POSITIVELY AWARE
HIV TREATMENT, PREVENTION, AND SUPPORT FROM **TPAN**
MARCH+APRIL 2019

YOUR TICKET

TO THE MOST COMMONLY PRESCRIBED MEDICATIONS FOR TREATING HIV—WITH INSIGHT FROM AN HIV SPECIALIST AND AN ACTIVIST

THE 23RD ANNUAL

HIV DRUG GUIDE

WITH **PULL-OUT HIV DRUG CHART**


FRESH
POPCORN

AN ENSEMBLE CAST

How drug classes play their parts

CLIFFHANGER FOR A CURE

We're ready for a cure—*aren't we?*

AND THE NOMINEES ARE...

Recommendations for first-time therapy

ON WITH THE SHOW!

Moving beyond your diagnosis

POSITIVELY AWARE
JOURNALISM. INTEGRITY. HOPE.

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LIVE LIFE POSITIVELY AWARE

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TPAN was founded in 1987 in Chicago as Test Positive Aware Network, when 17 individuals gathered in a living room to share information and support in response to the HIV/AIDS epidemic. POSITIVELY AWARE is the expression of TPAN's mission to share accurate, reliable, and timely treatment information with anyone affected by HIV.

POSITIVE ROLES: LEFT TO RIGHT, TOP ROW: JOSEPH HUTTO, DANIELLE KRUSE, ARMANDO RAMIEREZ-GUZMAN. MIDDLE ROW: D'EVA LONGORIA, JOSHUA F. STOVALL, DOUG FERGUSON. BOTTOM ROW: JUDY BROWN, RENÉ GARZA, DUANE CRAMER.

MARCH+APRIL 2019

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EVERY ISSUE

The experience is your own, but you're not alone in the room

THE ROLE OF A LIFETIME: LEFT TO RIGHT, TOP ROW: JOSEPH HUTTO, DANIELLE KRUSE, ARMANDO RAMIREZ-GUZMAN. MIDDLE ROW: D'EVA LONGORIA, JOSHUA B. STOVALL, DOUG FERGUSON. BOTTOM ROW: JUDY BROWN, RENÉ GARZA, DUANE CRAMER.

THERE'S SOMETHING to be said about sitting in a darkened room with a bunch of a strangers, watching a film in a movie theater. Everyone is sharing the same experience, but how they react is uniquely their own response. That's the concept behind the cover of this year's HIV drug guide.

The nine people who took part in the drug guide cover shoot are all living with HIV. They shared their experiences and insights.

Armando Ramirez-Guzman, 38, has been living with HIV since 2003. The cover's concept resonated with him: "I not only advocate, I want people to understand that living with HIV is not an obstacle. You can live life, go out and have fun, and enjoy a movie date."

Joshua B. Stovall, 37, has been HIV positive 14 years: "I decided to be a part of this photo shoot to show my support of being in care, staying in care, and becoming virally suppressed. The power we all possess is to know. Knowing is half the battle. Knowledge is the pursuit of happiness."

Danielle Kruse, 48, was diagnosed with HIV in July 2016: "I was told I had been HIV positive for 12–20 years prior to my diagnosis. I want to encourage people to use PrEP and to get tested. I was a naïve Iowa girl who never thought I would get HIV. Anyone can get it. I took part in this photo shoot to break the stereotype of 'who gets HIV,' and to erase stigma."

Duane Cramer, 56, has been living with HIV since 1996; his father passed away in 1986 as a result of complications from HIV/AIDS: "I want to ensure that people who look like me and are like me—black, same-gender-loving men—are always represented in the rainbow of those affected by HIV. Black men who have sex with men still account for more than half of newly diagnosed cases of HIV and those living with HIV. So, for me, it is critical that we are visible, vocal, and open about our status."

A noted professional photographer himself, Cramer commented on the images from the shoot. "A key message that comes through is that taking HIV meds is simply a routine for those of us who happen to be HIV positive. My HIV treatment program is a small part of my daily life. Though mundane—like taking a shower, having a meal, or simply going to a movie, it is important."

For **D'Eva Longoria**, 43, a heterosexual transgender Latina, living life openly raises awareness and combats stigma: "You are stronger than HIV! It has been almost 10 years since I was diagnosed and I am at the happiest moment of my life!"

Doug Ferguson, 47, reflected on living more than half his life with HIV: "When I first learned about my HIV status, there were only a couple of medications available to treat HIV. My first HIV specialist advised me that I likely had no more than 10 years before I would develop AIDS and die. I've now lived for more than twice that time, thanks to advances in treatment. I've been symptom-free, healthy, and happy! I even finished an Ironman competition in 2012!"

"Being HIV positive for over 17 years has not slowed me down," says **René Garza**, 55, who has been positive since February 2002. "In fact, it's made me make better choices about my diet and exercise, and take better care of myself. For me, life goes on."

"Stay positive and learn everything you can from your doctor and your own research," offers **Joseph Hutto**, 35, who has been reading POSITIVELY AWARE ever since he was diagnosed seven years ago. "Knowledge is power! Use every resource you can get your hands on to arm yourself with information so you can best manage and maintain your own health and well being. Live life loudly and proudly!"

As the photo shoot neared completion, 67-year-old **Judy Brown**, HIV positive 26 years, looked about the set and observed, "We've come a long way, baby!"

—RICK GUASCO

THE COVER and additional pictures from this series were photographed by **John Gress** and styled by **Wyll Knight**, at **Pride Arts Center**, in Chicago.

THE **PHARMICIST**

Dr. Eric K. Farmer is an HIV clinical pharmacist at the Indiana University Health LifeCare Clinic at Methodist Hospital in Indianapolis. He was instrumental in starting formal clinical pharmacy services in 2009 at LifeCare, one of the largest providers of HIV medical services in the state of Indiana. At LifeCare, Dr. Farmer provides pharmacy services that include medication adherence counseling and patient education, drug information services, medication procurement, medication therapy management, and medical care coordination services. He currently serves as a clinical preceptor for APPE students, PGY1 residents, and PGY2 residents at IU Health and is on the clinical faculty of the Midwest AIDS Training and Education Center. He is involved in the PGY2 ID Residency Advisory Committee as well as the Indiana HIV/STD Advisory Council with the Indiana State Department of Health. Dr. Farmer graduated from Butler University with his Doctor of Pharmacy in 2007. He then completed an ASHP-accredited PGY1 pharmacy residency at Eskenazi Health (formerly Wishard Health Services) in Indianapolis, and subsequently an ASHP-accredited PGY2 HIV specialty pharmacy residency at the Center for HIV/AIDS Care and Research at Boston Medical Center.

THE **DOCTOR**

Dr. W. David Hardy currently serves as Adjunct Professor of Medicine at Johns Hopkins University School of Medicine and lives in Washington, D.C. His previous professional experience includes serving as Senior Director of Research at Whitman-Walker Health in D.C. (2015-2018), Chief Medical Officer of Calimmune, a translational science company investigating gene-modified cellular therapies as a potential cure for HIV (2013-2015) and Director of the Division of Infectious Diseases at Cedars-Sinai Medical Center and Professor of Medicine at the David Geffen School of Medicine at UCLA (2002-2013). Dr. Hardy has cared for persons with HIV infection since 1982 and conducted research on HIV and related diseases since 1984. Dr Hardy currently serves as Chair of the Board of Directors of the HIV Medicine Association (HIVMA) and Chair of the Education Committee of the American Academy of HIV Medicine (AAHIVM). He has worked with several community-based organizations, including AIDS Research Alliance, Alliance for Housing and Healing, Being Alive-Empowering People with HIV/AIDS, Project Angel Food, and AIDS Project Los Angeles.

THE **ACTIVIST**

Moisés Agosto-Rosario is a longtime treatment advocate and educator for people living with HIV/AIDS. A frequent public speaker and writer in both English and Spanish, Moisés has played a crucial role in ensuring that communities of color have equal access to care, treatment, and lifesaving information and has won numerous awards for his work with the HIV community. He is currently the Director of Treatment for NMAC (formerly known as the National Minority AIDS Council). Before joining NMAC, he worked as program manager for the International Treatment Preparedness Coalition (ITPC) with the HIV Collaborative Fund for HIV Treatment Preparedness, a project of the Tides Foundation. In this role, he was responsible for grant making activities in Latin America, the Caribbean, and Eastern Africa. Previous to ITPC he served as the Vice President and Managing Director for Community Access, a Nelson Communications Company and member of the Publicis Healthcare Group. Moisés served as the editor of *SIDA Ahora*, the Spanish publication of the People with AIDS Coalition of New York, and was an active member of ACT UP. Moisés graduated from the University of Puerto Rico in Rio Piedras with a B.A. in Literature and Education.

THE **ASSOCIATE EDITOR**

Enid Vázquez has been Associate Editor of POSITIVELY AWARE ever since she joined the magazine in 1995. She earned her B.A. in journalism from the University of Wisconsin-Madison. She interned at *The Chicago Reporter* and was a cub reporter for *The Hartford Courant*, the oldest continuously published newspaper in the United States. Her freelance work has appeared in publications around the country. She became interested in health reporting because of the importance it has on people's lives. It is a privilege to work on behalf of people living with HIV/AIDS, Enid says. She believes that HIV is as a much condition fueled by societal discrimination as it is by a virus. As such, it makes her reporting socio-political as well as medical. She enjoys reporting on medical updates and making them relatable to readers' lives. Enid has a special interest in sexual violence and sexual freedom, and in serving the sex trade worker and transgender communities.

THE **EDUCATOR**

Carla Blieden, PharmD, MPH, AAHIVP completed her Doctor of Pharmacy, Master of Public Health, and PGY1 Residency at the University of Southern California. She is certified as an HIV pharmacist and has worked as the clinical pharmacist at the Maternal, Child, and Adolescent/Adult Center, a family-centered HIV clinic in Los Angeles, for almost a decade. She works directly with patients focusing on adherence to HIV medication, managing other chronic diseases, and analyzing HIV medication resistance. Carla is adjunct faculty at USC School of Pharmacy where she lectures on HIV and her primary focus is the integration of Public Health within the school curriculum. She reviewed the DHHS guidelines and pull-out drug chart for this guide.

AGOSTO-ROSARIO BY JONATHAN TIMMES · BLIEDEN BY ISAAC MORA · FARMER AND VÁZQUEZ BY JOHN GRESS

MIXED EMOTIONS

I identified with your recent Editor's Note [Jan+Feb 2019]. I turned 80 in November after 30 years of being positive. I have mixed emotions about being a long-term survivor because the increasingly painful effects of age-related degenerative diseases are threatening my joy of life.

As you pointed out, aging with HIV disease is a process of loss, both of loved ones and of self-image. Even though I consider myself to have lived a productive, successful life, I still have periods of depression and sadness. The emotional toll of this disease is profound, indeed.

Thanks for your work to publish an informative magazine.

—**JERE ERICKSON**
SAN DIEGO, CALIFORNIA

EDUCATING

I am a peer educator here at Telford Unit, New Boston, Texas and have been receiving your magazines for four months already (two issues). I just want to say thank you. I've learned a lot of valuable information and our peers have learned a lot, too. You're doing an awesome job. Your hard work is changing lives here in Telford Unit. Thank you once again.

NAME WITHHELD
NEW BOSTON, TEXAS

GET YOURS NOW

I work at JustUs Health (formerly the Minnesota AIDS Project). We have gotten drug guides from you every year in the past to help our HIV case managers as well as to put up in our client rooms. They have been *super* helpful and we are interested in getting more this year. The person at our agency responsible for getting copies of these in the past no longer works here, so I am reaching out to see if I could get connected to the right person to request some drug guides for this year. I know I am a bit early still, but wanted to start on this now to be prepared.

—**MATT JOHNSON**
MINNEAPOLIS, MINNESOTA

I'm Melissa Watkins, formerly of Accordant Health Services, and am starting off the new year with a new job with AHF in Lithonia, Georgia. I brought your wonderful HIV drug chart and posted it. The doctors here also saw the smaller tri-fold pocket edition of the chart, and wanted their own. Now *everybody* wants one!

When the 2019 pocket edition charts roll out, we want those, too! I so appreciate you all, and attribute my learning the meds to your work!

Much love to you, and yours in the mission.

—**MELISSA WATKINS**
LITHONIA, GEORGIA

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THINK GREEN.
PLEASE RECYCLE
THIS MAGAZINE
WHEN FINISHED.

PHOTO: JOHN GRESS

EDITOR'S NOTE

JEFF BERRY

STOP. LOOK. LISTEN.

Instead of hurrying through life, take a moment to breathe

In early September of last year I was attending the United States Conference on AIDS in Orlando and running late for a dinner I had been invited to that evening. AIDS conferences are the endurance marathons for AIDS activists, from the moment you wake up until you hit your pillow late at night you are literally running from session to meeting to workshop to reception, just to get up and do it all over again. This goes on for a number of days, and you're lucky if you get five to six hours of sleep each night. Invariably when you get home you are exhausted and spent—but in a good way.

As I was hurrying down a long, wide corridor filled with people scurrying to their own reception/dinner/meeting, one person headed toward me in the opposite direction caught my eye. She seemed to recognize me but I was pretty sure I didn't know her, and I was late for my dinner, so I smiled back but decided to keep moving. But then as we neared each other we both stopped, and she began to talk. And my eyes started to well up as she shared her story.

She introduced herself and said she wanted to thank me. When she was incarcerated (she explained then and in a subsequent conversation) they would send her to a local HIV clinic every three months, and that is where she discovered POSITIVELY AWARE. She told me it gave her hope—I think her exact words were, *it saved my life*. She told me that reading about my personal journey and my own struggles touched her deeply during a dark time in her life (she had learned she was HIV positive and had lost a friend due to complications from AIDS), but by reading the magazine somehow she knew she was going to be okay. She knew nothing about which regimens to take, or what resources were there for her, but she learned how to formulate questions for her doctor and get the care that she needed.

I told her how glad I was to have made a difference in some small way, and how much it meant to me that she shared her story with me. We exchanged cards, and both went on our busy way, but I have never forgotten that moment—it will stay with me for the rest of my life.

So this is why we do what we do, why this issue you are holding in your hands is so important, and demonstrates the incredible power that knowledge and sharing our stories can hold. This is our annual HIV Drug Guide, our 23rd to be exact (I always like to point out that there were only three drugs in the first drug guide). It's not meant to be read from cover to cover, although there is probably that one person out there who does that (*thank you!*). Rather, glean from it what you will, and keep the issue handy all year round for when you need it again. For some that means if you are starting treatment for the first time, the DHHS guidelines ("And the Nominess Are..." on page 13) show which regimens are recommended. If you are experiencing a side effect, or suspect a drug interaction, go to that section on the drug page to learn more. And if you like looking at pretty pictures of pills, the pullout HIV drug chart is just for you!

This is why we do what we do, why this issue you're holding in your hands is so important, and demonstrates the incredible power that knowledge and sharing our stories can hold.

I would be remiss not to thank all of the many people involved in the making of the drug guide, starting with Associate Editor Enid Vázquez and our pharmacist Eric Farmer, PharmD, who update the bulk of this huge bear (special thanks to Eric for his excellent writing and review); Creative Director Rick Guasco, whose fantastic design and amazing covers continue to blow me away; the talented Dr. W. David Hardy and Moisés Agosto-Rosario for their expertise and insight; Carla Blieden, PharmD, who came out of the blue to volunteer her help and is now part of the team; the mastery and beauty of photographer John Gress; our eagle-eye proofreader Jason Lancaster; with additional thanks to Drew Halbur, BSPharm, and all of the wonderful people at Walgreens; and the staff of TPAN for putting up with us and our craziness while we are on deadline.

It really does take a village, and it's important to stop and take the time to listen to each other. No one is an island. Individually we can make our own personal achievements, but collectively and working together we can change lives.

Take care of yourself, and each other.

@PAeditor

CLIFFHANGER FOR A CURE

Are we ready for a cure for HIV? Of course we are, *aren't we?*

BY **W. DAVID HARDY, MD**

A brief history of curing viral infections in humans

Almost as soon as HIV was identified in 1983 as the cause of AIDS, the clamor for a cure for this insidious viral infection began. The repeated failures and numerous tales of human tragedy that followed gave rise to a sense of unattainable loftiness reserved only for distant dreams, not reality. This sense of unattainability was shattered in 2007, with the initial reports of Timothy Brown—the Berlin patient—the only person to have ever been cured of HIV. The door was cracked opened at last; we were on our way. Right?

Maybe not so fast. Let's take a small dose of reality and look carefully at our medical track record for curing viral infections. In 1983, modern medicine had rarely ever cured a life-threatening viral infection, except perhaps herpes simplex (HSV) encephalitis (brain infection), initially with the old chemotherapy agent vidarabine and later with the more effective and less toxic acyclovir. But even in those cases, the virus causing the serious infection, while significantly tamped down and put into latency, was still able to recur in the surviving person's future. It was not eradicated. Since those early days, successful suppressive treatments for many members of the herpes family of viruses [HSV-1 & -2, VZV (chicken pox/shingles virus), CMV (retinitis, colitis), EBV (infectious "mono" virus)] have been developed to suppress these potentially life- and sight-threatening viral infections, but not to cure them.

The biggest breakthrough in truly curing a viral infection came only within the last 10 years with the development and approval of many all-oral, non-interferon-containing, single-tablet regimen (STR) combination treatments for hepatitis C (HCV). Currently 90–100% of persons with almost any type of HCV, at any stage of liver disease or treatment history, with or without HIV can be cured of this infection with 8 to 12 weeks of a one-pill-once-a-day treatment. The chances of cured HCV infection coming back is very, very low, unless the cured person re-engages in high-risk behavior for acquiring the infection.

So, why was HCV so "easy" to cure and HIV not so?

First, it is important to point out that HCV became curable based upon essential new scientific knowledge that came from research discoveries on HIV treatment. The four classes of direct-acting agents (DAAs) that have revolutionized HCV treatment to create a cure are heavily based upon scientific discoveries about viruses made while scientists were studying HIV. Second, there is a *big* difference between the two viral infections, which makes them very different targets for cure—HCV does not "integrate" or insert its genetic material into the DNA of human cells that it infects like HIV does to the human cells which it infects. Eradicating non-integrated HCV genes from a human cell is much easier than the task of cutting out integrated HIV genes from an infected human CD4+ T cell. When HIV "splices" its genetic material into the DNA of human cells, its genes continue to be carried in those cells and all "daughter" cells that come from those cells for as long as they live. Thus, the challenge of curing an integrated viral infection like HIV is a much higher bar.

But wait, what about our highly effective antiretroviral therapy? Why isn't it enough to cure HIV?

It's certainly true that our current antiretroviral treatment (ART) is highly effective and has greatly diminished the death and destruction that HIV has waged on humans in many parts of the world. But these agents have important limitations. First, they can only work when virus is in its "actively replicating" phase—that is, when it is churning out large numbers of new infectious viruses to travel throughout the body to infect new cells. Second, when virus enters its latent, or "sleeping," phase, antiretrovirals are no longer effective against the dormant, integrated virus that has been spliced into human CD4+ T cells. It is, in fact, this phase of HIV infection that makes up the often spoken about "latent viral reservoir," which is referring to those pieces of viral genetic material quietly sleeping inside of human immune cells (CD4+ T cells), that has the potential to reactivate and produce new viruses which can infect new cells. Fortunately, the number of these latently infected cells is small. It is estimated that only 1 to 60 per 1 million CD4+ T cells are latently infected with HIV. Even though this "1-in-a-milion" or so number sounds very small, it is enough to allow HIV to re-emerge in the blood of people living with HIV (PLWH) who stop their HIV medications

PHOTO: JOHN GRESS

after being undetectable for many, many years. And this generally happens within 4 to 8 weeks after stopping antiretrovirals in most PLWH on ART. Thus, this is our formidable, final hurdle between us and a cure for HIV.

Scaling the final hurdle of the latent viral reservoir

HIV researchers usually fall into two basic camps: the immunologists—the scientists who are experts on our incompletely understood human immune system which protects us from both foreign invaders (infections) and internal invaders (cancer)—and the virologists, those scientists who are experts on every aspect of how viruses reproduce themselves and cause disease, and then finding their "Achilles' heels" to attack and stop them from doing harm. We owe a great deal to the virologists for much of the success of combination ART.

When we think about curing HIV, many tough scientific questions are directed to both virologists and immunologists.

Virologists

The virologists will help us better understand and discover holes in the way that HIV goes into its latent (or sleeping) phase so that we can use that information to shock it awake and attack it, lock it in that phase for good, or prevent it from going latent in the first place. They will discover ways to protect CD4+ T cells from being susceptible to HIV; that is, to make them "uninfectable," by blocking the entrance sites that HIV uses to enter and infect T cells.

Finding creative ways to use "gene editing" technology to cut out the integrated HIV genes from the DNA of CD4+ T cells to free them from viral control will also be one of the virologists' goals. Gene therapy, the science of adding, deleting, or blocking genes within the human DNA, is still in its infancy for treating human disease; however, at least one gene therapy has been approved by the FDA as treatment for a childhood cancer.

Many of these areas of research are already well underway; some have shown promise, others have not and are being abandoned, and still others have already "gone back to the drawing board" for a second or third revision and re-try.

Immunologists

Immunologists will help us better understand how we can create "new immunity," or resistance against HIV in PLWH who did not have that immunity when they first encountered the virus and became infected. In other words, they will help us learn how to retrain or rebuild the immune systems of PLWH to become HIV-resistant without ART.

With previous serious viral infections, such as polio, small pox, and measles, many people became infected but survived the infection without treatment. This observation told us that the human immune system could be re-trained or re-engineered to resist those viruses.

The ability to "train" the human immune system to

Infections are rarely, if ever, truly eradicated from humans.
It's the immune system that is 'trained' to do the work.

resist viral infections has become a commonly used and effective preventative force against viral infections—better known as vaccination or immunization. In fact, immunization against viral illnesses has been the major way that we have controlled these infections for the last 150 years.

Unfortunately, there are no known human beings who have developed long-term, natural immunity against HIV. So, we do not have a proven natural pathway to follow as we have had with other viral infections. (Elite and viremic "controllers," those PLWH who have undetectable viral loads or less than 2,000 copies/mL without ART, are our closest guides to how humans can naturally resist HIV. Unfortunately, it is estimated that only 1% to 3% of PLWH fall into the controller category.)

How to best create new immunity for PLWH is going to be a challenge the likes of which human medicine has only overcome once before. That previous life-saving treatment is for advanced cancers (lymphoma, leukemia) which could not be cured with usual chemotherapy and radiation therapy.

That treatment is called stem cell transplantation. It involves taking the youngest, freshest cells of the immune system, called stem cells, from the bone marrow of the same person (for lymphoma) or from another person (for leukemia) and giving them to the person with cancer. This is done after all cancer (and immune system) cells of that person have been destroyed with large doses of chemotherapy and radiation therapy. In other words, the cancer and the immune system of the person are first destroyed and then replaced with healthy new immune cells. The slate is wiped clean of cancer and a new, healthy immune system is rebuilt.

This is the process that Timothy Brown underwent to cure his leukemia, and as an added benefit, cured him of HIV. However, the risk of destroying a person's immune system and replacing it with a new, cancer-free one is only balanced by the benefit of not dying from an otherwise fatal cancer. The risk-to-benefit ratio of using stem cell transplantation as a cure for both cancer and HIV has been positive, but in only 1 of over 10 attempts.

Is Timothy Brown's story enough to urge other PLWH to take on this risk? Certainly, if they have lymphoma or leukemia unresponsive to treatment, but what about PLWH without cancer?

Another potentially promising immune-boosting therapy already approved for cancer treatment and sometimes cure is a new class of medications called immune checkpoint inhibitors (ICIs). These human antibody treatments are aimed at reviving "overstimulated" and "exhausted" T cells which have been turned off by a natural immune shut-off valve. ICIs are designed to block this turn-off switch, a state commonly found in T cells in PLWH, and thereby turn the immune system back on.

Using one's own revitalized T cells to fight one's HIV makes good sense, right? While these treatments have shown promise in many cancers, they can also potentially cause the immune system to attack non-HIV-infected cells and cause long-term side effects such as low thyroid hormone levels, requiring the affected person to take thyroid hormone replacement for life.

Here again, are the now proven positive treatment results in persons with cancer adequate to explore these therapies in PLWH?

Are we ready for a cure for HIV? Of course we are, aren't we?

A growing number of research publications, from several parts of the world, written almost exclusively by PLWH and other community advocates, have documented the PLWH community's ever vigilant, but hopeful, attitudes, feelings, fears, and aspirations for a cure for HIV. In addition to providing a cogent, irreplaceable voice for the persons central to this entire discussion, these publications have reflected the need for continued frank discussion and education for both the research and PLWH advocacy communities to improve communication and avoid misunderstandings.

