Complera	Gilead Sciences
Crixivan	Merck & Co.
Edurant	Janssen Therapeutics
Emtriva	Gilead Sciences
Epivir	ViiV Healthcare
Epizcom	ViiV Healthcare
Evotaz	Bristol-Myers Squibb
Fuzeon	Genentech
Intelence	Janssen Therapeutics
Invirase	Genentech
Isentress	Merck & Co.
Kaletra	AbbVie, Inc.
Lexiva	ViiV Healthcare
Norvir	AbbVie, Inc.
Prezcobix	Janssen Therapeutics
Prezista	Janssen Therapeutics
Rescriptor	ViiV Healthcare
Retrovir	ViiV Healthcare
Reyataz	Bristol-Myers Squibb
Selzentry	ViiV Healthcare
Stribild	Gilead Sciences
Sustiva	Bristol-Myers Squibb
Tivicay	ViiV Healthcare
Triumeq	ViiV Healthcare
Trizivir	ViiV Healthcare
Truvada	Gilead Sciences

CONTINUES ON PAGE 76

CO-PAY PROGRAM	PATIENT ASSISTANCE	DETAILS
None	800-556-8317; rxhope.com or pparx.org	Patient assistance program only.
gileadcopay.com; 877-505-6986	866-290-4767	Co-pay program covers up to $6,000 per year with no monthly limit.
None	877-784-4842; viivhealthcareforyou.com	No co-pay card; generic available. Patient assistance program only.
gileadcopay.com; 877-505-6986	800-226-2056; gilead.com/us_advancing_access	Co-pay program covers up to $6,000 per year with no monthly limit.
None.	800-652-3430; merck.com/merckhelps	Patient assistance program only.
866-961-7169; edurant.com	800-652-6227; jjpaf.org	Co-pay program covers up to $7,500/year with no monthly limit. Card available through provider or at janssentherapeutics.com.
877-505-6986; gileadcopay.com	800-226-2056; gilead.com/us_advancing_access	Card available through your provider, AIDS service organization, and pharmacy. Co-pay program covers up to $3,600 per year with a monthly maximum of $300.
None	877-784-4842; viivhealthcareforyou.com	No co-pay card; generic available. Patient assistance program only.
mysupportcard.com	877-784-4842; viivhealthcareforyou.com	Card available online or through provider. Co-pay program covers up to $2,400 per year with no monthly limit.
888-281-8981; bmscustomerconnect.com/bms3assist/copay	888-281-8981; bmscustomerconnect.com/bms3assist	Co-pay program covers up to $6,800 per year with no monthly limit.
None	pparx.com	Patient assistance program only.
866-961-7169; intelence.com	800-652-6227; jjpaf.org	Co-pay program covers up to $7,500/year with no monthly limit. Card available through provider or at janssentherapeutics.com.
None	pparx.org	Patient assistance program through pparx.org.
866-350-9232; isentress.com	800-652-3430; merck.com/merckhelp	Co-pay program covers up to $400 per month per prescription.
800-441-4987; kaletra.com	800-222-6885; abbviepaf.org	Co-pay program covers up to $200 per month per prescription.
mysupportcard.com	877-784-4842; viivhealthcareforyou.com	Co-pay program covers up to $2,400 per year with no monthly limit.
800-441-4987; norvir.com	800-222-6885; abbviepaf.org	Co-pay program covers up to $50 per month per prescription.
866-961-7169; prezista.com	800-652-6227; jjpaf.org	Co-pay program covers up to $7,500/year with no monthly limit. Card available through provider or at janssentherapeutics.com.
866-961-7169; prezista.com	800-652-6227; jjpaf.org	Co-pay program covers up to $7,500/year with no monthly limit. Card available through provider or at janssentherapeutics.com.
mysupportcard.com	877-784-4842; viivhealthcareforyou.com	Co-pay program covers up to $2,400 per year with no monthly limit.
None	877-784-4842; viivhealthcareforyou.com	No co-pay card; generic available. Patient assistance program only.
888-281-8981; reyataz.com	888-281-8981; bms.com	Co-pay program covers up to $6,800 per year with no monthly limit.
mysupportcard.com	877-784-4842; viivhealthcareforyou.com	Co-pay program covers up to $2,400 per year with no monthly limit.
877-505-6986; gileadcopay.com	800-226-2056; gilead.com/us_advancing_access	Co-pay program covers up to $6,000 per year with no monthly limit.
888-281-8981; bmscustomerconnect.com/bms3assist/copay	888-281-8981; bmscustomerconnect.com/bms3assist	Co-pay program covers up to $6,800 per year with no monthly limit.
mysupportcard.com	877-784-4842; viivhealthcareforyou.com	Co-pay program covers up to $6,000 per year with no monthly limit.
mysupportcard.com	877-784-4842; viivhealthcareforyou.com	Co-pay program covers up to $6,000 per year with no monthly limit.
None	877-784-4842; viivhealthcareforyou.com	No co-pay card; generic available. Patient assistance program only.
877-505-6986; gileadcopay.com	800-226-2056; gilead.com/us_advancing_access	Co-pay program covers up to $3,600 per year with a monthly maximum of $300.

through certain exchange plans. According to an article by Michael Ruppal in the December 2014 issue of *HIV Specialist*, The AIDS Institute and others sent a letter in July 2014 to HHS Secretary Sylvia Mathews Burwell. In it they "pointed to limited benefits, high cost-sharing, and a lack of transparency on the part of some plans, all of which create barriers to accessing quality healthcare." Although plans with affordable HIV drug coverage co-pays exist in almost all areas, some plans may require you to pay $1,000 or more (up to 50%) in co-insurance for HIV drugs. Make sure you know what your plan will cost in terms of co-insurance, deductibles, and the monthly premium. In addition some plans do not cover all HIV medications, or price them in the highest tier, including generics. According to Ruppal, transparency improved for 2015 enrollment, but "issues of limited benefits and high-cost sharing may have to wait for further action by HHS." A ruling is expected soon.

Many state AIDS Drug Assistance Programs (ADAPs) can help pay out-of-pocket costs for HIV drugs obtained through some exchange plans. ADAPs can also help pay premiums in some states. Check with your state ADAP to learn what your state offers, as well as the income limits.

It is critical to consult a trained enrollment "navigator" when choosing an exchange plan. Contact your local HIV/AIDS service organization for help or a referral.

MEDICARE PART D

The Affordable Care Act provides for closing the Medicare Part D prescription drug benefit "donut hole" or coverage gap by 2020. Beneficiaries receive a 50% discount on covered brand name drugs while they are in the "donut hole," with increased savings on prescription drugs while they are in the coverage gap until the gap is fully closed. In addition, ADAP benefits are now considered as contributions toward Medicare Part D's True Out of Pocket spending limit ("TrOOP"), so ADAP clients who have Medicare Part D should be able to benefit.

HARBORPATH AND THE COMMON PAP FORM

HarborPath is a non-profit organization that helps uninsured people living with HIV/AIDS and/or hepatitis C to gain access to brand name prescription medicines at no cost, by providing case managers with a single online portal for PAP applications and medication fulfillment through a mail-order pharmacy. Go to harborpath.org.

The Department of Health and Human Services (DHHS), along with seven pharmaceutical companies, the National Alliance of State and Territorial AIDS Directors (NASTAD), and community stakeholders developed a common patient assistance program application that can be used by both providers and patients. To download the form, go to hab.hrsa.gov/patientassistance.

ADDITIONAL PROGRAMS

Co-pay and patient assistance programs are also available for hepatitis B and C drugs, and medications or treatments used for other HIV-related conditions such as lipodystrophy—some of these are included in the co-pay and PAP charts at right. There is even a separate assistance program for Truvada as prevention, or PrEP (pre-exposure prophylaxis).

The Patient Assistance Network Foundation recently expanded eligibility criteria for HIV treatment and prevention (including PEP and PrEP). Those who qualify (you must have insurance and income below 500% FPL) are eligible to receive a grant of up to $4,000/yr. to help cover out-of-pocket costs for meds. You may apply for a second grant during your eligibility period depending on available funding. Go to panfoundation.org/hiv-treatment-and-prevention.