For example, it has been reported that PLWH prefer the term "eradicating" rather than "sterilizing" when describing a cure that will remove all traces of HIV from a PLWH's body. This justifiably stems from the negative fertility connotations associated with the term "sterilizing". Further, PLWH prefer an "eradicating" versus a "functional" cure (ART-free remission from HIV without all traces of the virus removed but rather held in check by new anti-HIV immunity) due to concerns that the virus may return and become resistant to ART. From a scientific/medical standpoint, expectations of a truly eradicating cure may be too high and unattainable. The best outcome that medical science has ever accomplished in treating infectious diseases among humans has been to decrease the amount of infection to a level that the immune system can control it for a lifetime, or at least many years. Infections are rarely, if ever, truly eradicated from humans. It's the immune system that is "trained" to do the work.

It goes without saying that a renewed, reinvigorated, and mutually respectful partnership is needed between the PLWH and scientific/medical communities as we all embark on our greatest challenge to date—to cure HIV. Exceptional, new, out-of-the-box thinking and exquisitely refined new takes on old ideas will be needed as the journey unfolds. Voluntary altruism, once so evident and proudly practiced in the earlier years of the epidemic, will be encouraged and respected. Carefully worded, clear, and trusting communication, both oral and written, using language comfortable for all involved will be the order of the day. Borrowing from the lessons learned from the days of drug development of our currently available ART, successful cure strategies will most likely be given as combination treatments, perhaps in series, perhaps together. Unlike those drugs which are primarily oral and tablet-based, cure strategies may well involve more procedures, intravenous infusions, and longer periods of follow-up to see if they work. There is no doubt that the rationale for, the desire for, and the understanding of what a cure for HIV means will be different and perhaps unique to everyone involved, but the common purpose for treading this uncharted road together will make it bearable and successful. PA

W. DAVID HARDY, MD, is Adjunct Professor of Medicine, Division of Infectious Diseases at the Johns Hopkins University School of Medicine.

The category is DHHS guideline recommendations for first-time therapy

And the nominees are...

Most people starting HIV treatment for the first time (treatment-naïve) should take one of the following:

- Biktarvy
- Triumeq
- Tivicay plus Descovy or Truvada
- Isentress HD or Isentress, plus Descovy or Truvada

In certain clinical (health) situations, first-time folks may take one of the following regimens. They are effective and tolerable but have some disadvantages when compared with the regimens listed above or have less supporting data from randomized clinical trials.

- Symtuza; Prezcobix or Prezista plus Norvir, with Descovy, Truvada, or Epzicom
- Delstrigo; or Pifeltro plus Descovy
- Evotaz or Reyataz plus Norvir, with Descovy, Truvada, or Epzicom
- Odefsey or Complera
- Genvoya or Striblid
- Atripla; Sustiva plus Descovy; or Symfi or Symfi Lo
- Isentress or Isentress HD, plus Epzicom

That's according to HIV treatment guidelines from the U.S. Department of Health and Human Services (DHHS).

Lots of people, however, are not taking HIV therapy for the first time; for example, people who are on therapy and virally suppressed may choose to switch to another regimen for improved tolerability or to avoid drug interactions. The guidelines have lots to say about that and other situations.

A more detailed list

An antiretroviral (ARV) regimen for a treatment-naïve individual is usually made up of two nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (also known as a booster; the two drugs used for this purpose are cobicistat and ritonavir). (See charts on the following pages.)

A pregnancy test should be performed for those of childbearing potential prior to the initiation of INSTI therapy.

A regimen should be individualized on the basis of virologic efficacy (suppression of viral load to less than 50 copies per mL), toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, comorbid conditions (such as kidney disease, hepatitis B or C, etc.), and cost. More details including recommendations for treatment-experienced individuals and those for pregnant women are available online. Preliminary data have raised concerns about an increased risk of neural tube defects in infants born to people who were receiving dolutegravir (DTG) at the time of conception. Before prescribing DTG or another INSTI, refer to Table 6b in the guidelines for specific recommendations on initiating these drugs as part of initial therapy.

AIDSinfo has free mobile applications that allow access to federally approved HIV/AIDS treatment and research information, including a Guidelines mobile app, at aidsinfo.nih.gov/apps.

GRAZVYDAS-ISTOCKPHOTO

RATING OF RECOMMENDATIONS

A: Strong
B: Moderate
C: Optional

RATING OF EVIDENCE

I: Data from randomized controlled trials
II: Data from well-designed non-randomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies
III: Expert opinion

KEY TO ACRONYMS

3TC: lamivudine
ABC: abacavir
ART: antiretroviral therapy
ARV: antiretroviral
ATV: atazanavir
ATV/c: atazanavir/cobicistat
ATV/r: atazanavir/ritonavir
BIC: bictegravir
CD4: CD4 T lymphocyte, "T cell"
DOR: doravirine
DRV: darunavir
DRV/c: darunavir/cobicistat
DRV/r: darunavir/ritonavir
DTG: dolutegravir
EFV: efavirenz
EVG: elvitegravir
EVG/c: elvitegravir/cobicistat
FDA: Food and Drug Administration
FTC: emtricitabine
HLA: human leukocyte antigen
INSTI: integrase strand transfer inhibitor
NNRTI: non-nucleoside reverse transcriptase inhibitor
NRTI: nucleoside reverse transcriptase inhibitor
PI: protease inhibitor
RAL: raltegravir
RPV: rilpivirine
STR: single-tablet regimen
TAF: tenofovir alafenamide
TDF: tenofovir disoproxil fumarate

Rising to the

MOST PEOPLE STARTING HIV TREATMENT for the first time (treatment naïve) should take one of the following: Biktarvy; Triumeq; Tivicay plus Descovy or Truvada; or Isentress HD or Isentress, plus Descovy or Truvada.

Recommended initial regimens for most people with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI + 2 NRTIs

BIC FTC TAF

Biktarvy (BIC/FTC/TAF): AI

DTG ABC 3TC

Triumeq (DTG/ABC/3TC) if HLA-B*5701-negative: AI

DTG FTC TAF OR TDF

Tivicay (DTG) with **Descovy** (FTC/TAF) or **Truvada** (FTC/TDF): AI

RAL FTC TAF OR TDF

Isentress HD or Isentress (RAL) with **Descovy** (FTC/TAF): BII or **Truvada** (FTC/TDF): BI

Recommended initial regimens in certain clinical situations

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

Boosted PI + 2 NRTIs

(In general, boosted DRV is preferred over boosted ATV.)

DRV/c OR DRV/r FTC[1] TAF OR TDF

Symtuza (DRV/c/TAF/FTC) or **Prezcobix** (DRV/c) or **Prezista + Norvir** (DRV/r), with **Descovy** (FTC/TAF) or **Truvada** (FTC/TDF): AI

ATV/c OR ATV/r FTC[1] TAF OR TDF

Evotaz (ATV/c) or **Reyataz + Norvir** (ATV/r), with **Descovy** (FTC/TAF) or **Truvada** (FTC/TDF): BI

DRV/c OR DRV/r ABC 3TC

Prezcobix (DRV/c) or **Prezista + Norvir** (DRV/r), **with Epzicom** (ABC/3TC) If HLA-B*5701-negative: BII

occasion

Recommended initial regimens in certain clinical situations

NNRTI + 2 NRTIs

Delstrigo (DOR/TDF/3TC): BI;
or **Pifeltro** (DOR) with
Descovy (FTC/TAF): BIII

Atripla (EFV/FTC/TDF): BI;
or **Sustiva** (EFV) +
Descovy (FTC/TAF): BII;
or **Symfi** (EFV/3TC/TDF): BI

Odefsey (RPV/FTC/TAF) or
Complera (RPV/FTC/TDF)
If HIV RNA <100,000 copies/mL
and CD4 >200 cells/mm^3: BI

INSTI + 2 NRTIs:

Isentress HD
or **Isentress** (RAL)
with **Epzicom** (ABC/3TC)
If HLA-B*5701–negative and
HIV RNA < 100,000 copies/mL: CII

Genvoya (EVG/c/TAF/FTC) or
Stribild (EVG/c/FTC/TDF):
BI

Regimens to consider when ABC, TAF, and TDF cannot be used or are not optimal

Tivicay (DTG) with
lamivudine (3TC):
BI

Prezista + Norvir (DRV/r) with
Isentress (RAL):
If HIV RNA <100,000 copies/mL
and CD4 >200 cells/mm^3: CI

Prezista + Norvir (DRV/r)
with **lamivudine** (3TC):
CI

FOOTNOTE
1 **Lamivudine (3TC)** may substitute for emtricitabine (FTC) or vice versa.

NOTES:
- **Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF)** are two forms of tenofovir that are approved by the Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between the two.
- **raltegravir** (RAL) can be given as RAL 400 mg twice daily or RAL 1200 mg (two 600 mg tablets) once daily.

NOTE: THE FOLLOWING ARE AVAILABLE AS CO-FORMULATED DRUGS (NOT A COMPLETE LIST)

Epzicom
ABC/3TC

Evotaz
ATV/c

Biktarvy
BIC/FTC/TAF

Delstrigo
DOR/3TC/TDF

Prezcobix
DRV/c

Symtuza
DRV/c/FTC/TAF

Triumeq
DTG/ABC/3TC

Symfi
EFV 600 mg/3TC/TDF

Atripla
EFV/FTC/TDF

Genvoya
EVG/c/FTC/TAF

Stribild
EVG/c/FTC/TDF

Odefsey
RPV/FTC/TAF

Complera
RPV/FTC/TDF

Descovy
FTC/TAF

Cimduo or Temixys
3TC/TDF

Truvada
FTC/TDF

POSITIVELY AWARE

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WHEN DRUGS COLLIDE!

Understanding drug interactions

A DRUG INTERACTION is a reaction between two (or more) drugs (called a **drug-drug interaction**) or between a drug and a food or beverage (called a **drug-food interaction**). An existing medical condition can make certain drugs potentially harmful (called a **drug-condition interaction**). For example, taking a nasal decongestant if you have high blood pressure may cause an unwanted reaction.

Medicines help us feel better and stay healthy. But drug interactions can cause problems by reducing or increasing the action of a medicine or causing adverse (unwanted) side effects.

Are drug interactions a problem for people with HIV?

Treatment with HIV medicines (called antiretroviral therapy or ART) helps people with HIV live longer, healthier lives. But drug interactions, especially drug-drug interactions, can complicate HIV treatment.

Drug-drug interactions between HIV medicines are common, and may reduce or increase the concentration of an HIV medicine in the blood. This can make the affected HIV medicine less effective, or increase levels that also increase the risk of side effects.

Drug-drug interactions between HIV medicines and other medicines may make hormonal birth control less effective. Women using hormonal contraceptives may need to use an additional or different method of birth control to prevent pregnancy.

Can drug-food interactions and drug-condition interactions affect people with HIV?

Yes, the use of HIV medicines can lead to both drug-food interactions and drug-condition interactions.

Food or beverages can affect the absorption of some HIV medicines and increase or reduce the concentration of the medicine in the blood. Depending on the HIV medicine, the change in concentration may be helpful or harmful. Instructions for HIV medicines affected by food specify whether to take the medicine with or without food. (HIV medicines not affected by food can be taken with or without food.)

Pregnancy is a condition that can affect how the body processes HIV medicines.

Because of pregnancy-related changes, dosing of an HIV medicine may change during different stages of pregnancy. But pregnant women should always consult with their health care providers before making any changes to their HIV regimens.

How can I avoid drug interactions?

Tell your health care provider about all prescription and non-prescription medicines you are taking or plan to take. Also tell your health care provider about any vitamins, nutritional supplements, and herbal products you take.

Before taking a medicine, ask your health care provider or pharmacist these questions:

- How should I take the medicine?
- While taking the medicine, should I avoid any other medicines or certain foods or beverages?
- Can I take this medicine safely with the other medicines that I am taking? Are there any possible drug interactions I should know about? What are the signs of those drug interactions?
- In the case of a drug interaction, what should I do?

Take medicines according to your health care provider's instructions. Drug labels and package inserts include important information about possible drug interactions. Tell your health care provider if you have any side effect that bothers you or that does not go away.

LEARN MORE about drug interactions at aidsinfo.nih.gov/drugs and fda.gov.

Supporting role

HIV treatment can be costly, but there's help

Today's therapies are vastly improved over the first drugs used to treat HIV, but these advancements come at a cost. The prices of HIV drugs continue to rise every year at an average of 7–9 percent. While in the past these increases usually haven't directly affected someone who has drug coverage through their health insurance plan, increasingly individuals have to pay co-insurance (a percentage of the cost of the medication). The good news is that help is out there. State AIDS Drug Assistance Programs (ADAPs), several non-profit organizations, and the pharmaceutical companies themselves have programs in place to help you pay for the treatment you need.

A cost-sharing assistance program (CAP, also know as a co-pay program) is a program operated by pharmaceutical companies to offer cost-sharing assistance (including deductibles, co-payments, and co-insurance) to people with private health insurance to obtain HIV drugs at the pharmacy. Unfortunately many big health insurers have now introduced co-pay accumulators to their plans, and no longer allow the amount of the co-pay cards to be applied towards their deductible or out-of-pocket maximum, or steer them towards other cost-containing measures such as step therapy or individual generics that break up an STR. When choosing your healthcare plan, make sure your drug is covered (on the plan formulary) and know which drug tier it is in (your cost for the drug co-pay is based on which tier, or category, it falls under).

A patient assistance program (PAP) is a program run through pharmaceutical companies to provide free or low-cost medications to people with low incomes who do not qualify for any other insurance or assistance programs, such as Medicaid, Medicare, or AIDS Drug Assistance Programs (ADAPs). Each individual company has different eligibility criteria for application and enrollment in their patient assistance program.

HarborPath, a non-profit organization that helps uninsured individuals living with HIV gain access to brand-name prescription medicines at no cost, operates a special patient assistance program for individuals on ADAP waiting lists. An individual is eligible for the HarborPath ADAP waiting list program only if he or she has been deemed eligible for ADAP in his or her state and is verified to be on an ADAP waiting list in that state.

Applying for PAPs

In 2012, 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 form that can be used by both providers and patients. This combines common information collected on each individual company's form to allow individuals to fill out just one. Once the form is completed, case managers or individuals then submit the single form to each individual company, reducing the overall amount of paperwork necessary to apply for a patient assistance program.

In addition to serving as a special PAP for ADAP waiting list clients, HarborPath operates as a streamlined, online portal for PAP access. HarborPath creates a single place for application and medication fulfillment. This "one stop shop" portal provides a streamlined, online process to qualify individuals and deliver the donated medications of the participating pharmaceutical companies through a mail-order pharmacy.

INFORMATION IN THIS ARTICLE and the following tables is adapted from NASTAD's "HIV Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs": nastad.org/resource/pharmaceutical-company-hiv-patient-assistance-programs-and-cost-sharing-assistance-programs.

COST-SHARING ASSISTANCE PROGRAMS (CAP)

DRUGS COVERED	MANUFACTURER AND CONTACT INFORMATION	ASSISTANCE	RENEWAL
Kaletra and **Norvir**	**AbbVie** 800-441-4987, option 4; kaletra.com; norvir.com	**Kaletra:** Co-payment assistance covers the first $400 per prescription per month. **Norvir:** Covers up to $1,200 a year for co-payments.	Renews as long as criteria are met
Evotaz, **Reyataz**, and **Sustiva**	**Bristol-Myers Squibb** 888-281-8981; bmscustomerconnect.com/bms3assist	**Evotaz, Reyataz, and Sustiva:** Up to $7,500 annually for co-payments, deductibles, and co-insurance in all commercially-insured plans.	Automatic renewal
Atripla, **Biktarvy**, **Complera**, **Descovy**, **Emtriva**, **Genvoya**, **Odefsey**, **Stribild**, **Truvada**, and **Tybost**	**Gilead Sciences** 800-226-2056; gileadadvancingaccess.com	**Biktarvy, Genvoya, Stribild, and Truvada:** Covers the first $7,200 per year of co-payments. **Atripla, Complera and Odefsey:** Covers the first $6,000 per year of co-payments. **Descovy:** Covers the first $4,800 per year of co-payments. **Emtriva:** Covers the first $300 per month/$3,600 per year of co-payments. **Tybost:** Covers the first $50 per month/$600 per year of co-payments.	Automatic renewal
Edurant, **Intelence**, **Prezista**, **Prezcobix**, and **Symtuza**	**Janssen Therapeutics** 866-836-0114; edurant.com; intelence.com; prezista.com; prezcobix.com; symtuza.com	Covers the first $7,500 per year of co-payments, deductibles, and co-insurance.	Reapply each year
Delstrigo, **Isentress**, **Isentress HD**, and **Pifeltro**	**Merck and Co.** 800-444-2080; isentress.com	Covers the first $6,800 per year of co-payments, deductibles, and co-insurance for each of 12 eligible prescriptions.	Enrollment is valid until coupon expires, 12/31/2019
Cimduo, **Symfi**, and **Symfi Lo**	**Mylan** **800-657-6713**; cimduo.com; symfi.com; symfi-lo.com	**Symfi** and **Symfi Lo:** Covers up to $6,000 annually in out of pocket expenses for prescriptions for those with commercially available insurance. **Cimduo:** Covers up to $4,800 per year.	Reapply each year
Trogarzo	**Theratechnologies** 833-238-4372; trograzo.com; therapatientsupport.com	Contact program for details	
Juluca, **Lexiva**, **Rescriptor**, **Retrovir**, **Selzentry**, **Tivicay**, **Triumeq**, **Trizivir**, **Viracept**, and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVconnect.com	**Juluca**, $6,250; **Tivicay**, $5,000; and **Triumeq**, $7,500 per year/per patient maximum. **Lexiva, Rescriptor, Retrovir, Selzentry, Trizivir, Viracept, and Ziagen:** $4,800 per year/per patient maximum.	Automatic renewal
Invirase and **Viread**	**Patient Access Network Foundation** 866-316-7263; panfoundation.org	Maximum benefit is $3,600 per year. Patients may apply for a second grant during their eligibility period subject to availability of funding.	Reapply each year

PATIENT ASSISTANCE PROGRAMS (PAP)

DRUGS COVERED	MANUFACTURER AND CONTACT INFORMATION	FINANCIAL ELIGIBILITY
Kaletra, Norvir	**AbbVie** 800-222-6885; kaletra.com; norvir.com (co-pay information only); abbviepaf.org	**Kaletra:** 500% FPL **Norvir:** No income limits
Aptivus, Viramune XR	**Boehringer Ingelheim** 800-556-8317; bipatientassistance.com	500% FPL
Evotaz, Reyataz, and **Sustiva**	**Bristol-Myers Squibb** 888-281-8981; bmscustomerconnect.com/bms3assist	300–500% FPL
Atripla, Biktarvy, Complera, Descovy, Emtriva, Genvoya, Odefsey, Stribild, Truvada, and **Tybost**	**Gilead Sciences*** 800-226-2056; gileadadvancingaccess.com	500% FPL
Edurant, Intelence, Prezista, Prezcobix, and **Symtuza**	**Janssen Therapeutics** 800-652-6227; jjpaf.org	300% FPL
Crixivan, Delstrigo, Isentress, Isentress HD, and **Pifeltro**	**Merck and Co.** 800-727-5400; merckhelps.com; delstrigo.com; isentress.com; pifeltro.com	500% FPL
Trogarzo	**Theratechnologies** 833-238-4372; trogarzo.com	Call program for details
Combivir, Epivir, Epzicom, Lexiva, Juluca, Rescriptor, Retrovir, Selzentry, Tivicay, Triumeq, Trizivir, Viracept, and **Ziagen**	**ViiV Healthcare** 844-588-3288; ViiVconnect.com	500% FPL

* Patients who are insured and who do not meet their payer's coverage criteria are no longer eligible for support via Gilead's patient assistance program. This includes clients whose insurer has limited access based on: step-therapy or clinical criteria (e.g., drug and alcohol testing).

FOUNDATIONS

PROVIDING ACCESS TO CARE ASSISTANCE FOR PEOPLE LIVING WITH HIV

Harbor Path
harborpath.org
Provides access to free medications for uninsured people living with chronic illnesses; administers AIDS Drug Assistance Program (ADAP) Waiting List Program.

PAN Foundation
panfoundation.org
(866) 316-7263
Provides necessary healthcare treatments to the underinsured population.

Patient Advocate Foundation
patientadvocate.org
(800) 532-5274
Provides arbitration, mediation, and negotiation services to settle issues with access to care, medical debt, and job retention related to illness.

ADDITIONAL RESOURCES

THESE MAY BE OF INTEREST TO INDIVIDUALS LIVING WITH HIV

Clinical Trials
clinicaltrials.gov
A service of the U.S. National Institutes of Health, ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

Fair Pricing Coalition (FPC)
fairpricingcoalition.org
As part of their advocacy work, the Fair Pricing Coalition (FPC) negotiates with companies to ensure that cost-sharing and patient assistance programs are adequately generous and easy to apply for.

Health Insurance Marketplace
healthcare.gov
The official site of the Health Insurance Marketplace, Healthcare.gov allows individuals and families to sign up for insurance coverage through the Affordable Care Act.

Treatment Action Group
treatmentactiongroup.org
Treatment Action Group collaborates with activists, community members, scientists, governments, and drug companies to ensure that all people with HIV, TB, or HCV receive lifesaving treatment, care, and information.

On with the show!

Moving beyond your diagnosis—finding a provider, knowing your rights, and more

HIV treatment

It's recommended that everyone with HIV be on antiviral therapy. It's been shown that with early treatment, people living with HIV will live a near-normal lifespan. Treatment also prevents transmission of the virus.

Find an HIV specialist

It's good to find a medical provider who treats other people with HIV, or is knowledgable about treating HIV; look for an HIV specialist. The American Academy of HIV Medicine and the HIV Medicine Association each have a provider finder. Go to hivma.org and aahivm.org. In addition, your local AIDS service organization knows the HIV specialists in your area, and can help point you in the right direction.

Medical care

Ideally, people with HIV should have a CD4+ T cell count and HIV viral load measured every three to four months following suppression of HIV viral load with the use of effective antiretroviral therapy (ART). Testing every six months and even annually may be acceptable once your virus is undetectable for an extended period of time and you are in general good health.

- The T-cell count is a measure of immune function.
- Viral load is a measure of how much virus is in your blood.
- Generally, the viral load test result is given greater weight.

Baseline

At diagnosis or soon thereafter and before starting treatment, your clinic should check you for:

- Other STIs
- HIV drug resistance
- Hepatitis B and C

Insurance

Just because you have health insurance doesn't mean that treatment is free. There are co-pays and other costs for medical care. (See the cost-sharing and medication assistance charts beginning on page 21.) For those without insurance, check with your state's AIDS Drug Assistance Program (ADAP), or go to healthcare.gov, or call (800) 318-2596.

HIV and the ADA

How are people with HIV protected by the nation's disability law? Read the section on HIV from the Americans with Disabilities Act at ada.gov/archive/hivqanda.txt.

HIV anti-discrimination law

The National Center for HIV Law and Policy advocates for the rights of people living with HIV and covers several areas of concern (such as employment, housing, and immigration). Its website includes a link to organizations, by state, that can provide legal information to people living with HIV. Write the center: 65 Broadway, Suite 832, New York, NY 10006. Call (212) 430-6733. Go to hivlawandpolicy.org.

HIV prevention

When you are on effective antiretroviral treatment (ART) and your virus is undetectable (less than 200 copies) for at least six months, it also means you can't transmit HIV to your partner (Undetectable equals Untransmittable, or U=U). This is also called "treatment as prevention," or TasP.

Pre-exposure prophylaxis (PrEP) is when people vulnerable to HIV take medicine to lower their chance of acquiring HIV. Currently Truvada is the only drug approved for PrEP. Daily PrEP reduces the risk of acquiring HIV from sex by nearly 100%. Among people who inject drugs, it reduces the risk by more than 70%.

PEP (post-exposure prophylaxis) means taking antiretroviral medicines (ART) after being potentially exposed to HIV to prevent acquiring HIV. PEP should be used only in emergency situations and must be started within 72 hours after a recent possible exposure to HIV. If you think you've recently been exposed to HIV during sex, or through sharing needles and works to prepare drugs, or if you've been sexually assaulted, talk to your health care provider or an emergency room medical provider about PEP right away.

Sexually transmitted diseases (STIs) are infections that spread from person to person through sexual contact, including anal, vaginal, or oral sex. HIV is an STI, but TasP, PrEP, and PEP do not prevent transmission of other STIs such as gonorrhea or syphilis.

Having HIV and another STI may increase the risk of HIV transmission. Condoms and other methods can help prevent or lower your risk for STIs. People with HIV should get tested for STIs at least once every year if they are sexually active, and more often depending on individual risk factors or symptoms.

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Your map to the stars

Getting the most out of your drug guide

Below are tips to help you and your care providers make empowered, informed treatment decisions. Medications included in the 2019 HIV Drug Guide are those most commonly used, or expected to be approved in the coming year.

With so many choices out there, we order the drug pages by those that are the best options and list them first, followed by commonly prescribed drugs in each category. To quickly find your drug, go to the next page. On the pullout chart, drugs are listed by category and then alphabetically. Older drugs that are rarely used are only pictured (without dosing information) at the bottom of the pullout chart.

Goal of HIV therapy

Understanding HIV treatment is the key to success. The goal of therapy is to suppress the virus to an undetectable level (meaning the virus in your blood is so low, it cannot be detected by normal tests). This will keep you healthy, and the sooner you start therapy, the less damage to your immune system so you'll stay healthier, longer. When you are on effective antiretroviral treatment (ART) and undetectable (less than 200 copies) for at least six months, it also means you can't transmit HIV to your partner (undetectable equal untransmittable, or U=U). Getting to and staying undetectable means you need to take your medication as prescribed (for example, if it's with or without food), and not miss doses.

Drug names

When a drug is in development it's first given a "generic" or "scientific" name (such as dolutegravir). At medical conferences and in scientific publications you will often see three-character abbreviations used (DTG). Once it's approved, it's given its brand name (Tivicay), which most people know it by.

Drug classes and co-formulations

A fixed-dose combination (FDC) combines two or more drugs in one tablet, such as Prezcobix (darunavir/cobicistat). A single-tablet regimen (STR) contains drugs from different classes and is a complete regimen in one pill, such as Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide).

Anti-HIV drugs should always be taken in combination using two or more drug classes (for example, an integrase inhibitor plus two nukes). Single-tablet regimens (STRs) are in their own category, and combine multiple classes of drugs into one tablet. STRs are widely used for first-time treatment and for their convenience, but they are not for everybody, including some people who are treatment-experienced or have multi-drug resistance.

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. We include information on some of the recommendations on page 13, and at the top of each drug page, as well as in the pullout drug chart. DHHS and IAS-USA guidelines are very similar, but for consistency we reference only the DHHS guidelines. For complete guideline recommendations go to aidsinfo.nih.gov or iasusa.org/resources/guidelines.

Drug pricing and access

The Average Wholesale Price (AWP) is listed on each drug page and is a way to compare costs of drugs. It is not what you would pay if you were to pay the full retail price. In the drug cost-sharing and patient assistance program charts (beginning on page 21) we include information on how to access programs that can help cover all or part of the costs of these medications.

Talking to your doctor

You can play an active role in your health care by talking to your doctor. Clear and honest communication between you and your physician can help you both make smart choices about your health. It's important to be honest and upfront about your symptoms even if you feel embarrassed or shy. Have an open dialogue with your doctor—ask questions to make sure you understand your diagnosis and treatment.

Here are a few tips that can help you talk to your doctor and make the most of your appointment:

- Write down a list of questions and concerns before your appointment.
- Consider bringing a close friend or family member with you.
- Take notes about what the doctor says, or ask a friend or family member to take notes for you.
- Learn how to access your medical records, so you can keep track of test results, diagnoses, treatments plans, and medications and prepare for your next appointment.
- Ask for the doctor's contact information and their preferred method of communication.
- Remember that nurses and pharmacists are also good sources of information.

More information online

Operated by the National Institutes of Health, AIDSinfo maintains factsheets on each HIV medication at aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/58/fda-approved-hiv-medicines. Download iPhone and Android apps that provide drug info, treatment guidelines, and a glossary: aidsinfo.nih.gov/apps. You can also find the online version of your medication's drug page from our HIV Drug Guide by adding your drug's name after typing positivelyaware.com into your browser (for example, positivelyaware.com/*triumeq*).

Places!

In this guide, HIV drugs are grouped into eight categories— plus, one additional category for select non-HIV drugs. More information is available at positivelyaware.com

- **STR** — SINGLE-TABLET REGIMEN (MULTIPLE DRUG CLASSES)
- **LA** — LONG-ACTING INJECTABLE REGIMEN
- **INSTI** — INTEGRASE STRAND TRANSFER INHIBITOR (INTEGRASE INHIBITOR)
- **PI** — PROTEASE INHIBITOR
- **PKE** — PHARMACOKINETIC ENHANCER (BOOSTER)
- **NRTI** — NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR ("NUKE")
- **NNRTI** — NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR ("NON-NUKE")
- **EI/AI** — ENTRY INHIBITOR/ ATTACHMENT INHIBITOR

PAGE	BRAND NAME	CATEGORY	GENERIC NAME
38	**Atripla**	STR	efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF)
28	**Biktarvy**	STR	bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF)
51	**Cimduo**	NRTI*	lamivudine/tenofovir DF (3TC/TDF)
37	**Complera**	STR	rilpivirine/emtricitabine/tenofovir DF (RPV/FTC/TDF)
32	**Delstrigo**	STR	doravirine/lamivudine/tenofovir DF (DOR/3TC/TDF)
49	**Descovy**	NRTI*	emtricitabine/tenofovir alafenamide (FTC/TAF)
57	**Edurant**	NNRTI	rilpivirine (RPV)
53	**Emtriva**	NRTI	emtricitabine (FTC)
54	**Epivir**	NRTI	lamivudine (3TC)
52	**Epzicom**	NRTI*	abacavir/lamivudine (ABC/3TC)
45	**Evotaz**	PI/PKE	atazanavir/cobicistat (ATV/COBI)
34	**Genvoya**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF)
60	**Intelence**	NNRTI	etravirine (ETR)
42	**Isentress HD**	INSTI	raltegravir (RAL)
30	**Juluca**	STR	dolutegravir/rilpivirine (DTG/RPV)
47	**Norvir**	PKE	ritonavir (RTV)
36	**Odefsey**	STR	rilpivirine/emtricitabine/tenofovir alafenamide (RPV/FTC/TAF)
58	**Pifeltro**	NNRTI	doravirine (DOR)
43	**Prezcobix**	PI/PKE	darunavir/cobicistat (DRV/COBI)
44	**Prezista**	PI	darunavir (DRV)
46	**Reyataz**	PI	atazanavir sulfate (ATV)
61	**Selzentry**	EI	maraviroc (MVC)
35	**Stribild**	STR	elvitegravir/cobicistat/emtricitabine/tenofovir DF (EVG/COBI/FTC/TDF)
59	**Sustiva**	NNRTI	efavirenz (EFV)
39	**Symfi/Symfi Lo**	STR	efavirenz/lamivudine/tenofovir DF (EFV//3TC/TDF)
31	**Symtuza**	STR	darunavir/cobicistat/emtricitabine/tenofovir alafenamide (DRV/COBI/FTC/TAF)
41	**Tivicay**	INSTI	dolutegravir (DTG)
29	**Triumeq**	STR	dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)
62	**Trogarzo**	AI	ibalizumab-uiyk (IBA)
50	**Truvada**	NRTI*	emtricitabine/tenofovir DF (FTC/TDF)
48	**Tybost**	PKE	cobicistat (COBI)
55	**Viread**	NRTI	tenofovir disoproxil fumarate (tenofovir DF, or TDF)
56	**Ziagen**	NRTI	abacavir sulfate (ABC)

* Fixed-dose combination of two drugs from the same drug class.

HIV DRUGS EXPECTED TO BE APPROVED IN 2019

40	Brand name TBD	LA	injectable long-acting cabotegravir/rilpivirine (CAB LA/RPV LA)
33	Brand name TBD	STR	dolutegravir/lamivudine (DTG/3TC)
63	Brand name TBD	AI	fostemsavir (FTR)

HIV PREVENTION

68	**Truvada for PrEP**	PrEP	emtricitabine/tenofovir DF (FTC/TDF)

NON-HIV DRUGS

66	**Egrifta**	tesamorelin for injection	for HIV-related excess belly fat
66	**Mytesi**	crofelemer	for HIV/AIDS-associated diarrhea
67	**Serostim**	somatropin for injection	for HIV-related wasting

Biktarvy

bictegravir/emtricitabine/tenofovir alafenamide **(BIC/FTC/TAF)**

STR SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND TWO NRTIs

★ RECOMMENDED INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One tablet once daily without regard to food. Tablet contains 50 mg of the INSTI bictegravir plus 200 mg emtricitabine and 25 mg tenofovir alafenamide (TAF).

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. Biktarvy is not recommended for people with CrCl less than 30 mL/min or people with severe liver impairment.

➤ SEE ALSO DESCOVY, which is contained in this drug (bictegravir is not available separately).

➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects observed in study participants include nausea (5%), headache (5%), and diarrhea (6%). Five individuals in Study 1490 and none in Study 1489 stopped Biktarvy due to side effects, none of which were due to kidney problems. Serum creatinine, estimated creatinine clearance, urine glucose, and urine protein should be obtained before initiating Biktarvy and should be monitored during therapy. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

POTENTIAL DRUG INTERACTIONS

Do not take with rifampin, the anti-arrhythmic dofetilide, or St. John's wort. Not recommended to be taken with Epivir-HBV, Hepsera, or Vemlidy, all three for treatment of hepatitis B. Biktarvy should be taken two hours before taking laxatives or antacids, the ulcer medication sucralfate, oral iron or calcium supplements (but these two can be used with Biktarvy if taken together with food), or buffered medications. Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects. When starting or stopping Biktarvy in people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Can be taken with the hepatitis C medications Epclusa, Harvoni, Sovaldi, and Vosevi. Not intended to be taken with other HIV medications, unless prescribed that way.

Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Received FDA approval in February 2018. Biktarvy is quickly becoming a top dog in HIV treatment. The data show that the bictegravir drug resistance barrier is comparable to that of dolutegravir and protease inhibitors (like Prezista). That is a huge advantage. Biktarvy is the first unboosted INSTI-containing STR with TAF, and the second unboosted INSTI STR overall (the other is Triumeq). ("Unboosted" means that the primary antiretroviral drug, in this case bictegravir, does not require another medication such as Norvir or cobicistat to increase its drug levels in the body.) This is a really big deal due to less drug interactions when there's no boosting. Biktarvy is the second smallest INSTI-based STR tablet, which may help some individuals who have difficulty swallowing pills. Pediatric study is ongoing. New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir, which is chemically similar to bictegravir, at the time of conception. Consult your provider to discuss guidance on how to manage regimens containing an INSTI if there is any possibility of conception. At this time, the use of Biktarvy is not recommended during pregnancy due to lack of published data in pregnant women.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,534.78/month

DR. DAVID HARDY SAYS: Biktarvy became the eighth STR approved by the FDA, in February 2018. Many consider this three-drug, unboosted, integrase inhibitor-containing (bictegravir) and TAF-containing STR to be a crowning achievement of many years of HIV drug development. But is it any better than other ART regimens? Based on the clinical trial data, it is difficult to see distinct advantages of Biktarvy over Triumeq or Tivicay + Descovy or any clear advantage of switching from a suppressive and well-tolerated, boosted protease inhibitor or Triumeq—other than reducing the number of pills in an ART regimen or persistent nausea or other PLWH-reported side effects. One possible advantage of Biktarvy over Triumeq could be its use as a first-line ART regimen in same-day or rapid ART start programs due to the requirement for HLA-B*5701 testing for Triumeq. Data from two clinical trials (GS 380-1489 and 1490) comparing Biktarvy to Triumeq or to Tivicay plus Descovy showed very high and very close (92% vs. 93% and 89% vs. 93%, respectively) rates of undetectable viral loads among PLWH receiving their first ART regimen after one year of treatment. The conclusion from each study was that Biktarvy was as good as or similar to Triumeq or Tivicay plus Descovy. Although there was more mild to moderate nausea reported by PLWH receiving Triumeq versus those receiving Biktarvy, only 1 out of 315 PLWH stopped Triumeq due to nausea. The two-year follow-up of both of these studies continued to show high and similar rates of undetectable viral loads (87.9% vs. 89.8% and 84.1% vs. 86.5%, respectively) and no new differentiating characteristics between the regimens. Two clinical trials have studied the use of Biktarvy as a switch ART regimen for PLWH with undetectable viral loads receiving a boosted protease inhibitor regimen (Prezista + Norvir or Tybost, or Reyataz + Norvir or Tybost; GS 380-1878) or Triumeq (GS 380-1844). The one-year results of these studies showed that the PLWH who switched to Biktarvy and those who remained on their initial regimens both had excellent and similar results (1878: 92% vs. 89% and 1844: 94% vs. 95%) in terms of maintained undetectable viral loads and minimal side effects with both regimens. Of note, in the 1844 study, a decrease in nausea was reported in the PLWH who switched to Biktarvy. In all of these clinical trials studying Biktarvy, there were few PLWH who experienced virologic failure and when they did, their re-emerging HIV did not show any evidence of integrase inhibitor resistance—a finding very similar to Tivicay and Triumeq. To date, no emergent integrase resistance to Biktarvy has been reported in clinical practice.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Bikarvy is a good option for those recently infected and treatment virgins and those treatment-experienced that are facing difficulties with their current treatment regimen. As with any drug, there are side effects and drug interactions to be aware of by both the patient and the doctor. For example, you should not take Biktarvy if you take dofetilide to treat irregular heartbeat; it could be serious and possibly fatal. Avoid rifampin, which is used to treat some bacterial infections like tuberculosis. In general Biktarvy is well tolerated and is very effective.

Triumeq dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)

STR SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND TWO NRTIs

★ RECOMMENDED INITIAL REGIMEN FOR MOST PEOPLE IF HLA-B*5701 NEGATIVE

STANDARD DOSE

One tablet once daily, without regard to 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 INSTI drug resistance or are taking certain other medications. Tablet contains 50 mg of the INSTI dolutegravir plus 600 mg abacavir and 300 mg lamivudine.

For adults and children weighing at least 88 pounds (40 kg). 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 or liver problems. Triumeq should not be used in people with CrCl less than 50 mL/min or moderate or severe liver impairment.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN TRIUMEQ:** Tivicay, Ziagen, and Epivir.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Triumeq is generally well tolerated. The most common side effects that occurred in 2–3% of study subjects are insomnia, headache, and fatigue. Dolutegravir can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Conflicting data suggest a potential risk for heart problems when using abacavir-containing regimens in people with high risk for cardiovascular disease. Monitor for signs of hypersensitivity reaction (HSR) to abacavir. Prior to starting Triumeq, all individuals 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 by LabCorp/ViiV (see company contact on co-pay chart). Read more about HSR online. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the lamivudine component. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. See "More Information."

POTENTIAL DRUG INTERACTIONS

Do not take with the anti-arrhythmic dofetilide. Triumeq should be taken two hours before or six hours after taking antacids or laxatives, the ulcer medication Carafate, iron or calcium supplements, or buffered medications. Triumeq can be taken together with iron- or calcium-containing supplements if taken with food. Other acid reducers/heartburn medications (e.g., Aciphex, Dexilant, Prilosec, Pepcid, Zantac, Prevacid) are okay to use. Avoid co-administration with oxcarbazepine, phenobarbital, phenytoin, or St. John's wort. Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Triumeq is the only single-tablet regimen (STR) that contains Epzicom as the NRTI backbone. Compared to other INSTIs, dolutegravir has a relatively high genetic barrier against the development of drug resistance, similar to the protease inhibitors (such as Prezista). In addition, dolutegravir-containing regimens have demonstrated virologic superiority over Prezista-containing regimens. Triumeq has relatively few drug interactions and is well tolerated. Triumeq does not cover HBV as well as other STRs and therefore requires another anti-HBV medication in addition to its lamivudine component. Triumeq is a relatively large STR tablet, which can potentially be an issue for individuals who have difficulty swallowing. Another STR containing dolutegravir is Juluca. New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception. Until more information is available, regimens containing dolutegravir are not recommended for use in ART-naïve patients who are pregnant and within 12 weeks of conception. Consult your provider to discuss guidance on how to manage regimens containing dolutegravir if there is any possibility of conception.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
triumeq.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

$3,467.23/month

DR. DAVID HARDY SAYS: Triumeq was the fourth STR approved, in 2014, the second STR containing an integrase inhibitor (without a booster), and the first STR with Ziagen/Epivir instead of Viread/Emtriva. In three of four initial studies in PLWH starting their first ART regimen (including one study for women only) comparing Triumeq to either Sustiva, Prezista/Norvir, Reyataz/Norvir, or Isentress, Triumeq was shown to be superior to (better than) the comparison ART regimen (Atripla, Prezista/Norvir, and Reyataz/Norvir) and similar to the other integrase inhibitor-containing ART regimen (Isentress). These results were strengthened by the finding that in all of these studies, no HIV resistance (viral mutations) was found when a PLWH's viral load did not respond, or stopped responding, to Triumeq and their viral load became detectable. This was a new and unique finding for Triumeq compared to other integrase inhibitor-containing ART regimens (Stribild, Genvoya, and Isentress). In clinical trials, side effects seen with Triumeq have been uncommon and rarely a reason for PLWH to stop their treatment. HIV drug resistance associated with Triumeq has been seen in clinical practice in a handful of oftentimes poorly or incompletely documented anecdotal cases since its approval. Recently, the use of dolutegravir in HIV-positive women who desire to become pregnant or who could become pregnant without contraception has been strongly discouraged by many international and national regulatory and advisory organizations (WHO, DHHS/FDA, IAS-USA, EACS) due to the unexpected observation of an increased incidence of neural tube defects (serious birth defects affecting a baby's neurologic system) seen among HIV-positive women receiving dolutegravir at the time of conception in Botswana in a preliminary review of the Tsepamo study. Final results of the study will be reported later in 2019. Of note, these birth defects have not been seen in women who start dolutegravir in the second or third trimester of pregnancy. Some HIV-treating medical care providers and PLWH have avoided Triumeq due to reports of an increased risk of heart attacks with Ziagen, one of the medications in Triumeq. This sometimes limits the use of Triumeq. In addition, it is strongly encouraged that PLWH have a blood test to look for a genetic marker (HLA-B*5701) that is associated with a serious allergic reaction to the Ziagen. If the marker is present, no ART regimen with Ziagen should be used. Triumeq has been and continues to be a recommended first-line ART regimen since its approval in both DHHS and IAS-USA guidelines. An increasing, but still small, number of reports have noted increased cases of insomnia, mental stimulation, and worsening of mental health problems associated with Triumeq.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Make sure your doctor monitors your kidney function as well your heart. Abacavir has been associated with cardiovascular disease and a serious allergic reaction for which the drug must be discontinued immediately and never taken again. It's important to make sure you are not predisposed to this hypersensitivity reaction seen with abacavir. There is a blood test that can predict predisposition to it.

Juluca dolutegravir/rilpivirine (DTG/RPV)

STR SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND AN NNRTI

★ RECOMMENDED AS CONTINUATION THERAPY FOR PEOPLE WITH UNDETECTABLE HIV VIRAL LOAD FOR AT LEAST 6 MONTHS

STANDARD DOSE

One tablet once daily, with a meal (see Edurant), for adults who are virologically suppressed (have an undetectable viral load of less than 50 copies per mL) on a current ART (antiretroviral therapy) regimen for at least 6 months and who have no history of treatment failure or resistance mutations associated with rilpivirine or dolutegravir. Tablet contains 50 mg of the INSTI dolutegravir plus 25 mg of the NNRTI rilpivirine.

Take missed dose as soon as possible, with a meal, unless it is closer to the time of your next dose. Do not double up on your next dose. For proper absorption, rilpivirine must be taken with a meal that you chew—not just nutritional drinks or protein shakes.

➤ SEE THE INDIVIDUAL DRUGS CONTAINED IN JULUCA: Tivicay and Edurant.

➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Both dolutegravir and rilpivirine are generally well tolerated. Side effects observed in greater than 2% of study participants were diarrhea and headache. Dolutegravir and rilpivirine can each cause a small, reversible increase in a kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Liver enzymes should be monitored in people with hepatitis B or C and taking dolutegravir. Call your health care provider right away if you develop any of the following signs or symptoms: 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 pain, aching, or tenderness on the right side below the ribs. There may be a possibility of birth defects—see "More information."

POTENTIAL DRUG INTERACTIONS

Do not take Juluca with the anti-arrhythmic dofetilide. If taking rifabutin, add an Edurant tablet to Juluca dose. If you take antacids, laxatives, or other products that contain aluminum, calcium carbonate, magnesium, or buffered medicines, Juluca should be taken (with a meal, as always) at least 4 hours before or 6 hours after you take these medicines. Alternatively, these medications can be taken at the same time with Juluca and the meal. Take Juluca with a meal 4 hours before or 12 hours after you take H-2 blocker acid reducers (Pepcid, Zantac, Tagamet) or buffered medications. Juluca should not be taken with proton pump inhibitors (such as Aciphex, Dexilant, Prilosec, Prevacid, Protonix, Nexium). Avoid taking Juluca with some seizure medicines (carbamazepine, oxcarbazepine, phenobarbital, and phenytoin) or St. John's wort. HIV treatment guidelines suggest that metformin be started at the lowest dose and titrated based on glycemic control. Monitor for metformin adverse effects. When starting or stopping Juluca in people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Juluca is the first two-drug combination approved as a complete regimen for HIV. It replaces a three- or four-drug therapy for people with undetectable viral loads who want to switch to a simpler or smaller tablet regimen. People switching to Juluca must be virologically suppressed (with viral loads of less than 50 copies per mL) on a stable antiretroviral regimen for at least six months. This is a new HIV treatment strategy and potentially a game changer, especially with other dual-drug antiviral medications on the way. Those able to take their medications correctly, consistently, and achieve undetectable viral loads can take advantage of this drug-sparing strategy. Currently people taking HIV treatment must start out with a three-drug regimen (which may include the use of one of the single-tablet regimens, or STRs), then switch to Juluca after being undetectable for six months. Juluca still works against two steps of the life cycle of the virus, similar to 3-drug regimens. This is how the combination was used in clinical studies to date. This combination was listed in U.S. HIV guidelines as a "Strategy with good supporting evidence" around the time of its FDA approval. The guidelines also called Juluca "a reasonable option when using nucleoside drugs is not desirable" (for example, due to previous toxicity), with an A1 rating (strong recommendation based on randomized controlled trials). Juluca is the first nucleoside-free STR. Currently, all the STRs contain two nucleoside drugs. Juluca contains two currently available medications. Dolutegravir (available separately under the brand name Tivicay, from ViiV Healthcare) is available in the STR Triumeq. Rilpivirine (available separately under the brand name Edurant, from Janssen Therapeutics) is available in the STRs Complera and Odefsey. The benefits of using Juluca, a two-drug regimen for HIV-1, include less exposure to HIV medications while maintaining viral suppression. Juluca is the smallest STR, which may be advantageous to individuals who have difficulty swallowing. New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception. Until more information is available, regimens containing dolutegravir are not recommended for use in ART-naïve patients who are pregnant and within 12 weeks of conception. Consult with your provider to discuss guidance on how to manage regimens containing dolutegravir or a different integrase inhibitor if there is any possibility of conception.

DR. DAVID HARDY SAYS: Juluca, the seventh STR approved by the FDA, in late 2017, is a departure from the six previous STRs. This is because instead of being approved for initial treatment of PLWH and/or for use as a "switch regimen," Juluca is specifically and only approved as a "switch regimen" in PLWH with undetectable viral loads and *no* previous history of failed ART regimens. Juluca is also the first two-drug, instead of a three-drug, STR. What, you may ask, is the idea behind using only two drugs to keep HIV suppressed rather than the usual three drugs? The approval of Juluca as a two-drug "maintenance" ART regimen is unique and follows on the results of two large Phase 3 studies (SWORD 1 & 2) which enrolled more than 1,000 PLWH with undetectable viral loads receiving an NNRTI-, boosted PI-, or integrase inhibitor-containing ART regimen and no previous failed ART regimens. Half of the PLWH were switched to Juluca, the other half remained on their previous ART regimen. Ninety-five percent of both groups of PLWH maintained undetectable viral loads a year later; 89% of those switched initially maintained their undetectable viral loads two years later. More PLWH receiving Juluca reported side effects and stopped taking Juluca than those PLWH who stayed on their previous ART regimens, but no new or unexpected side effects were reported. The use of Juluca has shown a slow but steady rise since its approval among prescribing healthcare providers and PLWH. This may be due to reluctance to change virally suppressive ART with a multi-tablet regimen or uncertainty with a two-drug regimen.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Juluca was approved for patients who have been virally suppressed for at least six months and never experienced drug resistance to either of its component medications. If you are concerned about the exposure to HIV medicines and their side effects but want to make sure your viral load continues to be suppressed, Juluca might be your option. Keep an eye on your liver functions while taking Juluca.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

$3,249.54/month

Symtuza

darunavir/cobicistat/emtricitabine/tenofovir alafenamide **(DRV/COBI/FTC/TAF)**

STR — SINGLE-TABLET REGIMEN CONTAINING A PROTEASE INHIBITOR, A PHARMACOKINETIC ENHANCER (BOOSTER), AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily with food for treatment-naïve people or people with suppressed viral load on a stable HIV regimen for at least 6 months who have no known resistance to the darunavir or tenofovir components of the regimen. Tablet contains 800 mg darunavir, 150 mg cobicistat, 200 mg emtricitabine, and 10 mg tenofovir alafenamide.