To learn more about other patient assistance or co-pay programs for drugs used to treat HIV, certain opportunistic infectionsor other conditions, talk to your provider, contact the manufacturer directly, or go to pparx.org and needymeds.org. SurvivorRxPlan offers help in getting many medications not covered by ADAP, including alternative therapies and generics, even if you receive medicines through another discount program. Go to SurvivorRxPlan.com.

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. Use the adjacent chart to check specific details, or go to positivelyaware.com/copay for the most current information.

SPECIAL THANKS to Drew Halbur, BSPharm, AAHIVP, BCACP, and his team at Walgreens for updating the accompanying chart; thanks to John Peller, CEO of AIDS Foundation Chicago, and the Fair Pricing Coalition (FPC) for some of the information in this article. Go to fairpricingcoalition.org or hivhealthreform.org. [Note: author is a member of the FPC.]

HIV MEDICATIONS CONTINUED

DRUG	COMPANY
Tybost	Gilead Sciences
Videx EC	Bristol-Myers Squibb
Viracept	ViiV Healthcare
Viramune XR	Boehringer Ingelheim
Viread	Gilead Sciences
Zerit	Bristol-Myers Squibb
Ziagen	ViiV Healthcare

HIV PREVENTION

DRUG	COMPANY
Truvada for PrEP	Gilead Sciences, Inc.

HIV-RELATED CONDITIONS

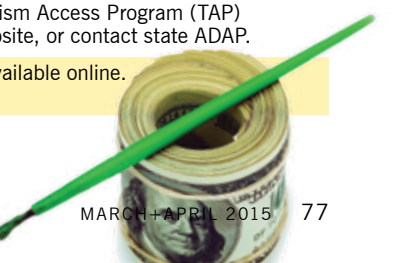
DRUG / ASSAY
Androgel (testosterone gel 1% & 1.62%) For adult males with low or no testosterone
Axiron (topical liquid testosteronel solution 30 mg/1.5 mL) For adult males with low or no testosterone
Egrifta Injectable for treating HIV-related excess belly fat (lipohypertrophy)
Fortesta (testosterone gel 2%) For adult males who have low or no testosterone)
Fulyzaq Anti-diarrheal approved for use in those with HIV/AIDS and on antiretroviral therapy.
HLA-Aware HLA-B*5701 test to determine if a person can start taking Ziagen, Epzicom, Trizivir, or Triumeq
Procrit Treats anemia due to zidovudine therapy
Radiesse Injectable facial filler approved for use in people with HIV to treat facial fat loss (lipoatrophy)
Sculptra Injectable facial filler approved for use in people with HIV to treat facial fat loss (lipoatrophy)
Serostim Injectable human growth hormone used for treating HIV-associated wasting in those on ART
Testim (testosterone gel 1%) For adult males with low or no testosterone
Trofile Assay A test to determine the tropism of a person's HIV to see if a CCR5 antagonist (such as Selzentry) would be effective
Vogelxo (testosterone gel 1%) For adult males with low or no testosterone

FOR HEPATITIS B AND C PROGRAMS, GO TO POSITIVELYAWARE.COM/COPAY

CO-PAY PROGRAM	PATIENT ASSISTANCE	DETAILS
877-505-6986; gileadcopay.com	800-226-2056; gilead.com/us_advancing_access	Co-pay program covers up to $600 per year with a monthly maximum of $50.
None	pparx.org	No co-pay card; generic available. Patient assistance program through pparx.org.
mysupportcard.com	877-784-4842; viivhealthcareforyou.com	Co-pay program covers up to $2,400 per year with no monthly limit.
None	pparx.org	No co-pay card for Viramune; available as generic. Patient assistance program through pparx.org.
877-505-6986; gileadcopay.com	800-226-2056; gilead.com/us_advancing_access	Co-pay program covers up to $3,600 per year with a monthly maximum of $300.
None.	pparx.org	No co-pay card; generic available. Patient assistance program through pparx.org.
None	877-784-4842; viivhealthcareforyou.com	No co-pay card; generic available. Patient assistance program only.