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 or liver problems. Symtuza can be used in people with an estimated creatinine clearance of at least 30 mL/min. It should not be used in people with severe kidney or liver impairment.

- SEE THE INDIVIDUAL DRUGS CONTAINED IN SYMTUZA: Prezista, Tybost, and Emtriva (TAF is not marketed separately for HIV, but see also Descovy).
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

As darunavir contains a sulfa component, use with caution in patients with sulfa allergies. Side effects most commonly reported in studied subjects include diarrhea (9%), rash (8%), nausea (6%), fatigue (4%), headache (3%), abdominal discomfort (2%), and flatulence (2%). While very rare, severe rash, accompanied in some cases by fever and/or elevations of AST/ALT (liver enzymes), can be life-threatening. Seek medical attention immediately. Observational cohort studies reported an association between some PIs (including darunavir when given with Norvir) and an increased risk of cardiovascular (CV) events, but data with darunavir/cobicistat is too limited to see such a connection. With PIs, there can be increased bleeding in hemophiliacs. Cobicistat can cause a small, reversible increase in serum creatinine (SCr, which indicates the eGFR or estimated CrCl lab values) within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Serum phosphorus in patients with or at risk for kidney impairment should also be monitored. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely, or never, seen with darunavir. IRIS (immune reconstitution inflammatory syndrome) may occur as the immune system regains strength; signs and symptoms from previous infections may occur soon after HIV treatment is initiated. Report symptoms of illness, such as shingles or TB, to a health care provider.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Use with other protease inhibitors or Intelence, Sustiva, or Viramune is not recommended. Do not take with betamethasone, budesonide, carbamazepine, dexamethasone, dronedarone, eslicarbazepine, ergot derivatives, fluticasone, triazolam, oral midazolam, lurasidone, methylprednisolone, oxcarbazepine, phenobarbital, phenytoin, pimozide, Revatio, simvastatin, lovastatin, St. John's wort, alfuzosin, ranolazine, or rifampin. Not recommended to be taken with apixaban, avanafil, dabigatran etexilate (in renal impairment), everolimus, rifampentine, salmeterol, ticagrelor, or voriconazole. Beclomethasone and prednisone as alternative corticosteriods may be considered, particularly for long-term use. Atorvastatin and rosuvastatin dose should not exceed 20 mg daily. Clinical monitoring is recommended with drospirenone, due to potential for hyperkalemia. Do not take with colchicine if there is kidney or liver impairment. Can be used with Daklinza. Cannot be taken with Zepatier. Based on the mechanism, drug interactions with other hepatitis C medications are probably similar to the interactions with Prezista + Norvir + Descovy. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

This medication was approved last year and is the first STR containing a protease inhibitor. This formulation is much more convenient and is associated with fewer copays. A benefit of the PIs is their high genetic barrier to the development of drug resistance. While medical providers may hate to say it out loud, this means greater forgiveness of missed doses; missing a dose here and there is never advisable but does happen. As such, a PI-based regimen such as Symtuza suits some people who may have trouble with the near-perfect drug adherence required of HIV treatment. In fact, the FDA allowed Janssen to advertise Symtuza as "help[s] protect against resistance." Symtuza may be used in rapid initiation, treatment given within 7 days of HIV diagnosis, before resistance test results are available. Treatment-experienced individuals with undetectable viral loads for at least six months may switch to Symtuza. Darunavir is available under the brand name Prezista and is also found in the co-formulated pill Prezcobix (with cobicistat). Compared with tenofovir DF, the tenofovir alafenamide in Symtuza is safer on kidney and bone health. Also as a result of the TAF, Symtuza can be taken by people with more advanced kidney disease, down to a renal function (CrCL) of 30 mL/min.

DR. DAVID HARDY SAYS: What makes Symtuza unique among STRs is that it is the first one to contain a boosted protease inhibitor. It will essentially combine two currently available medications, Prezcobix and Descovy, into one tablet which promises to be smaller (more pharmaceutical magic) than the size of a Prezcobix tablet (which is the largest STR tablet to date). For PLWH who are doing well with a boosted protease inhibitor-containing regimen, Symtuza offers these folks the opportunity to experience the benefits of a one-tablet, once-a-day regimen for the first time. It is thought that many HIV-treating healthcare providers now offer this new STR to their patients on protease inhibitor-containing regimens. For those PLWH whose access or adherence to their ART regimens is, or is predicted to be, difficult or unreliable, this new STR offers them an option for a proven "HIV resistance-resistant" ART regimen in one pill. On the other hand, many HIV-treating healthcare providers and PLWH are feeling increasingly confident that an integrase inhibitor-containing regimen (e.g., Triumeq, Biktarvy) is just as resistant-to-resistance as a boosted protease inhibitor regimen and has better tolerability. Clinical trial data with Symtuza and clinical experience with Prezcobix and Descovy show that PLWH tolerate this regimen fairly well, but not as well as they tolerate unboosted integrase inhibitors (Triumeq, Biktarvy, and Isentress). Nausea, queasiness, diarrhea, and rash are most common side effects seen with Symtuza or its components.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: This is the first once-a-day single-tablet regimen containing a protease inhibitor, darunavir. One good thing about darunavir is that it has a high barrier to resistance. This also makes it a good candidate for treatment-naïve individuals as initial therapy. Because of the way darunavir and cobicistat, a booster contained in Symtuza, are metabolized by the liver you will have to monitor for many drug-drug interactions that can cause serious problems. Among them, you will find commonly prescribed drugs such as statins and some benzodiazepines (Halcion, for example).

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$4,466.71/month

Delstrigo doravirine/lamivudine/tenofovir DF (DOR/3TC/TDF)

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily without regard to food. Tablet contains 100 mg of the NNRTI doravirine plus 300 mg lamivudine and 300 mg tenofovir DF (TDF). Approved only for adults at this time.

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; Delstrigo is not recommended in people with estimated creatinine clearance less than 50 mL/min. Should not be used in people with moderate or severe kidney impairment or severe liver impairment.

- SEE THE INDIVIDUAL DRUGS CONTAINED IN DELSTRIGO: Pifeltro, Viread, and Epivir.
- SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse reactions observed with Delstrigo in clinical trials (in more than at least 5% of people taking it) were dizziness (7%), nausea (5%), abnormal dreams (5%), and increased lipase (5%). In one study (DRIVE-AHEAD), an in-depth analysis was conducted of the incidence of neuropsychiatric adverse events associated with Delstrigo compared to Atripla. Neuropsychiatric events, such as depression, sleep disturbances, dizziness, etc., are another common side effect of the NNRTI class. The proportion of subjects who reported one or more neuropsychiatric adverse events overall was 24% for the Delstrigo group compared to 57% for the Atripla group. The neuropsychiatric adverse events associated with depression and suicide/self-injury were reported in 4% of the Delstrigo group compared to 7% of the Atripla group. Overall, sleep disturbances (e.g., abnormal dreams, insomnia, nightmares, etc.) were associated with 12% of people in the Delstrigo group compared to 26% of people in the Atripla group. Dizziness was associated with 9% in the Delstrigo group compared to 37% of the Atripla group. Altered sensorium (e.g., lethargy, drowsiness, etc.) was associated with 4% of people in the Delstrigo group compared to 8% of people in the Atripla group. The doravirine component of Delstrigo did not appear to negatively affect cholesterol in studied populations. Decreases in bone mineral density (BMD) have been observed in patients on TDF-containing regimens. 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. TDF may cause kidney toxicities. Creatinine clearance (CrCl) should be assessed before initiating treatment. In addition to CrCl, glucose and protein in the urine and serum phosphorus should be monitored more often in patients at risk for kidney problems. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. If you have HIV and HBV, guidelines recommend treatment for both viruses. Delstrigo can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Delstrigo without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

POTENTIAL DRUG INTERACTIONS

New interactions continue to be discovered after drug approval (doravirine is the new drug). Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for hepatitis B. When using with the antibiotic drug rifabutin (used for TB and to prevent MAC in AIDS patients), increase the doravirine dose by adding a Pifeltro tablet approximately 12 hours later. The following medications may lower the blood levels of doravirine, and therefore may decrease its effectiveness, and should not be used with Delstrigo: the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent (cancer drug) mitotane; and the herbal St. John's wort. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Epclusa and Harvoni each increase the concentration of TDF; monitor for adverse reactions. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Stand-alone versions of doravirine (Pifeltro) and lamivudine/tenofovir DF (Cimduo) were also approved; see those pages. Unfortunately, Delstrigo contains an older version of tenofovir, TDF. A safer version, TAF, is available and used in some STRs. TDF is still an effective and quite tolerable medication, but TAF has less toxicity to the kidneys and bones. Doravirine has not been directly compared to integrase inhibitor-based regimens in clinical trials yet. There is no data on the safety of Delstrigo use in pregnancy.

In the DRIVE-FORWARD study comparing doravirine to darunavir, results for the treatment-naïve individuals in the study were 80% (darunavir group) and 84% (doravirine group) undetectable (less than 50 viral load). That's a lower success rate than is expected in HIV treatment today, but was thought to be affected by the number of people who quickly dropped out of the study when they saw how many pills they had to take. Those drop-outs were counted as virologic failures. See more data online. Merck has applied to the FDA for a switch indication, so that people with undetectable viral load on their current treatment can switch to Delstrigo.

MANUFACTURER

Merck and Co.
(800) 622-4477
delstrigo.com

AVERAGE WHOLESALE PRICE

$2,520.00/month

DR. DAVID HARDY SAYS: Delstrigo was approved in August 2018 and is the twelfth STR and first "quasi-generic" STR approved by the FDA. The term "quasi-generic" means that two of the components of Delstrigo, tenofovir DF and lamivudine, are from a generic, non-branded manufacturer, and the Pifeltro (doravirine) is the branded drug made by the manufacturer, Merck. Doravirine is considered to be a "second generation" NNRTI due to its enhanced resistance profile compared to Sustiva and Viramune and similar to other NNRTIs such as Intelence and Edurant. In fact, lab studies predict that it may be effective after a first generation NNRTI has failed and caused HIV resistance mutations or in PLWH with transmitted NNRTI resistance. To test this laboratory finding, a clinical trial called the DRIVE BEYOND study, which enrolled ART treatment-naïve PLWH with transmitted HIV resistance (K103N, Y181C, or G190A mutations), completed its initial follow-up in late 2018. We look forward to hearing the outcome of this study in 2019. Data from two large clinical trials of treatment-naïve PLWH comparing Delstrigo to Sustiva (DRIVE AHEAD study) and to Prezista/Norvir (DRIVE FORWARD study) have shown that Delstrigo has similar anti-HIV potency as those two known potent medications with less treatment-limiting side effects and less cholesterol-elevating effects. Of note and what will hopefully be a growing trend which other newly approved STRs will follow, the 30-day wholesale acquisition cost (WAC) of Delstrigo is $2,100, compared to $2,950 for Biktarvy, $3,500 for Symtuza, $2,800 for Triumeq, $3,000 for Genvoya and Stribild, and $1,630 for Symfi and Symfi Lo.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Delstrigo was approved for patients who have not been treated with antiretrovirals before. In general, it is safe and well tolerated. If you have hepatitis B (HBV) and are taking Delstrigo, do not stop taking it and make sure you never run out of it. This is not only because you want to maintain HIV viral suppression, which is a good reason, but, if you stop the medicine, the HBV infection suddenly returns in a worse way than before. If for some reason you need to stop taking Delstrigo, your doctor will need to monitor your HBV infection by doing regular blood tests for a few months.

NOT YET APPROVED AT PRESS TIME.

PHOTO UNAVAILABLE

dolutegravir/lamivudine (DTG/3TC)

STR SINGLE-TABLET REGIMEN CONTAINING AN INSTI AND AN NRTI

✔ INITIAL REGIMEN TO CONSIDER WHEN ABC, TAF, AND TDF CANNOT BE USED OR ARE NOT OPTIMAL

STANDARD DOSE

One tablet once daily, without regard to food. Tablet contains 50 mg of the INSTI dolutegravir plus 300 mg of the NRTI lamivudine.

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. Lamivudine dosing needs to be adjusted for adults and children who have decreased kidney function (creatinine clearance less than 50 mL/min). See package insert when available for guidance on dosing in the setting of kidney impairment. Dolutegravir is not recommended for people with severe liver impairment. Lamivudine and dolutegravir are currently available separately.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN THIS MEDICATION:** Tivicay and Epivir.
- **SEE PACKAGE INSERT** when available for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Dolutegravir and lamivudine are both generally well tolerated. The most common adverse events (in 5% or more of people taking it) in the GEMINI-1 and GEMINI-2 studies combined were headache (10%), diarrhea (9%), and nasopharyngitis (allergy-like symptoms, 8%). Dolutegravir can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Liver enzymes should be monitored in people with hepatitis B or C and taking dolutegravir. 3TC can treat both HIV and HBV, but must be used in combination with another hep B drug (such as tenofovir) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop 3TC without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

POTENTIAL DRUG INTERACTIONS

Do not take DTG/3TC with Epivir-HBV. When starting or stopping dolutegravir in people on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Should be okay to take with Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

May be approved this year. Basically, this medicine is Triumeq without the abacavir (brand name Ziagen, also found in Epzicom). Dolutegravir is from the powerhouse drug class of integrase inhibitors, which are highly effective and generally tolerable. This coformulated STR is recommended by guidelines to be used in ART-naïve adults with baseline viral load less than 500,000 in instances where ABC, TDF, and TAF cannot be used or are not optimal. (Other considerations for switching meds when one has undetectable viral load are also given.) The benefits of using a two-drug regimen for HIV include less exposure to HIV medication while maintaining viral suppression and also minimizing the potential for side effects. See data online. New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception. Until more information is available, regimens containing dolutegravir are not recommended for use in ART-naïve patients who are pregnant and within 12 weeks of conception. Additionally, regimens containing dolutegravir should not be used in people of childbearing potential who are sexually active and not using effective contraception or who are planning to become pregnant. It is unclear whether dolutegravir is the only integrase inhibitor with the potential to cause these birth defects (neural tube defects), or if other integrase inhibitors also carry this risk. Consult your provider to discuss guidance on how to manage regimens containing dolutegravir or a different integrase inhibitor if there is any possibility of conception.

MANUFACTURER

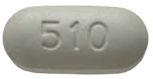
ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Not yet established.

DR. DAVID HARDY SAYS: This combination is based upon the results of the GEMINI 1 and 2 studies, in which treatment-naïve PLWH were assigned to receive either the 2-drug combination regimen of Tivicay plus Epivir or the 3-drug combination of Tivicay and Truvada, which showed undetectable viral loads in 91% vs. 93% of study participants, respectively, after one year of treatment. Adverse events were uncommon and similar between the two regimens, although there was more blood biochemical evidence of bone and kidney damage with the 3-drug (tenofovir DF-containing) regimen compared to the 2-drug regimen. Of note, virologic failure was seen in 4 and 2 study participants, respectively, with no evidence of any virologic resistance with either regimen. These two clinical trials are the first to show that a 2-drug, non-boosted regimen works as well as a 3-drug regimen. How HIV-treating medical care providers and PLWH will accept this paradigm-changing, 2-drug regimen as first-line therapy is yet to be seen. Of note, both the DHHS and IAS-USA guidelines include this regimen only as an alternative regimen when Truvada, TAF, or Epzicom cannot be tolerated. The TANGO study is randomizing 550 treatment-experienced PLWH with undetectable viral loads and no history of viral resistance to switch to Tivicay/Epivir (in a fixed-dose-combination tablet) or remain on their current ART regimen. TANGO began enrollment in February 2018 and is expected to produce results in 2020.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: When you are HIV positive, if you are in treatment, and virally suppressed, your life expectancy increases. Lifetime drug adherence is needed to fully get the benefits of the HIV drug regimen taken. By the same token, one is exposed to potential long-term adverse effects. Some are known and others, those that might show after longtime exposure, are still not known completely. Dual-drug HIV treatment regimens can potentially lessen drug exposure, not only for those on treatment but also for those considering treatment for the first time. Development of drug cross-resistance is something to take into consideration when you start treatment for the first time. The challenge is to find powerful drugs with a high genetic barrier to drug resistance. Recent research (GEMINI 1 and 2 studies) has proven that dual treatment with the two-drug combination of dolutegravir (DTG) plus lamivudine (3TC) is not inferior to triple ART combination. GEMINI 1 and 2 are identically designed studies. Both are large Phase 3 studies in which 700 treatment-naïve individuals were randomized to either DTG+3TC or DTG+TDF/FTC. The primary endpoint was reaching plasma viral load less than 50 copies at week 48. This treatment strategy looks promising. More research needs to be done.



Genvoya

elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide **(EVG/COBI/FTC/TAF)**

STR SINGLE-TABLET REGIMEN CONTAINING A BOOSTED INSTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily with food. Tablet contains 150 mg of the INSTI elvitegravir boosted by 150 mg cobicistat plus 200 mg emtricitabine and 10 mg tenofovir alafenamide (TAF).

For adults and children weighing at least 55 pounds (25 kg) and having a creatinine clearance of at least 30 mL/min (measurement of kidney function), as well as adults with creatinine clearance below 15 mL/min who are receiving chronic hemodialysis (HD). For those on HD, take tablet after completion of hemodialysis on days of HD treatment.

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 liver problems. Genvoya is not recommended for people who have severe liver problems, a CrCl between 15 to 30 mL/min, or a CrCl less than 15 mL/min who are not receiving chronic hemodialysis.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN GENVOYA:** Emtriva and Tybost (elvitegravir is not available separately, and neither is TAF for use in HIV, but see Descovy).
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Common side effects reported in at least 5% of study participants include nausea, diarrhea, headache, and fatigue. Before taking Genvoya, kidney function testing should be conducted, including serum creatinine, serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Genvoya. Cobicistat can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Separate by at least 2 hours from antacids containing aluminum, magnesium hydroxide, or calcium carbonate. Safe to take with other medications used for heartburn and GERD such as Nexium, Pepcid, Prevacid, Prilosec, and Zantac. Cobicistat has many drug interactions similar to Norvir. Do not take with cholesterol-lowering drugs containing lovastatin or simvastatin (Advicor, Altoprev, Mevacor, Simcor, Vytorin, Zocor), alfuzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methylergonovine, oral midazolam, lurasidone, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, or St. John's wort. Dose of clarithromycin may need to be reduced based on kidney function. An alternative corticosteroid to systemic dexamethasone should be considered. Risks versus benefits of using with voriconazole should be assessed with expert consultation. Some cholesterol-lowering drugs such as atorvastatin should be used with caution and started at the lowest dose possible. Monitor closely for increased side effects from these medications, such as muscle pain. Concentrations of antidepressants such as fluoxetine, paroxetine, bupropion, or amitriptyline may be increased, and their doses may need to be reduced. Genvoya increases levels of many nasal and inhaled steroids like fluticasone, which may lead to symptoms of Cushing's syndrome. An alternative corticosteroid to fluticasone is recommended. Cialis, Levitra, and Viagra levels are increased; doses should not exceed 10 mg Cialis or 2.5 mg Levitra per 72 hours, or 25 mg Viagra per 48 hours. Monitor for increased side effects of these medications. Effectiveness of oral contraceptives may be decreased; consider using alternative or additional contraception methods. Reduce Daklinza dose to 30 mg. Can be taken with Harvoni. Taking with Olysio, Viekira Pak, or Zepatier is not recommended. Monitor kidney function more closely with Epclusa. Not intended to be taken with other HIV medications, unless prescribed that way. 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 not listed here.

MORE INFORMATION

For a while very popular, Genvoya, along with its sister med Stribild, were recently downgraded in U.S. HIV treatment guidelines, from "recommended initial therapy for most people" to "recommended initial therapy in certain clinical situations." The change was made due to the presence of the booster cobicistat, which has many drug interactions, and because these meds do not have the high barrier to drug resistance that Biktarvy, Tivicay, and Triumeq have. Last year, Genvoya was approved for use in patients on hemodialysis; however, doctors are also using off-label prescribing of Biktarvy or Juluca for patients on hemodialysis. Genvoya is not recommended for use in pregnancy due to substantially lower exposures of cobicistat and elvitegravir during the second and third trimesters as well as reports of viral breakthrough. Switching regimens should be considered for pregnant women already taking this regimen. New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception. Consult your provider to discuss guidance on how to manage regimens containing an integrase inhibitor if there is any possibility of conception.

DR. DAVID HARDY SAYS: Genvoya, the fifth STR approved, in 2015, is commonly called the "new and improved" version of Stribild because it contains three of the four medications that Stribild contains. What makes Genvoya different is that the Viread component of Stribild has been "updated" with a new medication called TAF (tenofovir alafenamide fumarate). TAF is known as a "prodrug," which means that it's kind of like a "prequel"—it comes before the older, already known version and is changed into the active drug (tenofovir) within the body. TAF is kind of like tenofovir DF, but through pharmaceutical magic, the amount of tenofovir needed to effectively suppress HIV has been reduced from 300 mg in Stribild to only 10 mg in Genvoya. This 97% reduction means that there is much less tenofovir in the blood of PLWH taking Genvoya and therefore much less chance of kidney- or bone mineral density- (solidness of bone) harming side effects. Clinical trials have shown that Genvoya is similar to (just as good as) Stribild for treating HIV, and it has significantly fewer negative side effects on both kidneys and bones. Further, additional small studies proved that Genvoya can be safely used in PLWH with pre-existing mild to moderate kidney disease. Like Stribild, however, Genvoya contains a "booster" (cobicistat or Tybost) which is associated with interactions with other medications which PLWH may take. Of note, the most recent versions of both the DHHS and IAS-USA guidelines have removed both Stribild and Genvoya from their first line of "recommended for all PLWH" categories and placed them in a category for special situations.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Because cobicistat, a booster contained in Genvoya, is metabolized by the liver, you will have to monitor for many drug-drug interactions that can cause serious problems. Among them you will find commonly prescribed medications such as statins, erectile dysfunction drugs, and some benzodiazepines.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,534.78/month

Stribild elvitegravir/cobicistat/emtricitabine/tenofovir DF (EVG/COBI/FTC/TDF)

STR SINGLE-TABLET REGIMEN CONTAINING A BOOSTED INSTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily with food. Tablet contains 150 mg of the INSTI elvitegravir boosted by 150 mg cobicistat plus 200 mg emtricitabine and 300 mg tenofovir disoproxil fumarate (TDF).

For adults and children 12 years of age and older weighing at least 77 pounds (35 kg).

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 or liver problems. Stribild should not be started in individuals with estimated CrCl less than 70 mL/min and should be discontinued if CrCl decreases to less than 50 mL/min. Stribild is not recommended for patients with severe liver problems, or during pregnancy.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN STRIBILD:** Emtriva, Viread, and Tybost (elvitegravir is not available separately).
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Common side effects reported in 10% or more of study participants include nausea and diarrhea. Other less common side effects include abnormal dreams and headache. Before taking Stribild, kidney function testing should be conducted including serum creatinine, serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Stribild. Cobicistat can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. 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, and Zantac. Do not take Stribild with alfuzosin, carbamazepine, phenobarbital, phenytoin, ergotamine, dihydroergotamine, methylergonovine, oral midazolam, pimozide, Revatio, rifampin, rifabutin, rifapentine, Serevent, triazolam, or St. John's wort. An alternative corticosteroid to systemic dexamethasone should be considered. No significant interactions with beclomethasone or prednisolone. Risks versus benefits of using Stribild and voriconazole together should be assessed with expert consultation. Do not use with lovastatin or simvastatin (Advicor, Altoprev, Mevacor, Simcor, Vytorin, and Zocor). Cholesterol-lowering drugs such as rosuvastatin and atorvastatin should be used with caution and started at the lowest dose possible. Monitor closely for increased side effects from these medications, such as muscle pain. Concentrations of antidepressants such as fluoxetine, paroxetine, bupropion, or amitriptyline 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 many nasal and inhaled steroids like fluticasone, which may lead to symptoms of Cushing's syndrome. An alternative corticosteroid to fluticasone is recommended. Use caution with beta blockers 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. Monitor for increased side effects of these medications, such as visual disturbances. Effectiveness of oral contraceptives may be decreased; consider using alternative or additional contraception methods. Co-administer bosentan and immunosuppressants like Prograf, Gengraf, Neoral, and Sandimmune with caution. Reduce Daklinza dose to 30 mg. Taking with Harvoni, Olysio, Viekira Pak, or Zepatier is not recommended. Monitor kidney function more closely with Epclusa. Not intended to be taken with other HIV medications, unless prescribed that way. 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 not listed here.

MORE INFORMATION

The newer version of this drug, Genvoya, was approved for use in patients on hemodialysis last year; however, doctors are also using off-label prescribing of Biktarvy or Juluca for patients on hemodialysis. Genvoya along with its sister med Stribild were recently downgraded in U.S. HIV treatment guidelines, from "recommended initial therapy for most people" to "recommended initial therapy in certain clinical situations." The change was made due to the presence of the booster cobicistat, which has many drug interactions, and because these meds do not have the high barrier to drug resistance that Biktarvy, Tivicay, and Triumeq have. Stribild is not recommended for use in pregnancy due to substantially lower exposures of cobicistat and elvitegravir during the second and third trimesters as well as reports of viral breakthrough. Switching regimen or close monitoring should be considered for those already taking this regimen. New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception. It is unclear whether dolutegravir is the only integrase inhibitor with the potential to cause these birth defects (neural tube defects), or if other integrase inhibitors also carry this risk. Consult your provider to discuss guidance on how to manage regimens containing dolutegravir or a different integrase inhibitor if there is any possibility of conception.

DR. DAVID HARDY SAYS: Stribild was the third STR to be approved, in 2012, and the first STR to contain an integrase inhibitor medication (elvitegravir, formerly Vitekta) as well as the first to contain the "booster" Tybost (cobicistat). In order for the elvitegravir part of Stribild to be given once a day and effectively suppress HIV, it must be given with a "booster", like Tybost (cobicistat) or Norvir. Studies of Stribild comparing it to either Atripla or Reyataz/Norvir-containing ART regimens in PLWH starting their first ART regimen showed that it was similar to (just as good as) these two regimens. Due to these favorable comparisons, Stribild was recommended as a first-line ART regimen since it was first approved, but in 2018 it fell out of both the DHHS and IAS-USA guidelines as a recommended first-line ART regimen for all PLWH due to its booster (side effects and drug-drug interactions) and history of lower genetic barrier to viral resistance. Because Stribild contains Viread, PLWH who have pre-existing mild to moderate kidney disease, or who develop moderate kidney disease, should not receive Stribild. This limitation of Stribild has been improved with the availability of newer STRs. The use of Stribild was previously strong, but due to availability of newer STRs with less side effects and fewer drug interactions, its use continues to decrease.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: It is important to monitor the kidneys and bone density while taking Stribild. If there are changes in your bone density or your kidney functions, ask your doctor to switch you to Genvoya or Biktarvy. Because of cobicistat, Stribild has serious drug interactions that either increase or decrease the levels of commonly prescribed drugs such as some statins, benzos, and erectile dysfunction drugs. Remember to take it with food.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$3,707.99/month

Odefsey

rilpivirine/emtricitabine/tenofovir alafenamide **(RPV/FTC/TAF)**

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily, with a standard meal (more than 390 calories). See below. Tablet contains 25 mg of the NNRTI rilpivirine plus 200 mg emtricitabine and 25 mg tenofovir alafenamide (TAF).

Must be taken with a meal that you chew—not just nutritional drinks or protein shakes. Taking rilpivirine without food could result in a 40% decrease in drug absorption and may lead to resistance.

People taking HIV treatment for the first time must have an HIV RNA (viral load) of less than 100,000 copies/mL and a CD4 T-cell count of more than 200 cells/mm^3 before starting Odefsey due to higher rates of virologic failure in these patients.

For adults and children 12 years of age and older weighing at least 77 pounds (35 kg) and having a CrCl of at least 30 mL/min.

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.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN ODEFSEY:** Edurant and Descovy (co-formulation of Emtriva and TAF).
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Moderate to severe side effects are uncommon; insomnia, headache, and depressive disorders (depression, negative thoughts, suicidal thoughts or actions) were each reported in 2% of study participants on rilpivirine-containing regimens. Cases of rash and increased liver enzymes have also been reported with regimens containing rilpivirine. There may be a small increase in serum creatinine (SCr) and decrease in estimated creatinine clearance (CrCl) associated with rilpivirine. See Descovy page for other possible effects on kidney function. The most common (greater than 10%) side effect seen in clinical trials with Descovy (the fixed-dose combination of Emtriva and TAF) is nausea. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemildy (TAF), all three used for the treatment of hepatitis B. Proton pump inhibitors (PPIs, heartburn or stomach acid drugs like Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix, etc.) can't be taken with Odefsey. Antacids containing aluminum, magnesium hydroxide, or calcium carbonate can be taken two hours before or four hours after Odefsey. Stomach acid-reducing drugs like Pepcid, Tagamet, and Zantac can be taken 12 hours before or four hours after a dose of Odefsey. Do not take with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, or the herb St. John's wort. Taking Odefsey with rifabutin is not recommended. 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 fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, or telithromycin, because these drugs increase rilpivirine levels, which can increase the risk for side effects. Reduced methadone levels can occur and while dose adjustments are not necessary, it is recommended to monitor for withdrawal symptoms. Odefsey should also not be taken with other medications that prolong QTc interval or medications with a known risk of torsades de pointes. May be taken with Daklinza, Harvoni, Olysio, Sovaldi, Zepatier, or Epclusa. Cannot be taken with Viekira Pak. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Odefsey is a single-tablet regimen that is an option for people with impaired kidney function. Rilpivirine-containing regimens can be relatively difficult to take because of their food requirement and drug interactions. In addition, strict adherence is critical due to the relatively low barrier to the development of resistance. The Odefsey tablet is very small in size, which may be advantageous to individuals who have difficulty swallowing.

MANUFACTURER

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

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

AVERAGE WHOLESALE PRICE

$3,216.92/month

DR. DAVID HARDY SAYS: Odefsey is the sixth STR approved, in 2016, and is commonly considered the "new and improved" version of Complera. Clinical trials have shown that switching PLWH who are receiving Atripla or Complera to Odefsey results in similar (as good as) results in terms of suppressing their HIV compared to keeping them on their initial ART regimen. Those PLWH switched from Atripla to Odefsey also had decreased side effects (grogginess, vivid dreams) compared to those who continued Atripla. Odefsey continues to have the same potency problems that Complera has, that is, it is not as effective in suppressing initial high viral loads in PLWH (>100,000 copies/ml). Similar to Complera, Odefsey is well tolerated by PLWH, with minimal to rare side effects. Therefore, Odefsey has not been recommended for initial treatment for all PLWH, but rather only those with low initial viral loads (<100,000 copies/ml). Although not specifically studied, Odefsey's use as an ART switch regimen for PLWH with undetectable viral loads off of a regimen associated with side effects (e.g., protease inhibitor) would probably work well as it did with Complera.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Odefsey is a once-a-day single-tablet regimen that contains two HIV nucleoside analog reverse transcriptase inhibitors (emtricitabine, tenofovir alafenamide) and a non-nucleoside reverse transcriptase inhibitor (rilpivirine). Odefsey is comparable to Complera; the difference is that Odefsey contains tenofovir alafenamide instead of tenofovir disoproxil, reducing the risk for kidney toxicity and loss of bone density. This single-tablet regimen is recommended in certain clinical situations for individuals who have not yet been treated for HIV, and have a viral load less than or equal to 100,000 copies. It is also prescribed to individuals with previous HIV antiretroviral treatment who are virally suppressed (less than 50 copies) for at least six months, with no history of treatment failure related to developing resistance to the other medicines contained in Odefsey. Consult your doctor about all medications you are taking, prescribed or over-the-counter. Serious drug interactions can occur. If you feel extremely depressed or suffering insomnia, tell your doctor. Damage to the liver or kidneys is a possibility when taking Odefsey. Make sure your doctor monitors liver and kidney functions. If you experience an allergic reaction call your doctor immediately and stop taking Odefsey.

Complera

rilpivirine/emtricitabine/tenofovir disoproxil fumarate **(RPV/FTC/TDF)**

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily, with a standard meal (more than 390 calories) for adults and children 12 years of age and older weighing at least 77 pounds (35 kg). Tablet contains 25 mg of the NNRTI rilpivirine plus 200 mg emtricitabine and 300 mg tenofovir DF (TDF).

Must be taken with a meal that you chew—not just nutritional drinks or protein shakes. Taking rilpivirine without food could result in a 40% decrease in drug absorption and may lead to resistance.

People taking HIV treatment for the first time must have an HIV RNA (viral load) of less than 100,000 copies/mL and a CD4 T-cell count of more than 200 cells/mm^3 before starting Complera due to higher rates of virologic failure in these patients.

Take missed dose as soon as possible, unless it's closer to the time of your next dose. Do not double up on your next dose. Complera should not be used in people with CrCl less than 50 mL/min or severe liver impairment.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN COMPLERA:** Edurant and Truvada (co-formulation of Emtriva and Viread).

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Moderate to severe side effects are uncommon. Insomnia, headache, and depressive disorders (depression, negative thoughts, suicidal thoughts or actions) were each reported in 2% of study participants. Cases of rash and increased liver enzymes have also been reported with regimens containing rilpivirine. There may be a small increase in serum creatinine (SCr) and decrease in estimated creatinine clearance (CrCl) associated with rilpivirine. See Truvada page for other possible effects on kidney function. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted.

POTENTIAL DRUG INTERACTIONS

Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here. Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for treatment of hepatitis B. Proton pump inhibitors (PPIs, heartburn or stomach acid drugs like Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix, etc.) can't be taken with Complera. Antacids containing aluminum, magnesium hydroxide, or calcium carbonate can be taken at least two hours before or at least four hours after a Complera dose. Stomach acid-reducing drugs like Pepcid, Tagamet, and Zantac can be taken at least 12 hours before or at least four hours after a Complera dose. Do not take Complera with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, or the herb St. John's wort (other herbals have not been studied with Complera, but consult with a pharmacist before taking any herbals or OTC supplements). 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 fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, or telithromycin, because these drugs increase rilpivirine levels, which can increase the risk of side effects. Reduced methadone levels can occur and while dose adjustments are not necessary, it is recommended to monitor for withdrawal symptoms. Complera should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk of torsades de pointes. Complera may be taken with Daklinza, Harvoni, Olysio, Sovaldi, and Zepatier. Monitor for tenofovir toxicities with Epclusa. Complera cannot be taken with Viekira Pak. Not intended to be taken with other HIV medications, unless prescribed that way. Tell YOUR provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Complera can be relatively difficult to take because of its food requirement and drug interactions. In addition, strict adherence is critical due to its relatively low barrier to the development of resistance. A newer version of Complera, Odefsey, contains tenofovir alafenamide (TAF) instead of tenofovir DF; TAF is safer on kidney and bone health. Also as a result of the TAF, Odefsey can be taken by people with more advanced kidney disease, down to a renal function (CrCL) of 30 mL/min.

DR. DAVID HARDY SAYS: Complera was the second STR approved in the U.S., in 2011. At that time, it was the first alternative STR to Atripla and offered PLWH a single, once-a-day pill which could (and was recommended) to be taken with food. It does not have the pesky grogginess and vivid dreams associated with Atripla. While Complera's side effects are better than Atripla's, its potency has always been somewhat questionable in PLWH with high initial viral loads (greater than 100,000 copies/mL). On the other hand, Complera's side effects have been minimal and therefore well tolerated by PLWH. Primarily due to its lack of potency, it has never been recommended as a starting regimen for all PLWH. Since the development of the "new and improved" version of Complera, called Odefsey, Complera's use has decreased and, because it has fallen further out of the recommended ART guidelines due to the issues above, it is rarely prescribed today.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Complera is the combination of three HIV medicines contained in one single tablet and taken once a day. It is comparable to Odefsey as it combines rilpivirine with emtricitabine and the original tenofovir disoproxil fumarate while Odefsey contains tenofovir alafenamide. Complera is recommended as an initial therapy in certain clinical situations for individuals with a viral load less than 100,000 copies. It could also be prescribed to those wanting to replace their current regimen and have had suppressed viral load (less than 50 copies) for at least six months. It is not recommended if the reason for replacement is due to developing resistance to other antivirals, more so those contained in Complera. You need to watch for drug-drug interactions and changes in liver and kidney functions.

MANUFACTURER

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

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

AVERAGE WHOLESALE PRICE

$3,216.92/month

Atripla

efavirenz/emtricitabine/tenofovir disoproxil fumarate **(EFV/FTC/TDF)**

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily on an empty stomach, preferably at bedtime (food increases the risk of central nervous system, or CNS, toxicities). Tablet contains 600 mg of the NNRTI efavirenz plus 200 mg emtricitabine and 300 mg tenofovir disoproxil fumarate (TDF).

For adults and children 12 years of age and older weighing at least 88 pounds (40 kg).

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. 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.

A similar, but not exact, off-patent medication is available (see pages for Symfi and Symfi Lo, EFV/3TC/TDF).

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN ATRIPLA:** Sustiva and Truvada (co-formulation of Emtriva and Viread).

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Use with caution in individuals with depression or other psychiatric issues who are not receiving mental health care. A 2014 study (reference online) reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized the fact that efavirenz has an association with suicidality (reported suicidal ideation or attempted or completed suicide), and should be used with caution in patients with severe or uncontrolled depression and/or a history of suicidality. It is recommended for anyone on a regimen containing efavirenz to be screened for depression and suicidality. Common side effects may include dizziness, drowsiness, abnormal or vivid dreams, difficulty concentrating, rash, diarrhea, nausea, fatigue, headache, and insomnia. These 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. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the emtricitabine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. The efavirenz component of Atripla has been associated with central nervous system (CNS) birth defects in non-human primates, and cases of neural tube defects have been reported after first trimester exposure in humans. A link between efavirenz and birth defects in humans has not been supported in meta-analyses. The recommendation is that women in their first trimester continue taking efavirenz 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). Because of the association with suicidality and neuropsychiatric effects, it is also recommended to screen for antenatal and postpartum depression in women with HIV who are taking a regimen containing efavirenz. 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

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for the treatment of hepatitis B. Atripla should not be taken with voriconazole, ergot derivatives, midazolam, pimozide, triazolam, bepridil, or St. John's wort. Atripla should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk of torsades de pointes. No dose adjustment of Atripla needed with Sovaldi. Use caution when administering Atripla with Harvoni and monitor renal function closely due to possible increased tenofovir levels. Increase dose of Daklinza to 90 mg when used with Atripla. Atripla should not be taken with Epclusa, Olysio, Viekira Pak, or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

DR. DAVID HARDY SAYS: Atripla was the first STR to be approved, in 2006. It was a popular, heavily recommended regimen for many years, until better STRs were approved. Due to its at times persistent neuropsychiatric side effects (grogginess, vivid dreams, worsening of mental health conditions) and elevated cholesterol, along with a requirement to be taken without food and at bedtime, this STR fell out of the recommended guidelines several years ago. Clinical trials of Atripla versus integrase inhibitor-containing ART regimens have shown that the integrase inhibitor ART regimens were superior to Atripla. Atripla is now rarely, if ever, used in the U.S.; however, it remains a commonly used ART regimen in other parts of the world (Africa, India, South America) although its use is decreasing. Of note, two quasi-generic, nearly-identical versions of Atripla were approved in 2018, but their uptake has not been strong.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Atripla is a once-a-day single-tablet regimen that has been used to treat HIV infection for quite some time. It was the favorite for initial therapy due to its potency and relative safety. The medicines contained in Atripla are efavirenz, emtricitabine, and tenofovir disoproxil. Efavirenz is known for its neurotoxicity. Individuals taking it have reported vivid dreams, depression, fatigue, and insomnia. For some time people believed these side effects would go away while others believe that you just get used to them. Watch out for any liver, kidney, bone, or mental problems while taking this regimen. Make sure your doctor monitors you closely.

MORE INFORMATION

Atripla is listed as a "Recommended Regimen in Certain Clinical Situations" in the DHHS guidelines based on a high rate of central nervous system side effects and a possible association with suicidality. Be careful when stopping Atripla, so that you avoid the rapid development of HIV resistance to it—check with your provider or pharmacist first.

MANUFACTURER

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

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

AVERAGE WHOLESALE PRICE

$3,266.88/month

Symfi and Symfi Lo

efavirenz/lamivudine/tenofovir disoproxil fumarate (EFV/3TC/TDF)

STR SINGLE-TABLET REGIMEN CONTAINING AN NNRTI AND TWO NRTIs

✔ RECOMMENDED INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily on an empty stomach, preferably at bedtime (food increases the risk of central nervous system, or CNS, toxicities). The Symfi tablet contains 600 mg of the NNRTI efavirenz plus 300 mg lamivudine and 300 mg tenofovir DF (TDF). The Symfi Lo tablet contains a lower dose of efavirenz, 400 mg, plus 300 mg lamivudine and 300 mg tenofovir DF (TDF).

For adults and pediatric patients weighing at least 77 pounds (35 kg) for Symfi Lo and 88 pounds (40 kg) for Symfi.

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. Do not split or crush the tablet. Dose cannot be adjusted for people with kidney problems. Symfi and Symfi Lo are not recommended for patients with CrCl less than 50 mL/min or individuals requiring dialysis. Symfi or Symfi Lo should not be used in people with moderate or severe kidney or liver impairment.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN SYMFI:** Sustiva, Epivir, and Viread.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects occurring in 5% or more of studied individuals include headache (14%), body pain (13%), fever (8%), abdominal pain (7%), back pain (9%), asthenia (6%), diarrhea (11%), nausea (8%), vomiting (5%), arthralgia (joint pain, 5%), depression (11%), insomnia (5%), anxiety (6%), pneumonia (5%), and rash (18%). These side effects are most common at the start of treatment and usually diminish in two to four weeks. Bedtime dosing on an empty stomach can help reduce symptoms. Use with caution in individuals with depression or other psychiatric issues who are not under a psychiatrist's care. Prior to initiation, people should be tested for hepatitis B (HBV) infection. Severe exacerbations of hepatitis B have been reported in people who are co-infected with hepatitis B and have discontinued the lamivudine and/or tenofovir components. Monitor liver enzymes closely in people co-infected with hepatitis B and, if appropriate, initiation of anti-hepatitis B therapy may be warranted. The efavirenz component in these medications can cause a false positive for marijuana on certain drug tests. A more specific confirmatory test can be done.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), all three used for treatment of hepatitis B. Do not take with another nephrotoxic (harmful to the kidneys) medication, such as high-dose or multiple NSAIDs (non-steroidal anti-inflammatory drugs; these include aspirin, ibuprofen – Motrin, Advil, and others, and naproxen sodium – Aleve and others). Should not be taken with voriconazole, ergot derivatives, midazolam, pimozide, triazolam, bepridil, or St. John's wort. Efavirenz should also not be taken with other medications that prolong QTc interval (a heart problem) or medications with a known risk of torsades de pointes. May affect warfarin levels. Can decrease levels of buprenorphine and methadone—monitor for withdrawal. When taken with carbamazepine, phenobarbital, or phenytoin, periodic monitoring of anticonvulsant and efavirenz 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 posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. Monitor effectiveness of clarithromycin or consider using azithromycin instead. Levels of immunosuppressants should be monitored when starting or stopping Symfi or Symfi Lo. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). No dose adjustment of Symfi or Symfi Lo needed with Sovaldi. Use caution when administering with Harvoni and monitor renal function closely due to possible increased tenofovir levels. Increase dose of Daklinza to 90 mg when used with Symfi or Symfi Lo. Should not be taken with Epclusa, Olysio, Viekira Pak, or Zepatier. Not intended to be taken with other HIV medications, unless prescribed that way. See Atripla page for more potential side effects. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Symfi and Symfi Lo are basically alternative versions of Atripla, a well-established HIV medication that's no longer in favor when starting therapy. If you can't sleep, ask your doctor about gradually adjusting the timing of your dose until it's taken during the day. A rare genetic trait affecting drug metabolism of Sustiva, leading to a higher rate of side effects, occurs more in African Americans. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Randomized clinical trial data have demonstrated the efficacy of lower dose (400 mg) efavirenz found in Symfi Lo, however this dose has not been studied in a U.S. population, in pregnant women, or in patients with TB and HIV. The U.S. guidelines therefore preferentially recommends Symfi with higher dose efavirenz (600 mg) over the reduced dose of efavirenz found in Symfi Lo (400 mg) at this time.

Symfi and Symfi Lo are listed as a "Recommended Regimen in Certain Clinical Situations" in the DHHS guidelines, just as Atripla is, due to their association with a high rate of central nervous system side effects and possible association with suicidality. Be careful when stopping these medications, so that you avoid the rapid development of HIV resistance to it—check with your provider or pharmacist first.

DR. DAVID HARDY SAYS: Symfi and Symfi Lo are the ninth and tenth STRs approved by the FDA, in March 2018, and are the first fully generic STRs. Of note, while almost identical to the branded medication Atripla, the substitution of lamivudine for emtricitabine (Emtriva) makes them slightly different. The FDA approved these two fixed-dose combinations of previously approved antiretrovirals based not upon clinical trial data, but rather pharmacokinetic demonstration of bioequivalence, which means that Mylan, the manufacturer, had to show that the combination tablet of the three medications combined produced similar blood levels of the three drugs when given as three separate tablets. The lower dose of efavirenz in Symfi Lo (400 mg) is based upon supporting data from the ENCORE1 study which demonstrated similar virologic potency but fewer side effects with the lower dose of efavirenz. The uptake of these two new fully generic STRs in clinical practice is still uncertain as both the DHHS and IAS-USA guidelines removed efavirenz-containing regimens from their first-line recommended regimens many years ago, based primarily upon excessive side effects compared to newer STRs. A unique and distinguishing characteristic of these STRs is their lower monthly wholesale acquisition cost (WAC): $1,630 compared to $2,100 for Delstrigo, $2,950 for Biktarvy, $3,500 for Symtuza, $2,800 for Triumeq, and $3,000 for Genvoya and Stribild.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Symfi and Symfi Lo are once-daily single-tablet regimens that might offer powerful antiretroviral treatment at a much lower price than comparable antiretroviral treatments on the market. The difference between them is that Symfi Lo has a lower dose of efavirenz than Symfi. Research among adults living with HIV shows that treating them with tenofovir and emtricitabine was comparably effective regardless of whether they also received 400 mg or 600 mg of efavirenz. The advantage of the lower 400 mg dose vs. the 600 mg higher is that the exposure to neurotoxicities is less, therefore individuals with the lower dose report less insomnia, depression, and dizziness.

MANUFACTURER

Mylan
symfi.com; symfi-lo.com
mylan.com
(877) 446-3679

AVERAGE WHOLESALE PRICE

Symfi: **$1,961.33**/month
Symfi Lo: **$1,961.33**/month

INVESTIGATIONAL DRUG AT PRESS TIME.

PHOTO UNAVAILABLE

long-acting cabotegravir/rilpivirine (CAB LA/RPV LA)

LA LONG-ACTING INJECTABLE REGIMEN; CONTAINS AN INSTI AND AN NNRTI

DHHS RECOMMENDATION NOT YET ESTABLISHED

STANDARD DOSE

Clinical trials of this investigational regimen used a long-acting cabotegravir injection of 400 mg plus 600 mg rilpivirine injection every 4 or 8 weeks. The dose consisted of two 2 mL injections. Rilpivirine must be taken with food; see Edurant page for details. An induction phase with oral medication was used in research and will be used when approved. The cabotegravir tablet may not otherwise be available on the market.

➤ SEE EDURANT; cabotegravir is not yet available

➤ SEE PACKAGE INSERT when available for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

In one study, injection site reactions with mild, short-term (two to five days) redness, pain, and swelling was reported in 84% of all injections. Moderate symptoms were reported in 15% of injections. Less than 1% of patients discontinued the study due to injection site reactions. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients with pre-existing psychiatric conditions on an INSTI. There may be a possibility of birth defects—see "More information."