CO-PAY PROGRAM	PATIENT ASSISTANCE	DETAILS
855-330-5479; start.truvada.com/individual/truvadaprep-copay	855-330-5479; start.truvada.com/individual/truvadaprep-copay	For HIV-negative individuals to prevent HIV. Truvada for PrEP Medication Assistance Program (MAP) covers co-pays up to $3,600/yr. with a $300 monthly cap (additional support considered on case-by-case basis—call number); for uninsured provides free drug for those with incomes below 500% FPL.

COMPANY	CO-PAY PROGRAM	PATIENT ASSISTANCE	DETAILS
AbbVie, Inc.	855-2435-162; androgel.com	800-222-6885: abbviepaf.org; pparx.org	Co-pay: Patient pays first $10, then covers up to $50 per month for a total of 12 transactions. Card available through provider or print the card online.
Eli Lilly and Company	877-929-4766; axironmd.com	855-559-8783; lillytruassist.com	Co-pay: First month free, then $25 to $75 per month. Card available online. Free 30-day sample through Axiron representative.
Theratechnologies	844-347-4382; egrifta.com	844-347-4382; egrifta.com	Call number or go to egrifta.com for program details.
Endo Pharmaceuticals	800-462-3636; fortestagel.com	866-777-5702 whatismylowtcopay.com	Co-pay amount depends on the type of patient's insurance (commerical vs. government vs. no insurance).
Salix Pharmaceuticals	866-282-6583; fulyzaq.com	866-282-6583; fulyzaq.com	Co-pay covers first use up to $100, then patient pays first $25 up to $100. Card available online or from provider (good until 12/31/2015). Support program helps with PAP, prior authorization and access issues.
LabCorp/ ViiV Healthcare	viivhcdxresource.com/home	877-844-8872; viivhcdxresource.com	No co-pay program, PAP only. Covers entire cost of test for insured/uninsured. Test must be ordered by provider. Contact local ViiV rep, order online, or call.
Janssen Pharmaceuticals	None	800-652-6277; janssenprescription assistance.com/procrit-cost-assistance	No co-pay program, PAP only. Medicare Part D Extra Help with Low-Income Subsidy available (secure.ssa.gov/i1020/start)
Merz Aesthetics	None	866-862-1211; radiesse-fl.com	No co-pay program. PAP is sliding scale based on patient's annual income up to $50,000; reimbursement goes directly to physician.
Valeant Pharmaceuticals International	None	866-310-7551; needymeds.org	No co-pay program. PAP provides two kits and one follow-up kit. Free for those with an annual income below $22,340, and then on a sliding scale up to $61,940.
EMD Serono	877-714-2947; serostim.com	877-714-2947; serostim.com; 866-962-1128	Co-pay program covers up to $500 per prescription with a maximum of 12 discounts per lifetime.
Auxilium	None	877-663-0412	No co-pay program. PAP is sliding scale based on total household income.
Monogram Biosciences	None	877-436-6243; monogrambio.com; viivhcdxresource.com	Gateway coverage for uninsured/underinsured; assists in prior authorization or if insurance reimbursement is denied. ViiV also has Tropism Access Program (TAP) for ADAP eligible; see website, or contact state ADAP.
Upsher-Smith Laboratories, Inc.	None	None	A 30-day free trial card available online.



WHAT IS PREZCOBIX™?