POTENTIAL DRUG INTERACTIONS

New interactions continue to be discovered after drug approval (cabotegravir is the new medication). Not intended to be taken with other HIV medications, unless prescribed that way. If used with abacavir/lamivudine during the initial oral induction phase, as this regimen was also studied, be aware of possible drug interactions with these agents (see Epzicom page). During the initial oral induction phase with rilpivirine, it is not recommended to co-administer carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, proton pump inhibitors (Aciphex, Dexilant, Nexium, Prevacid, Prilosec, Protonix), or St. John's wort. Antacids should be taken two hours before or at least four hours after oral Edurant. Acid-reducing drugs (Pepcid, Tagamet, Zantac, and Axid) should be taken 12 hours before or four hours after an oral Edurant dose. Some of these interactions will no longer be relevant once injection therapy begins, or a maintenance phase containing rilpivirine starts; however, see package insert when available for guidance. Monitor for worsening of any fungal infections when rilpivirine is used with antifungal medications like fluconazole, itraconazole, ketoconazole, posaconazole, or voriconazole; dose adjustment for these medications may be needed. Use azithromycin when possible instead of the antibiotics clarithromycin, erythromycin, or telithromycin. Methadone levels are reduced slightly and patients should be monitored for symptoms of withdrawal. Should be used with caution when taken with other medications with a known risk of torsades de pointes or QT prolongation (these abnormal heart rhythms can make the heart stop). Tell YOUR provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

May be FDA approved this year. This drug is taken once a month, as two shots, into the muscle. That's it. Or as ViiV Healthcare pointed out, it changes HIV treatment from 365 dosing days per year to just 12. People who are adherent to their HIV regimen now may be eligible to switch to this med when approved. The trade-off with long-acting treatment is the requirement for near-perfect adherence and visiting your doctor's office 12 times a year instead of two or three. The treatment is also one injection per butt muscle. Cabotegravir is from the top-of-the-line HIV medications right now, the INSTI drug class. They have great efficacy and are, in general, easy to take. Rilpivirine is already on the market in a variety of oral formulations (Complera, Edurant, Juluca, and Odefsey). Rilpivirine is not sold separately as an injectable. Cabotegravir is also being studied for HIV prevention as one PrEP shot taken every two months. The lead-in oral dosing is used to establish the tolerability of cabotegravir prior to long-acting injection. For example, if an allergic reaction occurs, it can be out of the system in a day or two. In the LATTE-2 study with people on first-time HIV therapy, cabotegravir plus rilpivirine given every 4 weeks or every 8 weeks was found to be as effective as the traditional three-med (even if only as one pill) oral combination given to people in the control group of the trial. There was some virologic failure in the 8 week group vs. none in the 4 week; hence, research went forward with only 4 week dosing. This success was out to 96 weeks (nearly two years). Moreover, the majority of participants given shots in the Phase III ATLAS study (more than 96%) said they preferred the injections every month or two months to taking their previous daily HIV oral regimen, despite any side effect or injection site reaction. New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception.

DR. DAVID HARDY SAYS: One strategy for making ART simpler and more convenient would be to change the frequency that anti-HIV medications need to be taken or administered. Two anti-HIV medications have been developed into long-acting, injectable (into muscle) forms and have completed testing in a successful phase 2 study (LATTE-2) and are now in phase 3 clinical trials. Cabotegravir is an investigational integrase inhibitor similar to Tivicay (dolutegravir). Rilpivirine is already approved by the FDA as an oral anti-HIV medication (Edurant). Both have been developed into injectable forms which maintain high enough drug levels in the blood to suppress HIV and allow for monthly or every two-months dosing. This combination of co-administered (one injection of each drug per butt muscle) monthly or every two months regimen was studied first in a Phase 2 study called LATTE-2. In October 2018, the LATTE-2 investigators reported that at 160 weeks (3 years) of follow-up, 104 of 115 participants (90%) and 95 of 115 participants (83%) receiving the injectable regimen, every 8 and 4 weeks respectively, remained virally suppressed. Of the patients on the oral comparator arm who chose to switch to the injectable regimen at week 96, 33 of 34 participants (97%) and 10 of 10 participants (100%) remained virally suppressed on every 8- and 4-week dosing, respectively. Building on the success of LATTE-2, this injectable ART regimen is being studied for HIV treatment in two Phase 3 studies: FLAIR (treatment-naïve) and ATLAS and ATLAS-2M (treatment-experienced with ART switch in PLWH with undetectable viral loads). Results from ATLAS-2M are expected in 2019. We know that the LATTE-2 showed very good HIV suppression and few generalized side effects, but nearly 100% of the PLWH receiving the monthly or two-monthly injections in their butt muscles reported mild, short-term (2–5 days) "injection site reactions," consisting of pain, redness, and swelling where they received the injections. Interestingly, the majority of PLWH in the study preferred the injections over their previous daily tablet ART regimens. This was reported to be due to greater convenience of monthly or two-monthly dosing, lack of being reminded daily of their HIV-positive status, and not having to remember and manage tablet prescriptions. More will be revealed regarding this new way of receiving ART as results from the studies above become available. [See more data online.] It is important to note that injectable cabotegravir given every two months by itself is also being compared to Truvada for pre-exposure prophylaxis (PrEP) in two large studies being conducted by the HIV Prevention Trials Network (HPTN).

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: A few long-acting HIV regimens are under investigational. These regimens will change HIV care radically and further on will do so with PrEP as well. The ATLAS study showed long-acting cabotegravir and rilpivirine, injected once a month, had similar efficacy to a standard of care, daily, oral three-drug regimen at week 48. This study was designed for individuals on HIV treatment that were virally suppressed for at least six months.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Not yet established.

Tivicay dolutegravir (DTG)

INSTI INTEGRASE STRAND TRANSFER INHIBITOR ★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One 50 mg tablet once daily without regard to food, for people on HIV therapy for the first time (treatment-naïve) or treatment-experienced people who have never taken an INSTI. One 50 mg tablet twice daily, without regard to food, for people who have or who are suspected to have certain INSTI drug resistance or who are taking certain other medications. Must be taken in combination with another antiretroviral(s) which does not contain this medication or medication from the same drug class.

Tivicay is approved for adults and children weighing at least 66 pounds (30 kg). For patients weighing 66 pounds (30 kg) to 88 pounds (40 kg), the dose is one 10 mg tablet and one 25 mg tablet (35 mg total dose) once daily without regard to food. For patients weighing at least 88 pounds (40 mg), the dose is one 50 mg tablet once daily without regard to 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. 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.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

In general, Tivicay is well tolerated with infrequent side effects. 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. Additionally, increased CPK (creatine kinase, a lab value indicating muscle damage), rhabdomyolysis (breakdown of muscle), and myopathy or myositis (muscle pain) were reported. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring patients on an INSTI who have pre-existing psychiatric conditions. Tivicay can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function. Liver enzymes should be monitored in people with hepatitis B or C. There may be a possibility of birth defects—see "More information."

POTENTIAL DRUG INTERACTIONS

Do not take with the anti-arrhythmic dofetilide. Intelence decreases Tivicay levels by 88%, therefore, these two medications must be co-administered with Kaletra, boosted Prezista, or boosted Reyataz. Tivicay should be taken two hours before or six hours after taking laxatives or antacids, the ulcer medication sucralfate, oral iron or calcium supplements, or buffered medications. It can be taken with iron- or calcium-containing supplements if taken together with food. Acid reducers (Pepcid, Zantac, Tagament) and proton pump inhibitors (for example, Aciphex, Dexilant, Prilosec, Prevacid, Protonix, and Nexium) are okay to use. Avoid taking with Viramune, oxcarbazepine, phenytoin, phenobarbital, and St. John's wort. Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects. Use alternatives to rifampin, carbamazepine, efavirenz, Aptivus/Norvir, and Lexiva/Norvir when possible in people with confirmed or suspected INSTI drug resistance, but these medications can be taken with Tivicay 50 mg twice daily. Should be okay to take with Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Tivicay is part of Juluca as well as Triumeq, both single-tablet regimens. Tivicay is considered a second-generation INSTI—it may work in many individuals whose virus has developed resistance to other INSTIs, but it needs to be dosed twice daily in these people. Compared to other INSTIs, Tivicay has a high genetic barrier against the development of resistance, similar to the protease inhibitors (such as Prezista). Tivicay has also demonstrated superiority to Prezista when looking at virologic results. Pediatric HIV guidelines added Tivicay as part of a preferred regimen. Tivicay is particularly useful when drug interactions are a concern with the HIV protease inhibitor (PI) drugs. Tivicay is a small tablet, a benefit for patients who have difficulty swallowing.

Tivicay as part of Juluca is used as a medication to switch to for people with undetectable viral loads on their current regimen for at least six months; see Juluca. Another ART (antiretroviral therapy) switch strategy with some supporting evidence for its consideration in people with viral suppression in the DHHS guidelines that uses Tivicay is switching to a boosted protease inhibitor + integrase inhibitor. In two small observational studies, individuals were switched from their current ART regimens to Prezista + Norvir + Tivicay, and viral suppression was maintained in over 97% of participants. Another strategy with some supporting evidence suggests switching patients with a suppressed viral load to a regimen of Tivicay + Epivir (lamivudine, 3TC) for maintenance therapy. A fixed-dose combination pill with these two medications is expected to be approved this year; see dolutegravir/3TC page.

New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception. Until more information is available, regimens containing dolutegravir are not recommended for use in ART-naïve patients who are pregnant or within 12 weeks of conception. It is unclear whether dolutegravir is the only integrase inhibitor with the potential to cause these birth defects (neural tube defects), or if other integrase inhibitors also carry this risk. Consult your provider to discuss guidance on how to manage regimens containing dolutegravir or a different integrase inhibitor if there is any possibility of conception.

DR. DAVID HARDY SAYS: Tivicay was the third integrase inhibitor approved, in 2013, initially as a single agent and a year later as a component of the STR Triumeq (Tivicay/Ziagen/Epivir). What makes Tivicay stand out from other integrase inhibitors or STRs containing integrase inhibitors is its proven high barrier to HIV resistance. To date (more than five years since initial approval), there have been few, if any, well-confirmed cases of resistance to Tivicay in PLWH taking this medication as first-time ART. In addition, clinical trial data show that Triumeq is superior to (better than) Atripla and both Prezista/Norvir and Reyataz/Norvir in terms of suppressing viral loads as well as having fewer side effects. As mentioned before, many HIV treaters are not always comfortable with prescribing Triumeq due to the Ziagen (abacavir) which it contains for reasons mentioned on other pages. For those treaters, the two-pill combination of Tivicay and Descovy has become their favorite "go-to" first-line ART regimen. How this is now changing with the availability of Biktarvy is not yet clear. Some HIV treaters and the PLWH for whom they prescribe antiretrovirals may opt to simplify to Biktarvy or stick with what is already working well. In 2018, preliminary results from the Tsepamo study from Botswana unexpectedly showed an increased occurrence of neural tube defects in infants of HIV-positive women who were taking Tivicay at the time of conception. Until the final results of this study are known sometime in 2019, the use of Tivicay in HIV-positive women desiring to become pregnant and those able to become pregnant who are not using contraception is recommended to be avoided (see Triumeq).

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Tivicay is approved once a day for HIV-positive individuals initiating HIV treatment for the first time and for those on HIV treatment who have not taken integrase inhibitors before. It is prescribed twice a day, however, for those who have developed resistance to other integrase inhibitors.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
tivicay.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

50 mg tablets:
$2,088.59/month

Isentress HD (and Isentress) raltegravir (RAL)

INSTI INTEGRASE STRAND TRANSFER INHIBITOR

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

ISENTRESS HD: Two 600 mg film-coated tablets once daily for individuals new to HIV therapy (treatment-naïve) or who are virologically suppressed (have undetectable viral load) on an initial regimen of Isentress.

ISENTRESS: One 400 mg film-coated tablet twice daily for people with HIV treatment experience; this Isentress dose may also be taken by those new to HIV therapy.

Must be taken in combination with another antiretroviral(s) which does not contain this medication or medication from the same drug class. Isentress HD is for adults and children weighing at least 88 pounds (40 kg). Isentress is for adults and children weighing at least 4 pounds (2 kg). Both Isentress HD and Isentress can be taken without regard to food.

Isentress (but not Isentress HD) pediatric formulations are available as oral granules for suspension and flavored chewable tablets. Isentress dosing for neonates (birth to 4 weeks [28 days] of age) (for oral granules for suspension) and children less than 55 pounds (for chewable tablets) is based on weight; see package insert for dosing. The chewable tablets may be chewed or swallowed whole. Do not substitute chewable tablets or oral suspension for film-coated tablets.

Take missed dose as soon as possible, unless it's closer to the time of your next dose. Do not double up on your next dose.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

In general, raltegravir is very well tolerated with infrequent side effects. Those reported in up to 3–4% of study subjects include insomnia, nausea, and headache. The side effect profile in children is comparable to adults. Isentress may cause elevated levels of creatine kinase (a muscle enzyme). Inform your provider or pharmacist if you have a history of rhabdomyolysis, myopathy, or increased creatine kinase, or if you also take medications that may contribute to these conditions such as statins, fenofibrate, or gemfibrozil (cholesterol medications). There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. The DHHS guidelines recommend closely monitoring people with pre-existing psychiatric conditions on an INSTI. Chewable tablets contain phenylalanine, which can be harmful to patients with phenylketonuria.

POTENTIAL DRUG INTERACTIONS

Isentress HD cannot be used with rifampin, but Isentress can; increase Isentress to 800 mg twice daily when using with rifampin. Remember to decrease the raltegravir back to its original dose when you finish taking rifampin. There are no data on dosing of the chewable tablets with rifampin. There is no need to increase the raltegravir dose with rifabutin. With both Isentress HD and Isentress, avoid Gaviscon and other antacids containing aluminum or magnesium. Calcium-containing antacids like Tums (calcium carbonate) can be used with Isentress, but not Isentress HD. Other acid reducers (such as Pepcid, Zantac, Prilosec, and Prevacid) are okay to use. Raltegravir is not recommended with carbamazepine or phenobarbital. Raltegravir can be used with Daklinza, Harvoni, Olysio, Sovaldi, Viekira Pak, Zepatier, or Epclusa. Unlike Isentress, Isentress HD cannot be used with Intelence or boosted Aptivus. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

The newer formulation of Isentress HD was approved in 2017. While the previous version, Isentress, was well tolerated and highly effective, its twice-daily dose was seen by some as a small hindrance. Raltegravir-based regimens may be preferred for patients with high cardiovascular risk. Isentress is the preferred INSTI medication in HIV treatment guidelines for pregnancy, 400 mg twice a day in combination with 2 NRTIs. In pediatric HIV guidelines, Isentress was downgraded in 2017 from "preferred" to an "alternative" part of an initial regimen last year for children ages 6–12.

New preliminary data from an observational study in Botswana suggest that there may be an increased risk of birth defects in infants born to those who were receiving dolutegravir at the time of conception. It is unclear if other integrase inhibitors also carry this risk. Consult your provider to discuss guidance on how to manage regimens containing dolutegravir or a different integrase inhibitor if there is any possibility of conception.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

Isentress HD:
$1,800/month
Isentress 400 mg:
$1,800/month

DR. DAVID HARDY SAYS: Isentress HD was approved by the FDA in May 2017. It was developed to offer PLWH the option for a once-daily Isentress regimen. The total daily Isentress dose is 1,200 mg/day (600 mg x 2) along with two NRTIs (one tablet of Truvada, Epzicom, or Descovy). It's hard to imagine what the advantage of taking two Isentress HD plus another pill, all once-daily, would be over taking one of the STRs. Isentress was the first integrase approved, in 2007. Initially, it has to be taken twice daily (two tablets 8–12 hours apart). Early clinical trials demonstrated very rapid (and still the most rapid) drops in viral loads (compared to protease inhibitor and NNRTI regimens), suggesting that it was more potent than older classes of antiretrovirals. However, we soon learned that this rapid drop in viral load did not correlate with resistance to HIV resistance, as this occurs with Isentress at a rate similar to that for Atripla. At the time when Isentress was approved, it provided a critical new medication for many PLWH who had run out of treatment options and kept them alive. Isentress is one of, if not, *the* antiretrovirals with the fewest side effects. With the development of newer once-daily integrase inhibitors (Tivicay) and STRs (Genvoya, Biktarvy), the use of Isentress has waned in favor of simpler ART regimens.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Isentress and Isentress HD are both the brand names for the integrase inhibitor known as raltegravir. It is prescribed to treat HIV infection in patients with multi-drug resistance who have not taken integrase inhibitors before, as well as for individuals initiating treatment for the first time. The differences between regular Isentress and the HD version are the contained dose and the frequency that it is taken. With regular Isentress, you take one 400 mg pill twice a day, while with Isentress HD you take two 600 mg pills once a day. Isentress (not HD) can also be prescribed to children as an oral suspension or as chewable tablets. If a skin rash or an allergic reaction develops, stop the drug and call your provider. Liver and kidney functions must be monitored.

Prezcobix darunavir/cobicistat (DRV/COBI)

PI/PKE FIXED-DOSE COMBINATION CONTAINING A PROTEASE INHIBITOR AND A PHARMACOKINETIC ENHANCER (BOOSTER)

✔ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet (800 mg of the PI darunavir boosted by 150 mg cobicistat) once daily with food, in people with no darunavir-associated drug resistance, including both treatment-experienced individuals and those who are treatment-naïve (taking HIV therapy for the first time). Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug or medication from the same drug classes. Use with non-nucleosides or other protease inhibitors is not recommended.

Prezcobix is only available for people taking darunavir once daily, not those who require darunavir twice daily. It is not recommended to co-administer Prezcobix with tenofovir disoproxil fumarate (brand name Viread, found in Truvada), with creatinine clearance (CrCl) less than 70 mL/min (a measure of kidney function).

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. Prezcobix is not recommended during pregnancy due to substantially lower exposures of darunavir and cobicistat during pregnancy. Cobicistat has not been studied in individuals under 18 years of age, thus Prezcobix should not be used in pediatric patients. Do not use in people with severe liver impairment.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN PREZCOBIX:** Prezista and Tybost.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

As darunavir (contained in Prezcobix) contains a sulfa component, patients with a known sulfonamide allergy should be monitored for rash after starting it. The most common side effects reported in at least moderate intensity in 5% or more of study participants were diarrhea, nausea, rash, headache, abdominal pain, and vomiting. Cobicistat can cause a small, reversible increase in serum creatinine (SCr, which indicates the eGFR or estimated CrCl lab values) within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Serum phosphorus in patients with or at risk for kidney impairment should also be monitored. Kidney impairment, including cases of acute kidney failure and Fanconi syndrome, has 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; CrCl, urine glucose, and urine protein should be monitored regularly while taking Tybost-containing regimens. While very rare, severe rash (in 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. Observational cohort studies reported an association between some PIs (including darunavir) and an increased risk of cardiovascular (CV) events. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely, or never, seen with darunavir. With PIs, there can be increased bleeding in hemophiliacs.

POTENTIAL DRUG INTERACTIONS

Cobicistat interacts with many drugs because, as a booster, it inhibits liver enzymes involved in drug metabolism. Do not take with betamethasone, budesonide, carbamazepine, ciclesonide, dexamethasone, dronedarone, ergot derivatives, eslicarbazepine, fluticasone, triazolam, oral midazolam, lomitapide, lurasidone, methylprednisolone, mometasone, oxcarbazepine, phenobarbital, phenytoin, pimozide, rivaroxaban, Revatio, simvastatin, lovastatin, St. John's wort, triamcinolone, alfuzosin, ranolazine, or rifampin. Not recommended to be taken with avanafil, everolimus, rifapentine, salmeterol, ticagrelor, or voriconazole. Apixaban dose may need to be adjusted. Beclomethasone, prednisolone, and prednisone as alternative corticosteroids may be considered, particularly for long-term use. Atorvastatin and rosuvastatin dose should not exceed 20 mg daily. Clinical monitoring is recommended with drospirenone, due to potential for hyperkalemia. Do not take with colchicine if there is kidney or liver impairment. Can be used with Daklinza. Cannot be taken with Zepatier. Based on the mechanism, drug interactions with other hepatitis C medications are probably similar to the interactions with Prezista + Norvir. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

Since Prezista (darunavir) must be used with a PK enhancer such as cobicistat or ritonavir, this formulation makes for greater convenience, one less pill, and one less co-pay. The resulting co-formulation, however, is rather large in size, but the tablets are designed as an immediate-release formulation, so no potential problem with absorption is anticipated if the tablets are chewed, split, or crushed.

DR. DAVID HARDY SAYS: Approved in early 2015, this two-drug tablet consolidated Prezista and the booster Tybost into one tablet. It assures that Prezista will always be taken with its necessary booster. It has the "distinction" of being the largest antiretroviral tablet, which may be a problem for some PLWH to swallow. It was developed not only to ensure boosting and reduce pill number, but also as part of the run-up to the development of Symtuza. Its side effects are identical to those mentioned in Prezista.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: This is a protease inhibitor (PI) combined in one tablet with the booster known as cobicistat (COBI). Because of COBI, this PI can be taken once a day and should be used in combination with other HIV medicines. This protease inhibitor is superior in efficacy and tolerability when compared to Kaletra (lopinavir/ritonavir), another boosted PI. Darunavir is lipid-friendly and less likely to cause metabolic complications. If prescribed with Truvada, it is important to then monitor kidney functions and bone density. As with the other protease inhibitors, darunavir is metabolized by the liver; many drug-drug interactions can occur, either increasing or decreasing drug levels, causing serious problems. Your doctor must be aware of all the medications you take, even if they are over-the-counter or supplements.

A single-tablet, once-daily regimen containing darunavir/COBI/FTC/TAF is now available (see Symtuza). Darunavir is recommended as part of an initial regimen "in certain clinical situations" in DHHS guidelines. DHHS wrote this is "in part because of greater tolerability" with the integrase inhibitor medications compared to Prezista + Norvir or Prezcobix. According to the guidelines, "An example of a situation in which a darunavir-based regimen may still be preferred is when a high genetic barrier to resistance is particularly important, such as when there is substantial concern regarding a person's adherence or when antiretroviral therapy (ART) should be initiated before resistance test results are available [go to aidsinfo.nih.gov]." Examples of people needing to start treatment immediately before resistance test results are available include newly infected individuals, pregnant women, and those who are experiencing certain opportunistic infections (an indication of advanced disease).

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,317.55/month

Prezista darunavir (DRV)

PI PROTEASE INHIBITOR

✔ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One 800 mg tablet with 100 mg Norvir or 150 mg Tybost once daily with food for treatment-naïve people (those taking HIV therapy for the first time) 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 who have at least one Prezista-related resistance mutation. Prezista should always be taken with Norvir or Tybost. Must also be taken in combination with another antiretroviral(s) which does not contain this medication or medication from the same drug class.

For adults and children 3 years of age and older weighing at least 22 pounds (10 kg).

Prezista for children is dosed based on weight. There are 75 mg and 150 mg tablets as well as an oral suspension (100 mg/mL) (strawberry cream flavor) available for children three and older and adults who can't swallow pills.

Suspension needs to be taken with Norvir or Tybost, 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.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Prezista contains a sulfa component and should be used with caution in patients with severe 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 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 increase in serum creatinine (SCr) may be seen which does not translate to a decrease in kidney function. Observational cohort studies reported an association between some PIs (including darunavir) and an increased risk of cardiovascular (CV) events. Although some older PIs have been associated with liver toxicity, lactic acidosis, diabetes, or fat redistribution, these conditions are only rarely, or never, seen with darunavir. IRIS (immune reconstitution inflammatory syndrome) may occur as the immune system regains strength; signs and symptoms from previous infections may occur soon after HIV treatment is initiated. Report symptoms of illness, such as shingles or TB, to a health care provider. Protease inhibitors can cause increased bleeding in hemophiliacs.

POTENTIAL DRUG INTERACTIONS

Drug interactions of Prezista + Norvir may be different than those for Prezista + Tybost. Do not take with alfuzosin, dronedarone, colchicine (in patients with kidney or liver impairment), lomitapide, lurasidone, ranolazine, pimozide, ergot derivatives, triazolam, oral midazolam, rifampin, Revatio, Xarelto, or St. John's wort. Tramadol dose decrease may be needed. Monitor therapeutic effects and adverse reactions with use of some analgesics, such as fentanyl and oxycodone. Monitoring of clonazepam is recommended. Reduced dose of rifabutin is recommended. Do not use lovastatin or simvastatin, or co-formulations containing these drugs (Advicor and Vytorin). Cholesterol-lowering alternatives are rosuvastatin, atorvastatin (should not exceed 20 mg per day), pitavastatin, and pravastatin, but should be used with caution and started at the lowest dose possible. Monitor for increased side effects from these medications. Reduce clarithromycin dose by 50 to 70% in kidney impairment. The antifungal drugs itraconazole or ketoconazole should be used with caution (maximum dose is 200 mg per day for either). Voriconazole should not be used unless the benefits outweigh the risks. Prezista increases levels of nasal and inhaled fluticasone (found in Advair, Flonase, Breo Ellipta, Arnuity Ellipta, and Flovent) and budesonide, as well as systemic corticosteroids ciclesonide, betamethasone, dexamethasone, methylprednisolone, mometasone, and triamcinolone. Use alternative corticosteroid and monitor for signs of Cushing's syndrome. Beclomethasone, prednisolone, and prednisone as alternative corticosteriods may be considered, particularly for long-term use. Effectiveness of oral contraceptives may be decreased; consider using alternative methods of contraception. Monitoring is recommended with methadone. Titration or decreased dose may be needed for buspirone, diazepam, estazolam, and zolpidem. Therapeutic drug monitoring is recommended for antiarrhythmics amiodarone, bepridil, disopyramide, flecainamide, systemic lidocaine, mexiletine, propafenome, and quinidine. 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 not listed here.