- PREZCOBIX™ is a prescription HIV-1 (Human Immunodeficiency Virus 1) medicine used with other antiretroviral medicines to treat HIV-1 infection in adults. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome). PREZCOBIX™ contains the prescription medicines PREZISTA® (darunavir) and TYBOST® (cobicistat).
- It is not known if PREZCOBIX™ is safe and effective in children under 18 years of age.
- **When used with other antiretroviral medicines to treat HIV-1 infection, PREZCOBIX™ may help:**
  - reduce the amount of HIV-1 in your blood. This is called "viral load."
  - increase the number of CD4+ (T) cells in your blood that help fight off other infections.
- PREZCOBIX™ is always taken in combination with other HIV medications for the treatment of HIV-1 infection in adults. PREZCOBIX™ should be taken once daily with food.
- PREZCOBIX™ does not cure HIV-1 infection or AIDS, and you may still experience illnesses associated with HIV-1 infection. You must keep taking HIV-1 medicines to control HIV-1 infection and decrease HIV-related illnesses.
- Ask your healthcare provider if you have any questions on how to prevent passing HIV to other people.
- **Please read the Important Safety Information below and talk to your healthcare provider to learn if PREZCOBIX™ is right for you.**

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about PREZCOBIX™?

- **PREZCOBIX™ may cause liver problems.** Some people taking PREZCOBIX™ may develop liver problems which may be life-threatening. Your healthcare provider should do blood tests before and during your treatment with PREZCOBIX™.
  - Chronic hepatitis B or C infection may increase your chance of developing liver problems. Your healthcare provider should check your blood tests more often.
  - Signs and symptoms of liver problems include 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. Tell your healthcare provider if you develop any of these symptoms.
- **PREZCOBIX™ 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. Call your healthcare provider right away if you develop a rash.
  - **Stop taking PREZCOBIX™** and call your healthcare provider right away if you develop any skin changes with symptoms such as fever, tiredness, muscle or joint pain, blisters or skin lesions, mouth sores or ulcers, red or inflamed eyes like "pink eye" (conjunctivitis).
- **PREZCOBIX,™ when taken with certain other medicines, can cause new or worse kidney problems, including kidney failure.** Your healthcare provider should check your kidneys before you start and while you are taking PREZCOBIX™.

Who should not take PREZCOBIX™?

- **Do not take PREZCOBIX™** with any of the following medicines: alfuzosin (Uroxatral®), cisapride (Propulsid,® Propulsid® Quicksolv), colchicine (Colcrys,® Mitigare,® if you have liver or kidney problems), dronedarone (Multaq®), dihydroergotamine (D.H.E.45,® Embolex,® Migranal®), ergotamine tartrate (Cafergot,® Ergomar,® Ergostat,® Medihaler,® Migergot,® Wigraine,® Wigrettes®), methylergonovine (Methergine®), lovastatin or a product that contains lovastatin (Altoprev,® Advicor,® Mevacor®), lurasidone (Latuda®), oral midazolam (Versed®), pimozide (Orap®), ranolazine (Ranexa®), rifampin (Rifadin,® Rifater,® Rifamate,® Rimactane®), sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH), simvastatin or a product that contains simvastatin (Simcor,® Vytorin,® Zocor®), St. John's Wort (*Hypericum perforatum*) or a product that contains St. John's Wort, or triazolam (Halcion®).
- Serious problems can happen if you take any of these medicines with PREZCOBIX™.

What should I tell my healthcare provider before taking PREZCOBIX™?

- **About all health problems.** Tell your healthcare provider if you have liver problems, including hepatitis B or hepatitis C, have kidney problems, are allergic to sulfa (sulfonamide), have diabetes, have hemophilia, or have any other medical condition, are pregnant, breastfeeding, or plan to become pregnant or breastfeed. Tell your healthcare provider if you become pregnant while taking PREZCOBIX™.
- **About all medicines you take.** Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with PREZCOBIX™. **Keep a list of your medicines to show your healthcare provider and pharmacist. Do not start taking a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take PREZCOBIX™ with other medicines.

What are the possible side effects of PREZCOBIX™?

- **The most common side effects of darunavir, one of the medicines in PREZCOBIX,™ include** diarrhea, nausea, rash, headache, stomach area (abdominal) pain, and vomiting.
- **Other possible side effects include:**
  - **High blood sugar, diabetes or worsening diabetes, and increased bleeding in people with hemophilia** have been reported in patients taking protease inhibitor medicines, including PREZCOBIX™.
  - **Changes in body fat can happen in people who take HIV-1 medicines.** The exact cause and long-term health effects of these changes 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.