DR. DAVID HARDY SAYS: Approved in 2006, it is still the "newest" protease inhibitor (this tells you something about recent progress in this class of medications). It must always be given with a booster, Norvir (ritonavir) or Tybost (cobicistat), to be effective. It is approved to be given as a part of a first-time ART regimen dosed once-daily (800 mg tablet + booster) with two NRTIs or dosed twice-daily (600 mg tablet + booster) for PLWH whose HIV has some resistance to protease inhibitors. Its major side effects are nausea, queasiness, diarrhea, and rash. It is the first and only protease inhibitor which is now approved as part of an STR (see Symtuza).

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Darunavir is lipid-friendly and less likely to cause metabolic complications. If prescribed with Truvada, it is important to monitor kidney function and bone density. As with the other protease inhibitors, darunavir is metabolized by the liver; many drug-drug interactions can occur either increasing or decreasing drug levels, causing serious problems. Your doctor must be aware of all the medications you take even if they are over-the-counter or supplements.

MORE INFORMATION

Prezista, which is now found in the recently approved single-tablet regimen Symtuza (see that page), is recommended as part of an initial regimen "in certain clinical situations" in DHHS guidelines. DHHS wrote this is "in part because of greater tolerability" with the integrase inhibitor medications compared to Prezista + Norvir or Prezcobix. There is growing evidence that a protease inhibitor-based regimen, boosted by ritonavir plus Epivir (lamivudine), can maintain viral suppression in patients who initiated triple-drug therapy, who achieved sustained viral suppression for at least 1 year, and who have no evidence of, or risk of resistance to, either darunavir or lamivudine. Use of Prezista with Norvir and Epivir may be a reasonable option when the continued use of TDF, TAF, or ABC is contraindicated or not desirable. Additionally, another ART switch strategy with some supporting evidence in patients with viral suppression in the DHHS guidelines is to switch patients to a boosted protease inhibitor + integrase inhibitor. In two small observational studies, patients were switched from their current ART regimens to Prezista + Norvir + Tivicay, and viral suppression was maintained in over 97% of participants. For patients on a complicated salvage regimen with current viral suppression and a history of treatment failure, there is evidence to support simplifying the regimen to a combination of Genvoya + Prezista. A single-tablet, once-daily regimen containing darunavir/COBI/FTC/TAF is now available (See Symtuza). Prezista + Norvir is a preferred component in the DHHS perinatal guidelines for use in pregnancy. Prezista is also found in the fixed-dose tablet Prezcobix.

MANUFACTURER

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

AWP

800 mg tablets:
$2,027.65/month

Evotaz atazanavir/cobicistat (ATV/COBI)

PI/PKE FIXED-DOSE COMBINATION CONTAINING A PROTEASE INHIBITOR AND A PHARMACOKINETIC ENHANCER (BOOSTER)

✔ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily with food. Each tablet contains 300 mg of atazanavir boosted by 150 mg cobicistat. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug or medication from the same drug classes. Use with Intelence or Sustiva is not recommended.

Use in treatment-experienced patients depends on protease inhibitor drug resistance. Co-administration with drugs containing tenofovir disoproxil fumarate (Viread, found in Atripla, Cimduo, Complera, Delstrigo, Stribild, Symfi, Symfi Lo, and Truvada) is not recommended if kidney function as measured by creatinine clearance is below 70 mL/min. Co-administration with drugs containing tenofovir alafenamide (Vemlidy, found in Biktarvy, Descovy, Genvoya, Odefsey, and Symtuza) is not recommended if kidney function as measured by creatinine clearance is below 30 mL/min.

Not recommended in people with any degree of liver impairment or those who are treatment-experienced and on hemodialysis.

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. Evotaz is not recommended during pregnancy due to substantially lower exposures of atazanavir and cobicistat during pregnancy. Cobicistat has not been studied separately from Genvoya and Stribild in individuals under 18 years of age; thus, Evotaz should not be used in pediatric patients.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN EVOTAZ:** Reyataz and Tybost.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common (greater than 10%) side effects reported in clinical trials were nausea, ocular icterus (yellowing of the eyes), and jaundice. Rash has also been reported, though less common. Cobicistat can cause a small, reversible increase in serum creatinine (SCr, which indicates the eGFR or estimated CrCl lab values) within the first few weeks of treatment without affecting actual kidney function (see Tybost for more information). Patients experiencing a confirmed increase in serum creatinine of greater than 0.4 mg/dL from baseline should be closely monitored for renal safety. Serum phosphorus in patients with or at risk for kidney impairment should also be monitored. Kidney impairment, including cases of acute kidney failure and Fanconi syndrome, has 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; CrCl, urine glucose, and urine protein should be monitored regularly while taking Tybost-containing regimens. Observational cohort studies reported an association between some PIs (including darunavir, found in Prezista and Prezcobix, and lopinavir/ritonavir, brand name Kaletra) and an increased risk of cardiovascular (CV) events; however, this has not been observed with Reyataz (atazanavir, or ATV), found in Evotaz. Another observational cohort study of predominantly male participants found a lower rate of cardiovascular events in those receiving atazanavir-containing regimens compared with other regimens. Further study is needed.

POTENTIAL DRUG INTERACTIONS

Cobicistat interacts with many drugs, because as a booster it inhibits liver enzymes involved in drug metabolism. Do not take with ergot derivatives, triazolam, oral midazolam, lurasidone, pimozide, Revatio, simvastatin, lovastatin, St. John's wort, Viramune, alfuzosin, ranolazine, rifampin, dronedarone, or irinotecan. Do not take with colchicine if there is kidney or liver impairment. Do not use with Olysio, Viekira Pak, or Zepatier. Can be used with Sovaldi, Daklinza (reduce Daklinza dose to 30 mg), or Harvoni (if TDF is not part of the HIV regimen). Monitor for tenofovir toxicities with Epclusa if TDF is part of the regimen. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Evotaz is an alternative PI for first-time therapy in DHHS HIV treatment guidelines, and is one of two PIs that are co-formulated with the booster cobicistat (the other is Prezcobix). Since most 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 is not an HIV medication. Similar to ritonavir, it is used to boost blood levels of other drugs. The two PK enhancers have a long list of drug interactions. Maintaining adequate hydration is important with Evotaz. Reyataz + Tybost + Epzicom is no longer included in the list of "Recommended Initial Regimens in Certain Clinical Situations" because it has disadvantages when compared with other regimens in this category.

DR. DAVID HARDY SAYS: Approved in early 2015 (at the same time as Prezcobix), this two-drug tablet combines Reyataz with a booster (Tybost) to ensure boosting and reduce pill number. There is and will not be (any time soon) an STR containing Reyataz. As discussed on the Reyataz page, the use of Reyataz as a first-time regimen for PLWH has significantly decreased due to its increased side effects compared to other ART options.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Evotaz is atazanavir boosted with cobicistat, and is prescribed for treatment-experienced patients and those initiating HIV treatment for the first time. Evotaz is a once-a-day, single-tablet two-drug treatment for use in combination with other HIV medicines. Compared to previous PIs, it has a friendly lipid profile, eliminating any worries about metabolic complications. Even though cobicistat is not clinically inferior to boosting with ritonavir, as a single-tablet dual therapy it makes treatment easier for individuals by eliminating one pill and an extra co-payment. AbbVie, the maker of ritonavir, never licensed ritonavir to be used in a co-formulation with other HIV drugs. Drug interactions are a concern. Acid reflux medications can interfere with the absorption of atazanavir. With atazanavir there is an increase of bilirubin that, although not harmful, causes yellowing of the eyes and skin. Watch the kidneys and the liver. The brand name for atazanavir is Reyataz and it was originally boosted with ritonavir.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,926.56/month

GENERIC IS AVAILABLE.

Reyataz atazanavir sulfate (atazanavir, or ATV)

PI PROTEASE INHIBITOR

✔ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

For most treatment-naïve (first time on HIV therapy) and treatment-experienced individuals, the dose is one 300 mg capsule plus 100 mg Norvir or 150 mg Tybost once daily with food. Must be taken in combination with another antiretroviral(s) which does not contain this drug or medication from the same drug class. See package insert for dosing recommendations during pregnancy, liver or kidney impairment, and with certain drug interactions. Capsules also available in 150 mg and 200 mg. Take Norvir or Tybost at same time as Reyataz. Pediatric dose with 50 mg oral powder available based on body weight for children at least 3 months of age weighing at least 11 pounds (5 kg).

Take missed dose as soon as possible, unless it's 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. Oral powder may be used by adult patients who cannot swallow the capsules.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects may include nausea, ocular icterus (yellowing of the skin or eyes as a result of increased bilirubin levels), jaundice, and rash. The ocular icterus and jaundice was reversible on discontinuation of the drug. Other less common side effects may include kidney stones, gallstones, abnormal heart rhythm, and elevated liver enzymes (more common in people with hepatitis B or C). Capsules do not contain phenylalanine but oral powder does; thus use with caution in individuals with phenylketonuria (PKU). Kidney laboratory testing should be performed in all patients prior to initiation of Reyataz and continued during treatment. Renal laboratory testing should include serum creatinine, estimated creatinine clearance, and urinalysis with microscopic examination. Rarely, chronic kidney disease has been observed. A cross-sectional cohort study reported Reyataz with Norvir was associated with less progression to atherosclerosis (a symptom of cardiovascular disease). Large observational cohorts found an association between some PIs (DRV/r, FPV, IDV, and LPV/r) and an increased risk of cardiovascular events, while this association was not noted with Reyataz. Another observational cohort study of predominantly male participants found a lower rate of cardiovascular events in those receiving Reyataz-containing regimens compared with other regimens. Further study is needed. With protease inhibitors, there can be increased bleeding in hemophiliacs.

POTENTIAL DRUG INTERACTIONS

Do not use with alfuzosin, rifampin, irinotecan, ergot derivatives, triazolam, oral midazolam, St. John's wort, Revatio, or Viramune (nevirapine). Do not use lovastatin, simvastatin, or co-formulations containing them (Advicor and Vytorin) for treatment of high cholesterol. Alternatives for these are atorvastatin, rosuvastatin, pravastatin, pitavastatin, and fluvastatin, but should be used with caution and started at the lowest dose possible; monitor for increased side effects. Proton pump inhibitors (PPIs, like Aciphex, Dexilant, Nexium, Protonix, 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. H2RAs like Pepcid may be taken (no more than 20 mg twice a day if treatment-experienced or 40 mg twice a day if treatment-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 or at least 10 hours after an H2RA. If taking chewable antacids like Rolaids and Tums, take Reyataz with food two hours before or one hour after. Treatment-experienced people should not take Reyataz with Sustiva. Viread decreases the levels of Reyataz and Reyataz/Norvir increases Viread levels; monitor for adverse events. Reyataz can be taken unboosted with Epzicom if necessary. Bepridil, amiodarone, quinidine, and lidocaine should be used cautiously because of the risk of worsening abnormal heart rhythm. Close monitoring is 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 + Norvir increases levels of fluticasone (found in Advair, Flonase, and Flovent); monitor for signs of Cushing's syndrome. An alternative corticosteroid is recommended. 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 for sedation. Do not take with Zepatier. Taking with Olysio is not recommended. Reyataz/Norvir is not recommended with Harvoni if tenofovir DF (TDF, in Truvada) is part of HIV regimen. With Epclusa, monitor for tenofovir toxicities if TDF is part of HIV regimen. Take Reyataz with morning Viekira Pak dose, without Norvir. 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 not listed here.

DR. DAVID HARDY SAYS: Approved in 2003, Reyataz was the first effective and better-tolerated protease inhibitor alternative to the now forgotten Kaletra (a drug credited with saving many PLWH lives in the early 2000s, but loaded with significant side effects). Reyataz can be given with or without a booster (Norvir or Tybost), but it is almost always given with a booster due to better resistance to HIV resistance when taken that way. In a 3-way clinical trial to find the best first-time ART regimen for PLWH, Reyataz + Norvir came in third after both Prezista + Norvir (second) and Isentress (first) due to its greater side effects (nausea, queasiness, diarrhea, and yellow eyes and skin). Reyataz's use has progressively fallen off over the past several years due to these study results. Of note, Reyataz went off patent (marketing exclusivity) in the summer of 2017 and became available as a generic form of the medication (atazanavir) in late December 2017. What effect this new generic, and most likely cheaper, version of Reyataz will have on its use will probably be minimal.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Compared to previous PIs, Reyataz has a friendly lipid profile, eliminating any worries about metabolic complications. Drug interactions are a concern. Acid reflux medications can interfere with the absorption of atazanavir. With atazanavir there is an increase of bilirubin that, although not harmful, causes yellowing of the eyes and skin. Watch the kidneys and the liver.

MORE INFORMATION

Yellowing of the eyes and skin is a common reason for discontinuation. Reyataz plus Norvir and 2 NRTIs is still recommended as a preferred regimen during pregnancy. Reyataz plus Tybost is not recommended during pregnancy. Maintaining adequate hydration is important with Reyataz. Reyataz + Norvir + Epzicom is no longer included in the list of "Recommended Initial Regimens in Certain Clinical Situations" because it has disadvantages when compared with other regimens in this category.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

300 mg, 30 capsules:
$1,739.30/month
Generic atazanavir
300 mg, 30 capsules:
$1,565.37/month

GENERIC IS AVAILABLE.

Norvir ritonavir (RTV)

PKE PHARMACOKINETIC ENHANCER (BOOSTER); ALSO AN ANTIRETROVIRAL (PROTEASE INHIBITOR)

✔ USED ONLY ONLY AS A BOOSTER FOR OTHER DRUGS; RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

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

Take missed dose as soon as possible (at the same time as the other PI prescribed) unless it's closer to the time of your next dose. Do not double up on your next dose. Do not crush or chew tablets or capsules; always swallow whole.

Approved for children older than one month with dosing based on body surface area; the use in children depends on the co-administered PI. Capsule formulation requires refrigeration, but tablet does not. Liquid formulation available (80 mg/mL) in peppermint and caramel flavor, but is not very palatable. The taste of the liquid can be improved by mixing with chocolate milk, peanut butter, Ensure, or Advera within one hour of dosing. Liquid formula should not be taken by pregnant women, as it contains 43% alcohol. Norvir oral powder available in 100 mg packets, is free of alcohol and propylene glycol (both of which are found in the liquid formula), and thus safer for pediatric use.

➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The side effect potential of Norvir is much lower now that it is only used as a booster at low doses. Most common side effects include stomach pain, nausea, diarrhea, and vomiting. Other less common side effects may include fatigue; tingling/numbness around the mouth, hands, or feet; loss of appetite; and taste disturbances. Norvir can also increase cholesterol and triglyceride levels. 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 Norvir is not recommended for those with severe liver impairment.

POTENTIAL DRUG INTERACTIONS

Norvir interacts with many drugs. Do not take with alfuzosin, amiodarone, flecainide, lurasidone, propafenone, oral midazolam, triazolam, pimozide, ranolazine, Revatio, rifapentine, rifampin, voriconazole, ergot derivatives, or the herb St. John's wort. Do not use lovastatin or simvastatin or co-formulations containing these drugs (Advicor and Vytorin) for the treatment of high cholesterol. Cholesterol-lowering alternatives are atorvastatin, rosuvastatin, pravastatin, pitavastatin, and fluvastatin, but should be used with caution and started at the lowest dose possible; monitor for increased side effects. Norvir increases levels of nasal and inhaled fluticasone (found in Advair, Flonase, Breo Ellipta, Arnuity Ellipta, and Flovent), which may lead to Cushing's syndrome. Use an alternative corticosteroid 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. Norvir may decrease levels of methadone, therefore titrate dose of methadone to clinical effect. Use caution with anticonvulsants such as carbamazepine, phenobarbital, and phenytoin. Use calcium channel blockers (amlodipine, nifedipine, and others) with caution. Norvir may alter warfarin levels; additional monitoring is required. Norvir use with other blood thinners (anticoagulants), such as Xarelto, is not recommended. Norvir can increase anticoagulant concentrations (and thereby increase risk of bleeding) or decrease their concentrations (and thereby decrease effectiveness). 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. Monitor for increased side effects of these medications, such as visual disturbances, low blood pressure, dizziness, and prolonged painful erection lasting longer than 4 hours. Effectiveness of oral contraceptives may be decreased; consider using other or alternative methods of contraception. Levels of the street drug ecstasy are greatly increased by Norvir, and at least one death has been attributed to the combination. Using Norvir with methamphetamines can result in up to 2–3 fold increase in methamphetamine concentrations and puts user at risk for overdose. GHB, another street drug, is also dangerous with Norvir. Clarithromycin levels can increase by up to 80%. Co-administer bosentan, salmeterol, and immunosuppressants with caution. If co-administered, a lower dose of colchicine is recommended. Norvir, when combined with another PI, may be taken with Sovaldi, Daklinza (dose may need adjustment), Epclusa (monitor for tenofovir toxicity if TDF is part of regimen), and Harvoni (if TDF is not part of HIV regimen). Norvir + PI should not be taken with Olysio, Viekira Pak, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

DR. DAVID HARDY SAYS: Norvir was the second protease inhibitor approved to treat HIV, in early 1996. Over a short period of time its significant side effects of nausea, vomiting, severe queasiness, and explosive diarrhea (when taking 1,200 mg/day) reduced its use as a protease inhibitor. By the late 1990s, it was used as the first booster (taking 100-400 mg/day) for almost all other protease inhibitors (except Viracept) and markedly increased the potency and reduced the number of doses of protease inhibitors. Even at lower doses, some PLWH have side effects such as nausea, queasiness, and diarrhea.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Once upon a time Norvir, or ritonavir, was approved as a treatment for HIV. It was one of the first PIs that slowed the death rates of HIV. For many, it was the rescuer from certain death. As with the other first generation PIs, it causes many debilitating side effects, including gastrointestinal problems and increased risk for liver toxicity. Because of the way it is metabolized, ritonavir increases the blood level of other drugs. It was hard to take because of its toxicities and drug interactions. Even though it failed as a treatment, it has proven to be, at a lower dose, an effective booster for newer and safer PIs.

MORE INFORMATION

The advantage of Norvir is its use with other PIs as a boosting agent (officially in the drug class called "pharmacokinetic enhancers"). As such, it's used to increase the levels of some HIV protease inhibitor (PI) medications. 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.

MANUFACTURER

AbbVie
norvir.com
(800) 633-9110

AVERAGE WHOLESALE PRICE

100 mg, 30 tablets:
$308.60/month
generic **$277.74**

Tybost cobicistat (COBI)

PKE PHARMACOKINETIC ENHANCER (BOOSTER); NOT AN ANTIRETROVIRAL

✔ USED ONLY AS A BOOSTER FOR OTHER DRUGS; RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

150 mg once a day with food taken at the same time with either Prezista 800 mg (co-formulated as Prezcobix), Reyataz 300 mg (co-formulated as Evotaz), or co-formulated in the single-tablet regimens Stribild and Genvoya.

Tybost is not an HIV drug; it is a pharmacokinetic enhancer or a "booster" used to increase the levels of Prezista 800 mg once daily, Reyataz 300 mg once daily, or elvitegravir 150 mg in Stribild and Genvoya. Tybost is not interchangeable with Norvir when used to increase the levels of other HIV medications.

Take missed dose as soon as possible (at the same time as any separate medication prescribed) unless it's closer to the time of your next dose. Tybost is not recommended for people with CrCl less than 70 mL/min when co-administered with a regimen containing TDF or for people with severe liver problems.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Side effects observed in clinical studies (greater than 2% of patients) include nausea, jaundice, and yellowing of the eyes. However, it was studied with Reyataz so the jaundice and yellowing of eyes were most likely due to the Reyataz component. Before taking Tybost, kidney function testing should be conducted, including serum creatinine, serum phosphorus, urine glucose, and urine protein. These measurements should continue to be monitored while taking Tybost. Cobicistat can cause a small, reversible increase in serum creatinine within the first few weeks of treatment without affecting actual kidney function. The SCr increase occurred within weeks of starting cobicistat and was reversible within a few days after stopping it. The co-adminstration of Tybost and Viread (tenofovir DF or TDF, also found in Complera, Stribild, and Truvada) is not recommended if the CrCl is less than 70 mL/min.

POTENTIAL DRUG INTERACTIONS

Tybost interacts with many drugs. Do not take with alfuzosin, colchicine, dihydroergotamine, dronedarone, ergotamine, irinotecan, simvastatin, lovastatin, lurasidone, methyl-ergonovine, ranolazine, rifampin, pimozide, triazolam, oral midazolam, Revatio, or St. John's wort. Tybost may increase levels of nasal or inhaled fluticasone (Flonase, Advair, Breo Ellipta, Arnuity Ellipta, and Flovent). Use an alternative corticosteroid 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). No significant interactions with beclomethasone. Tybost may increase levels of certain calcium channel blockers, beta blockers, HMG-CoA reductase inhibitors (statins or cholesterol medicines), anticoagulants, antiplatelets, antiarrhythmics, antidepressants, sedative-hypnotics, rifabutin, bosentan, erectile dysfunction agents, inhaled corticosteroids, and norgestimate. Caution should be taken, with possible dose adjustments of these medications, when used with Tybost. Sporonox (antifungal) and Biaxin (antibiotic) may increase Tybost concentrations. Tybost may also increase Biaxin levels. Rifabutin and some anti-seizure medications, such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin) may decrease Tybost drug levels. Do not take with Olysio, Viekira Pak, or Zepatier. Avoid Harvoni if tenofovir disoproxil fumarate (TDF) is part of the HIV regimen. Tybost has similar drug interactions as Norvir, but they are not interchangeable and there may be some drug interactions with Tybost that are not observed with Norvir. Tybost may increase levels of methamphetamines. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

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 regimens Genvoya and Stribild, both recommended therapies in the DHHS treatment guidelines in certain clinical situations. Tybost shares some of the same side effects of increased cholesterol and increased triglycerides as Norvir; however in clinical trials they were less pronounced. Tybost co-administered with darunavir or atazanavir should not be initiated in pregnant individuals and is not recommended during pregnancy. Inadequate levels of ART in second and third trimesters as well as viral breakthroughs have been reported. Tybost is not recommended during pregnancy. Tybost has not been studied separately from Genvoya, Stribild, Symtuza, Prezcobix, or Evotaz in individuals under 18 years of age; thus Tybost should not be used in pediatric patients.

DR. DAVID HARDY SAYS: Tybost was originally developed as a booster for the integrase inhibitor elvitegravir (see Stribild and Genvoya). In a head-to-head comparison of Reyataz (plus 2 NRTIs) boosted with Tybost or Norvir, no significant differences in effectiveness or side effects between the two boosters was seen. In fact, on a molecular basis, the two drugs are almost identical. A few small molecular changes in Tybost have taken away its anti-HIV activity, so it is not considered an antiretroviral, unlike Norvir. Tybost has fewer unwanted drug-drug interactions compared to Norvir.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Tybost, or cobicistat, is a drug developed to work as an enhancer to boost the level of other HIV drugs. Cobicistat is not an antiviral. This enhancer inhibits a liver enzyme used by many HIV drugs to be metabolized in the liver. Being a CYP3A4 inhibitor like ritonavir, it might cause the same side effects as ritonavir: increased triglycerides and cholesterol, as well as drug-drug interaction with many other drugs. One good thing about cobicistat is that it is less expensive and licensed for use in fixed-dose combinations.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$263.87/month

Descovy

emtricitabine/tenofovir alafenamide **(FTC/TAF)**

NRTI FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One tablet once daily, without regard to food. Tablet contains 200 mg emtricitabine and 25 mg tenofovir alafenamide. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug or medication from the same drug class.

For adults and children weighing at least 55 pounds (25 kg). Crushing or splitting tablets has not been studied and is not recommended; TAF is soluble in water, but has a bitter and burnt aromatic flavor profile.