These are not all of the possible side effects of PREZCOBIX™. For more information, ask your healthcare provider.

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

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 accompanying full Product Information for more details.

Janssen Therapeutics,
Division of Janssen Products, LP

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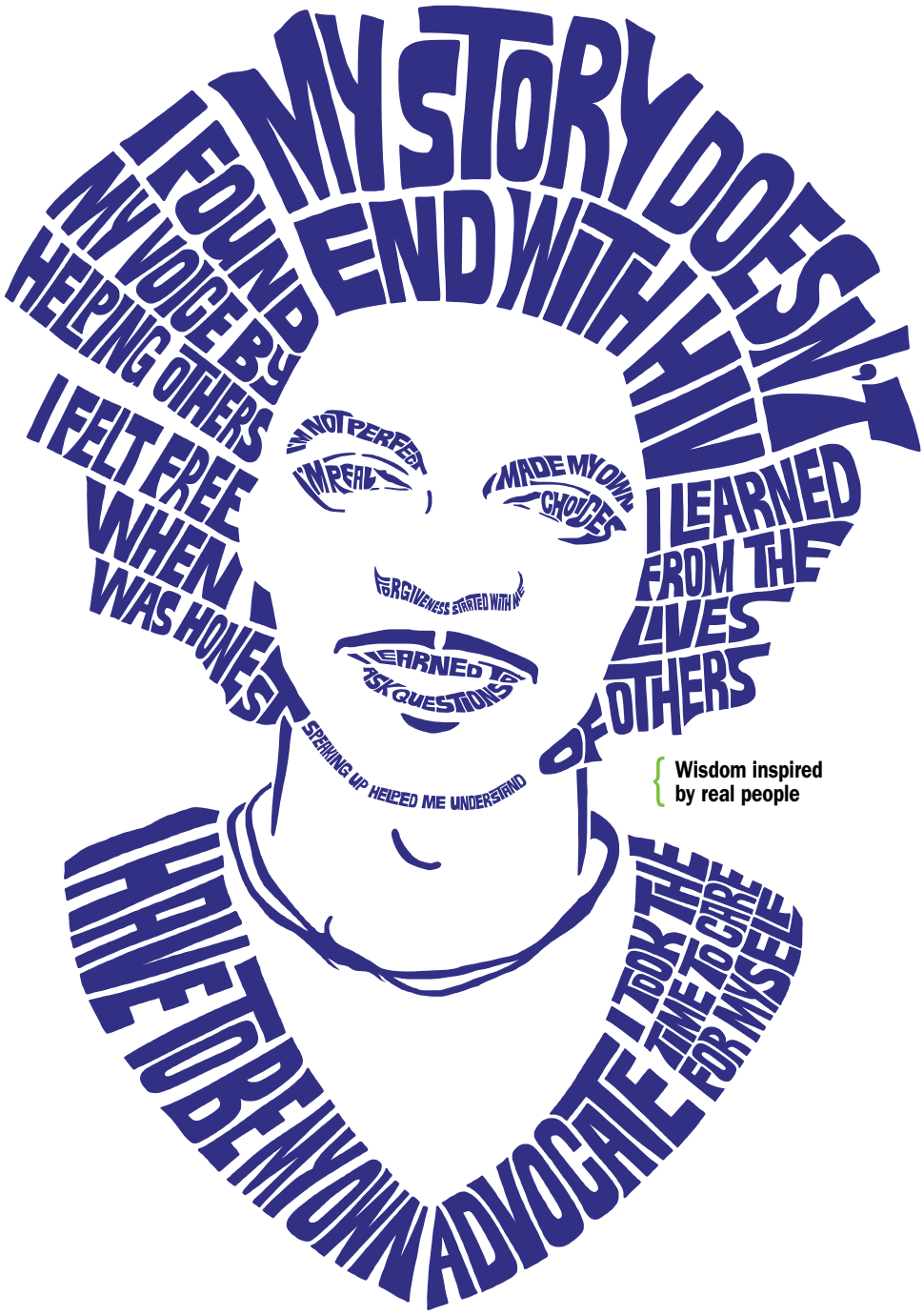

DISCOVER YOUR WISDOM WITHIN

Visit **PREZCOBIX.com** to hear wisdom inspired by experts and people like you living with HIV.

Ask your provider if Once-Daily* PREZCOBIX™ is right for you.

PREZCOBIX™
(darunavir 800 mg/
cobicistat 150 mg) tablets

PREZCOBIX.com

*PREZCOBIX™ is taken in combination with other HIV medications for the treatment of HIV-1 infection in adults.

IMPORTANT PATIENT INFORMATION

PATIENT INFORMATION
PREZCOBIX (prez-koe-bix)
(darunavir and cobicistat)
tablets

Please read this information before you start taking PREZCOBIX and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment. **What is the most important information I should know about PREZCOBIX?**

- **PREZCOBIX may cause liver problems.** Some people taking PREZCOBIX may develop liver problems which may be life-threatening. Your healthcare provider should do blood tests before and during your treatment with PREZCOBIX. If you have chronic hepatitis B or C infection, 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
- **PREZCOBIX 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. Call your healthcare provider right away if you develop a rash. **Stop taking PREZCOBIX** and call your healthcare provider right away 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)
- **PREZCOBIX when taken with certain other medicines can cause new or worse kidney problems, including kidney failure.** Your healthcare provider should check your kidneys before you start and while you are taking PREZCOBIX.

See **"What are the possible side effects of PREZCOBIX?"** for more information about side effects.

What is PREZCOBIX?

PREZCOBIX is a prescription HIV-1 (Human Immunodeficiency Virus 1) medicine used with other antiretroviral medicines to treat HIV-1 infection in adults. HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

PREZCOBIX contains the prescription medicines PREZISTA (darunavir) and TYBOST (cobicistat).

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

When used with other antiretroviral medicines to treat HIV-1 infection, PREZCOBIX may help:

- reduce the amount of HIV-1 in your blood. This is called "viral load".
- increase the number of CD4+ (T) cells in your blood that help fight off other infections.

Reducing the amount of HIV-1 and increasing the CD4+ (T) cells in your blood may help improve your immune system. This may reduce your risk of death or getting infections that can happen when your immune system is weak (opportunistic infections).

PREZCOBIX does not cure HIV-1 infection or AIDS. You must keep taking HIV-1 medicines to control HIV-1 infection and decrease HIV-related illnesses.

Avoid doing things that can spread HIV-1 infection to others.

- Do not share or re-use needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.
- Do not have any kind of sex without protection. Always practice safe sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

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

Who should not take PREZCOBIX?

Do not take PREZCOBIX with any of the following medicines:

- alfuzosin (Uroxatral®)
- cisapride (Propulside®, Propulsid® Quicksolv)
- colchicine (Colcrys®, Mitigare®), if you have liver or kidney problems
- dronedarone (Multaq®)
- ergot-containing medicines:
  - dihydroergotamine (D.H.E. 45®, Embolex®, Migranal®)
  - ergotamine tartrate (Cafergot®, Ergomar®, Ergostat®, Medihaler®, Migergot®, Wigraine®, Wigrettes®)
  - methylergonovine (Methergine®)
- lovastatin or a product that contains lovastatin (Altoprev®, Advicor®, Mevacor®)
- lurasidone (Latuda®)
- midazolam (Versed®), when taken by mouth
- pimozide (Orap®)
- ranolazine (Ranexa®)
- rifampin (Rifadin®, Rifater®, Rifamate®, Rimactane®)
- sildenafil (Revatio®), when used for the treatment of pulmonary arterial hypertension (PAH)
- simvastatin or a product that contains simvastatin (Simcor®, Vytorin®, Zocor®)
- St. John's Wort (*Hypericum perforatum*), or a product that contains St. John's Wort
- triazolam (Halcion®)

Serious problems can happen if you take any of these medicines with PREZCOBIX.

What should I tell my healthcare provider before taking PREZCOBIX?

Before taking PREZCOBIX, tell your healthcare provider if you:

- have liver problems, including hepatitis B or hepatitis C
- have kidney problems
- are allergic to sulfa (sulfonamide)
- have diabetes
- have hemophilia
- have any other medical condition

- are pregnant or plan to become pregnant. It is not known if PREZCOBIX will harm your unborn baby. Tell your healthcare provider if you become pregnant while taking PREZCOBIX.
  - **Pregnancy Registry:** There is a pregnancy registry for women who take antiretroviral medicines during pregnancy. The purpose of the registry 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 breastfeeding or plan to breastfeed. Do not breastfeed if you take PREZCOBIX.
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV to your baby.
  - It is not known if PREZCOBIX can pass into your breast milk.
  - Talk to your healthcare provider about the best way to feed your baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with PREZCOBIX. **Keep a list of your medicines to show your healthcare provider and pharmacist.**

- You can ask your healthcare provider or pharmacist for a list of medicines that interact with PREZCOBIX.
- **Do not start taking a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take PREZCOBIX with other medicines.

How should I take PREZCOBIX?

- Take PREZCOBIX exactly as your healthcare provider tells you.
- Do not change your dose or stop taking PREZCOBIX without talking to your healthcare provider.
- Take PREZCOBIX 1 time a day with food.
- If you miss a dose of PREZCOBIX by less than 12 hours, take your missed dose of PREZCOBIX right away. Then take your next dose of PREZCOBIX at your regularly scheduled time.
- If you miss a dose of PREZCOBIX by more than 12 hours, wait and then take the next dose of PREZCOBIX at your regularly scheduled time.
- If a dose of PREZCOBIX is skipped, do not double the next dose. Do not take more or less than your prescribed dose of PREZCOBIX at any one time.
- If you take too much PREZCOBIX, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of PREZCOBIX?

PREZCOBIX may cause serious side effects including:

- See **"What is the most important information I should know about PREZCOBIX?"**
- **Diabetes and high blood sugar (hyperglycemia).** Some people who take protease inhibitors including PREZCOBIX can get high blood sugar, develop diabetes, or your diabetes can get worse. Tell your healthcare provider if you notice an increase in thirst or urinate often while taking PREZCOBIX.
- **Changes in body fat can happen in people who take HIV-1 medications.** The changes may include an increased amount of fat in the upper back and neck ("buffalo hump"), breast, and around the middle of your body (trunk). Loss of fat from the legs, arms, and face may also happen. The exact cause and long-term health effects of these conditions are not known.
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 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 right away if you start having new symptoms after starting your HIV-1 medicine.
- **Increased bleeding for hemophiliacs.** Some people with hemophilia have increased bleeding with protease inhibitors including PREZCOBIX.

The most common side effects of darunavir, one of the medicines in PREZCOBIX, include:

- diarrhea
- nausea
- rash
- headache
- stomach area (abdominal) pain
- vomiting

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

These are not all of the possible side effects of PREZCOBIX. For more information, ask your health care provider.

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

How should I store PREZCOBIX?

- Store PREZCOBIX tablets at room temperature between 68°F to 77°F (20°C to 25°C).

Keep PREZCOBIX and all medicines out of reach of children.

General information about PREZCOBIX

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

If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about PREZCOBIX that is written for health professionals.

For more information call 1-800-526-7736.

What are the ingredients in PREZCOBIX?

Active ingredients: darunavir and cobicistat

Inactive ingredients: colloidal silicon dioxide, crospovidone, hypromellose, magnesium stearate, and silicified microcrystalline cellulose. The tablets are film-coated with a coating material containing iron oxide black, iron oxide red, polyethylene glycol, polyvinyl alcohol (partially hydrolyzed), talc, and titanium dioxide.

Manufactured by:
Janssen Ortho LLC, Gurabo, PR 00778

Manufactured for:
Janssen Therapeutics, Division of Janssen Products, LP, Titusville NJ 08560

Issued: January 2015

027415-150108

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- Prescription alignment that makes it easy to fill all your medications on the same date.
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