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. Descovy should not be used if CrCl is less than 30 mL/min or if you are on dialysis. In children weighing 55 to 77 pounds (25 – 35 kg), taking Descovy with a boosted HIV protease inhibitor medication is not recommended. Unlike Truvada, Descovy is not approved for and should not be used for prevention of HIV (pre-exposure prophylaxis, or PrEP).

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN DESCOVY:** Emtriva (but TAF is not available separately for HIV).

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Overall, Descovy is well tolerated, but some may experience nausea, headache, stomach pain, or weight loss. Rare skin discoloration on palms and soles may also occur. May affect the bones and kidneys. In clinical trials, fewer bone and kidney issues were observed with the TAF formulation compared to the TDF formulation. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. If you have HIV and HBV, guidelines recommend treatment for both viruses. Descovy can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Descovy without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), used for the treatment of hepatitis B. Use caution with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain like Advil or Motrin (ibuprofen) and Aleve (naproxen). Descovy should not be taken with certain anticonvulsants (including carbamazepine, oxcarbazepine, phenobarbital, and phenytoin), Aptivus/Norvir, rifabutin, rifampin, rifapentine, or St. John's wort. Can be used with hepatitis C drugs such as Epclusa, Harvoni, Sovaldi, Olysio, Daklinza, Viekira Pak, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Descovy is the newer version of Truvada. Instead of TDF, Descovy contains TAF (tenofovir alafenamide), which reduces serum tenofovir concentration by 90%. This results in lessened impact on kidney and bone mineralization but maintains potent antiviral activity inside the CD4 cell. In clinical trials, fewer kidney and bone issues were observed with TAF than with TDF, and significant improvements were seen when switching from TDF to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown. Both Descovy and Truvada are currently recommended by DHHS HIV treatment guidelines for first-time therapy for most people.

DR. DAVID HARDY SAYS: Descovy was approved in mid-2016 as the "new and improved" version of Truvada as it maintained the Emtriva (FTC) and changed the Viread (tenofovir DF) to TAF. This change was prompted by the finding that TAF (originally discovered and developed in 2002, but then shelved for several years) produced similar HIV-suppressing effects as Viread with much lower levels of the same drug in the blood. The lower tenofovir levels have been shown to have less harmful effects on the kidneys and bone mineral density (bone strength). Descovy is the most preferred two-nuke combination used by HIV treaters when building first-time ART regimens for their PLWH.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Descovy is the new Truvada, in the sense that it contains emtricitabine plus tenofovir alafenamide instead of the original tenofovir disoproxil fumarate. What is better about combining with TAF is that TAF has fewer kidney and bone density problems. Descovy has not been approved for PrEP, however. It is to be used to treat HIV in combination with other antivirals prescribed by your doctor. Many new STRs contain TAF already. Drug interactions may occur, so discuss with your doctor all medications taken, including over-the-counter medicines. A Phase 3, randomized, double-blind trial named Discover is under way, comparing Descovy and Truvada's efficacy in preventing HIV.

However, unlike Truvada, Descovy is not approved for and should not be used for PrEP. A clinical trial called DISCOVER is currently in progress comparing Descovy to Truvada for PrEP (prevention) in HIV-negative individuals. Because both FTC and TAF are also active against hepatitis B (HBV), Descovy is recommended by DHHS for individuals co-infected with both HIV and hepatitis B. Pediatric HIV guidelines list Descovy as part of a preferred regimen. There is insufficient data in pregnancy for the DHHS to recommend the routine use of Descovy in pregnant women at this time. Descovy tablets are relatively small compared to Truvada and other combination tablets, which may be an advantage for patients who have difficulty swallowing.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,010.95/month

APPROVED AS GENERIC, WHICH IS NOT YET COMMERCIALLY AVAILABLE.

Truvada emtricitabine/tenofovir DF (FTC/TDF)

NRTI FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One tablet once daily without regard to food for adults and children weighing at least 77 pounds. In children weighing 37–76 pounds, Truvada is dosed based on body weight. See package insert for weight-based dosing. Truvada tablets are available in the following emtricitabine/tenofovir DF dosages: 100/150 mg tablets, 133/200 mg tablets, 167/250 mg tablets, and 200/300 mg tablets. Tablets can disintegrate in water, grape juice, or orange juice with minor stirring and pressure from a spoon; however, no studies have been performed to evaluate the pharmacokinetics (PK) or stability of crushed vs. intact tablets. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug or medication from the same drug class.

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. The dose of Truvada should be adjusted if CrCl is less than 50 mL/min and Truvada should not be used if CrCl is less than 30mL/min or if you are on dialysis.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN TRUVADA:** Viread and Emtriva.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL DRUG INTERACTIONS

Overall, it is well tolerated, but some may experience nausea, headache, gas, stomach pain, or weight loss. Rare skin discoloration on palms and soles may also occur. The TDF in Truvada is associated with long-term 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. While calcium and vitamin D levels can be checked to assess the need for these supplements, talk with your provider before starting on your own. Truvada can cause kidney toxicities. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in all individuals with mild kidney impairment. If you have HIV and HBV, guidelines recommend treatment for both viruses. Truvada can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Truvada without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. Truvada is associated with lower lipid levels than Ziagen or tenofovir AF (TAF) due to tenofovir DF's favorable effect on cholesterol. Truvada contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), used for the treatment of hepatitis B. 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/Norvir, Prezista/Norvir, and Kaletra increase tenofovir concentrations. It is recommended that patients taking Reyataz/Norvir, Prezista/Norvir, or Kaletra with Truvada should be monitored for Truvada-associated adverse events, particularly decreases in kidney function. Avoid taking Truvada with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain like Advil or Motrin (ibuprofen) and Aleve (naproxen). Truvada may be used with hepatitis C drugs such as Daklinza, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier, depending on the third drug in the HIV regimen. Monitor for tenofovir toxicities if used with Epclusa. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug ineractions not listed here.

MORE INFORMATION

Current DHHS HIV treatment guidelines recommend Truvada (or Descovy) over Epzicom as the preferred NRTI component for initial therapy (unless Epzicom is paired with Tivicay). The newer version of Truvada, called Descovy, was approved in 2016. The ACTG A5202 study 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 copies/mL, the times to virologic failure and the first adverse event were both significantly shorter in patients taking Epzicom compared to Truvada. In studies using Tivicay in the regimen, however, Truvada and Epzicom were equally effective regardless of baseline viral load. 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. Fewer kidney and bone issues were seen with the TAF formulation compared to TDF in clinical trials. Approved in 2012 for HIV prevention (pre-exposure prophylaxis, or PrEP) in confirmed HIV-negative adults; see Truvada for PrEP page. Truvada is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy.

DR. DAVID HARDY SAYS: Truvada was approved in 2004 (on the same day as Epzicom, see that page) as a two-drugs-in-one-pill, two-nuke combination "backbone" to which a third drug is added to create a three-drug combination or "cocktail" ART regimen. Truvada was the most commonly prescribed antiretroviral for the majority of PLWH from the late 2000s until Descovy was approved in 2016. This was due to Truvada's solid track record as a potent, well-tolerated, and durable two-nuke combination, data showing its higher potency over Epzicom, and concerns (still controversial) about Epzicom's cardiovascular side effects. Truvada's use has steadily declined since the approval of three TAF-containing medications (Genvoya, Odefsey, and Descovy) due to less long-term side effects (kidney and bone strength). Truvada became the first, and still only, medication approved for pre-exposure prevention (PrEP) of HIV, in 2012. In mid-December 2017, a generic form of Truvada was approved in the U.S. With the availability of TAF-containing medications, the use of generic Truvada, while probably less expensive, has yet to be seen.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Truvada is the brand name of a fixed-dose combination containing emtricitabine and tenofovir disoproxil fumarate. Both drugs have a long half-life and when combined can be taken once a day. Truvada is the most prescribed NRTI fixed-dose combination with other antiretrovirals. It may cause damage to the kidneys and loss of bone density. It is important to monitor kidney function and bone density. Besides that, it is well tolerated and potent.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$2,010.95/month;
Approved as generic; not yet commercially available

Cimduo lamivudine/tenofovir DF (3TC/TDF)

NRTI FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED FOR INITIAL ART FOR MOST PERSONS WHEN COMBINED WITH TIVICAY OR ISENTRESS

STANDARD DOSE

One tablet once daily without regard to food for adults and children weighing at least 77 pounds (35 kg). Tablet contains 300 mg lamivudine (3TC) and 300 mg tenofovir disoproxil fumarate (TDF). Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug from the same drug class.

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. Cimduo and Temixys should not be used if CrCl is less than 50 mL/min or if you are on dialysis.

➤ **SEE THE INDIVIDUAL DRUGS CONTAINED IN CIMDUO AND TEMIXYS:** Epivir and Viread.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common adverse events (in more than 10% of people taking it) are headache (14%), pain (13%), depression (11%), diarrhea (11%), and rash (18%) (when studied in combination with efavirenz). Rare skin discoloration on palms and soles may also occur. The TDF in Cimduo is associated with long-term 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. While calcium and vitamin D levels can be checked to assess the need for these supplements, talk with your provider before starting on your own. TDF can cause kidney toxicities. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in all individuals with mild kidney impairment. If you have HIV and HBV, guidelines recommend treatment for both viruses. Cimduo can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Cimduo without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. Cimduo contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, Hepsera, or Vemlidy (TAF), used for the treatment of hepatitis B. Tenofovir decreases the concentration levels of Reyataz, therefore when Reyataz is taken with Cimduo or Temixys, it is recommended that Reyataz 300 mg is taken with Norvir 100 mg (all as a single daily dose with food). In addition, Reyataz/Norvir, Prezista/Norvir, and Kaletra increase tenofovir concentrations; therefore, it is recommended patients be monitored for TDF-associated adverse events, particularly decreases in kidney function. Avoid taking Cimduo with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain like Advil or Motrin (ibuprofen) and Aleve (naproxen). Avoid administration of sorbitol with Cimduo and Temixys. Hepatic (liver) decompensation, some fatal, has occurred when using lamivudine and interferon alfa (with or without ribavirin) for hep C treatment. (Of note, interferon alfa is no longer used for the treatment of hepatitis C). Cimduo and Temixys may be used with hepatitis C drugs such as Daklinza, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier, depending on the third drug in the HIV regimen. Monitor for tenofovir toxicities if used with Epclusa. Avoid use of sorbitol-containing medicines with lamivudine. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here.

MORE INFORMATION

This slightly different version of Truvada was FDA approved last year. It contains 3TC instead of Truvada's FTC. The three meds are essentially equivalent. The niche for Cimduo is that it may be a cheaper option for some insurance plans because it contains generic drugs. It also allows for some new or unique co-formulations (such as with Delstrigo, Symfi, and Symfi Lo). Cimduo has received DHHS HIV treatment guidelines recommendation as a component for initial ART in most people with HIV when combined with dolutegravir or raltegravir. TDF is falling out of favor since the newer formulation tenofovir alafenamide, or TAF, was approved. TAF is safer on kidneys and bones than TDF. Unlike Truvada, Cimduo is not approved for PrEP (HIV prevention). DHHS treatment guidelines recommend Cimduo, Truvada, or Descovy (which contains TAF) over Epzicom as the preferred NRTI component for initial therapy (unless Epzicom is paired with Tivicay). Kidney function must be monitored before and during treatment with Cimduo and it may not be a good option for patients with underlying kidney problems. When the virologic efficacy of Cimduo was compared to Truvada (each combined with Sustiva or nevirapine or a boosted PI) in a study, Cimduo was associated with higher rates of virologic failure compared to Truvada when paired with an NNRTI; however, there was no difference in the rates of virologic failure when paired with a boosted PI. It should be noted that the people in the study who were taking Cimduo generally had higher viral loads, lower CD4 counts, and were more likely to be using injection drugs at the start of the study compared to patients taking Truvada. Another study examining historical data noted viral resistance was more common with Cimduo than with Truvada, however this was not observed in clinical trials. Cimduo is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy. Another drug containing the same medications as Cimduo, Temixys, was FDA approved but is not commercially available.

DR. DAVID HARDY SAYS: Cimduo became the second generic two-nucleoside fixed-dose-combination tablet when it was approved by the FDA in March 2018 (see Epzicom). Like the FDA approval of Symfi and Symfi Lo (also manufactured by Mylan; see that page), Cimduo was approved based upon pharmacokinetic bioequivalence data, not clinical trial data, as the two agents in it, tenofovir DF and lamivudine, were already approved as antiretroviral medications (see Symfi/Symfi Lo). Similar to Symfi and Symfi Lo, Cimduo is not an exact generic version of Truvada, as lamivudine is used in place of Emtriva (emtricitabine), but even the FDA accepted clinical data from trials using tenofovir DF plus lamivudine in their original review and approval of Truvada, so the difference between Cimduo and Truvada is minimal and not clinically important. Comparing the cost of Cimduo: the wholesale acquisition cost (WAC) for a 30-day supply is $1,005, compared to $1,676 for both Truvada and Descovy, $1,292 for Ziagen, and $185–$1,116 for generic abacavir/lamivudine.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Cimduo is a fixed-dose combination containing lamivudine and tenofovir DF, and is to be used in combination with other antiretrovirals. It has proven to be highly effective and relatively safe. The most common adverse effects are associated with tenofovir DF: potential kidney damage and bone density loss. Similar to other HIV drugs, it is important to monitor liver functions. Cimduo was developed by Mylan.

MANUFACTURER

Mylan Specialty L.P.
mylan.com
cimduo.com
(877) 446-3679

AVERAGE WHOLESALE PRICE

$1,206.56/month

GENERIC IS AVAILABLE.

Epzicom abacavir/lamivudine (ABC/3TC)

NRTI FIXED-DOSE COMBINATION OF TWO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE WHEN USED IN COMBINATION WITH DOLUTEGRAVIR (AS TRIUMEQ)

STANDARD DOSE

One tablet once daily, without regard to food. Tablet contains 600 mg abacavir and 300 mg lamivudine. Must be taken in combination with another antiretroviral(s) which does not contain the medications in this drug or medication from the same drug class.

Take missed dose as soon as possible, unless it is closer to the time of your next dose. Do not double up on your next dose. Approved for adults and children weighing 55 pounds (25 kg) or more. Not recommended for those with decreased kidney function (creatinine clearance less than 50 mL/min) due to lamivudine component, or those with mild liver impairment due to abacavir component. Alternative doses may be obtained by using the individual components of this medication.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN EPZICOM:** Epivir and Ziagen.
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The length of this section is meant to be informative, not scary. Common side effects may include headache, nausea, fatigue, depressed mood, dizziness, diarrhea, and insomnia. Of note is the hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir (see Ziagen for details of symptoms). To minimize the risk for HSR, a blood test for HLA-B*5701 (a genetic marker) should be done prior to starting an HIV regimen containing Epzicom to identify patients at higher risk for this reaction. A negative HLA-B*5701 test does not mean you won't have HSR, but the risk is reduced to 1% from clinical studies. This test is covered by most insurance and also by LabCorp/ViiV (see company contact on co-pay chart).

An HSR can technically occur at any time, regardless of how long you have taken the medication, however, it is much more likely to occur when you start (or re-start) the medication (90% occur within the first 6 weeks of treatment). Symptoms of an HSR usually worsen, very slowly, with every dose. Call your healthcare provider right away to find out if you should stop taking Epzicom. If you stop Epzicom because of an allergic reaction, never take Epzicom or an abacavir-containing regimen such as Triumeq, Trizivir, or Ziagen again (called "rechallenging"). Rechallenging could cause a rare life-threatening reaction. This does not apply to a missed dose when HSR is not suspected, but talk with your healthcare provider and watch for symptoms if you've stopped the drug for at least a few days.

Some large observational studies suggest abacavir may increase the risk of cardiovascular events, including myocardial infarction (MI, or heart attack), in people with greater risk factors such as smoking, diabetes, high blood pressure, older age, high cholesterol, family history of heart disease, and drug use. Other studies have found no increased risk. 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 should discuss risks with their provider, and they should be monitored more closely. If you have HIV and HBV, guidelines recommend treatment for both viruses. The lamivudine component of Epzicom can be used to treat HIV and HBV simultaneously. If you are co-infected with HBV and HIV, you should not stop Epzicom without medical supervision because it can cause your HBV to flare up and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

POTENTIAL DRUG INTERACTIONS

Do not take with Epivir-HBV, used for the treatment of hepatitis B. Alcohol can increase the levels of abacavir and therefore can increase the possibility of side effects. Epzicom may be used with hepatitis C drugs such as Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier, depending on the third drug in the HIV regimen. There have been rare reports of depression and suicidal ideation, primarily in patients with a history of psychiatric illnesses, in people receiving INSTI-based regimens. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others). Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here.

MORE INFORMATION

Triumeq, a single-tablet regimen (STR) containing Tivicay and Epzicom, is a DHHS recommended initial therapy in most people (again, test for HLA-B*5701 first). Otherwise, the guidelines recommend Descovy or Truvada over Epzicom as the backbone NRTI component of an HIV drug combination for first-time therapy, with Epzicom listed as an alternative NRTI backbone. One of the reasons abacavir is a DHHS alternative drug is that the ACTG A5202 study found that abacavir/lamivudine (Epzicom) was inferior to tenofovir/emtricitabine (Truvada) in getting people undetectable when their pre-treatment viral load was over 100,000 copies/mL. However, when combined with Tivicay (dolutegravir), Epzicom performed just as well as Truvada in people with high viral loads (over 100,000 copies/mL). Hence, Triumeq is the only abacavir-containing regimen recommended by DHHS as initial therapy for most HLA-B*5701 negative people. The lamivudine portion of Epzicom is also used to treat the hepatitis B virus (HBV); see Epivir. Epzicom is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy.

DR. DAVID HARDY SAYS: Approved on the same day in 2004 as Truvada, Epzicom is also a two-drugs-in-one-pill, two-nuke combination "backbone" to which a third drug is added to build a three-drug combination or "cocktail" ART regimen (just like Truvada). Because Epzicom contains Ziagen (abacavir), a one-time blood or mouth swab test must be done to look for a genetic marker (HLA-B*5701) which predicts a severe allergic reaction to Ziagen if present. In 2008, a European cohort study raised concern about an association of Ziagen with the increased occurrence of heart attacks. Although many other studies have weighed in, trying to confirm or refute this finding, there still remains controversy whether cardiovascular disease (heart attacks) is a true side effect of Ziagen or a false association. Not long after this, a large clinical trial comparing first-time ART regimens for PLWH with either Epzicom or Truvada found that Epzicom was not as potent for PLWH with high viral loads (greater than 100,000 copies/mL). These two findings diminished the use of Epzicom and Ziagen in favor of Truvada. A generic version of Epzicom has been available in the U.S. since September 2016. Today most Epzicom use is prescribed as two of the three medications in the STR Triumeq (Tivicay/Ziagen/Epivir).

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Epzicom is a fixed-dose combination tablet containing abacavir and lamivudine. Epzicom is used as an alternative to Truvada in patients who can't tolerate tenofovir due to kidney toxicity or loss of bone density. Epzicom may increase the risk of heart attacks and cardiovascular disease due to abacavir. It is not as effective in patients whose viral load is more than 100,00 copies. It is combined with dolutegravir in the fixed-dose tablet branded as Triumeq. Epzicom is recommended as first-line treatment in combination with dolutegravir.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872
epzicom.com

AVERAGE WHOLESALE PRICE

$1,550.05/month;
generic: **$1,395.05**/month

Emtriva emtricitabine (FTC)

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One 200 mg capsule once daily without regard to food. Dosing needs to be adjusted for adults and children who have decreased kidney function (creatinine clearance less than 50 mL/min). See package insert for guidance on dosing in the setting of kidney impairment. Must be taken in combination with another antiretroviral(s) which does not contain the medication in this drug.

Indicated for adults and children regardless of age. Emtriva is dosed based on body weight for children. See the package insert for weight-based dosing.

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. It is also available as an oral solution (10 mg/mL) (cotton candy flavor) for children any age and adults who are not able to swallow the capsules. Can be substituted for Epivir.

- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.
- **TELL YOUR PROVIDER OR PHARMACIST** about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

POTENTIAL SIDE EFFECTS AND TOXICITY

Emtriva is very well tolerated. The most common side effects (rarely reported) may include headache, diarrhea, and nausea. If you have HIV and HBV, guidelines recommend treatment for both viruses. Emtriva can treat both HIV and HBV, but must be used in combination with another hep B drug (such as tenofovir) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop Emtriva without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. Rare skin discoloration (darkening of the skin on the palms and the soles) can occur and was more frequent in children, but is generally mild and not concerning.

POTENTIAL DRUG INTERACTIONS

No significant drug interactions. Emtriva may be used with hepatitis C drugs such as Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier, depending on the other components in the HIV regimen.

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. If your HIV develops resistance to Epivir or Emtriva, it does not mean that your HBV is also resistant to them. Both Descovy and Truvada (both contain Emtriva) are currently recommended by DHHS HIV treatment guidelines for first-time therapy for most people. Emtriva is also found in several single-tablet regimens (Atripla, Biktarvy, Complera, Genvoya, Stribild, Symtuza, and Odefsey). Sometimes, drug resistance that the virus develops against emtricitabine makes the virus reproduce at a slower rate. This drug resistance can also improve the antiviral activity of Retrovir (zidovudine) and Viread (tenofovir), and for that reason, some providers continue Emtriva treatment in combination with other antiretrovirals 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. The capsule is small, which is an advantage for people with difficulty swallowing.

DR. DAVID HARDY SAYS: Emtriva was approved in 2003 and has been a closely related medication to Epivir (lamivudine or 3TC). Note the similar chemical names FTC and 3TC. For many HIV treaters, ART guidelines writers, and even the FDA, the two medications are interchangeable. Emtriva is almost always used in combination with Viread (Truvada) or with TAF (Descovy). It is a potent antiretroviral, but its anti-HIV activity is almost completely lost when a very common, single mutation (M184V) occurs in the virus. It has very few, if any, significant side effects and therefore is almost always included in most ART regimens.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Emtriva or emtricitabine is a very safe and well-tolerated drug. Its chemical structure is the same as lamivudine. They are both equally effective and have an equal safety profile. The only difference is that emtricitabine has a longer half-life than lamivudine. Emtriva is one of the two drugs in Truvada, which became an alternative to Combivir, the first fixed-dose combination tablet containing zidovudine and lamivudine. It is also in single-tablet regimens such as Atripla, as well as Complera, Stribild, and the newer version of these drugs containing TAF, in addition to STRs containing integrase inhibitors (Biktarvy, Genvoya). It is also used to treat HBV.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

200 mg, 30 capsules:
$643.82/month

GENERIC IS AVAILABLE.

Epivir lamivudine (3TC)

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE WHEN USED IN COMBINATION WITH DOLUTEGRAVIR AND ABACAVIR

STANDARD DOSE

One 300 mg tablet once daily (or one 150 mg tablet twice daily), without regard to food. Dosing needs to be adjusted for adults and children who have decreased kidney function (creatinine clearance less than 50 mL/min). See package insert for guidance on dosing in the setting of kidney impairment. Must be taken in combination with another antiretroviral(s), which does not contain the medication in this drug.

According to the package insert, it is indicated for adults and children at least 3 months of age and older. Based on pediatric DHHS guidelines, it can be used as part of an empiric HIV regimen in infants of at least 32 weeks' gestation at birth for higher risk perinatal HIV exposure. Epivir for children is dosed based on body weight. See the package insert and/or DHHS guidelines for weight-based dosing.

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. The 150 mg tablets are scored and may be split. Based on drug properties, tablets may be crushed and added to a small amount of semi-solid food or liquid for immediate consumption. Epivir is also available as an oral solution (10mg/mL) (strawberry-banana flavor) for children and adults who are not able to swallow the tablets. Can be substituted for Emtriva.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Epivir is very well tolerated. The most common side effects with incidence greater than or equal to 15% were headache, diarrhea, nausea, malaise (general ill feeling), fatigue, nasal symptoms, diarrhea, and cough. If you have HIV and HBV, guidelines recommend treatment for both viruses. Emtriva can treat both HIV and HBV, but must be used in combination with another hepatitis B drug (such as tenofovir) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop Epivir without medical supervision because it can cause your HBV to flare up and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider.

POTENTIAL DRUG INTERACTIONS

No significant drug interactions. Epivir may be used with hepatitis C drugs such as Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier, depending on the other components in the HIV regimen. Avoid use of sorbitol-containing medicines with lamivudine; there are many, such as acetaminophen liquid (Tylenol liquid and others).

MORE INFORMATION

Epivir (lamivudine) is similar to Emtriva (emtricitabine): 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. If your HIV develops resistance to lamivudine, it doesn't mean that your HBV is also resistant to it. Sometimes, drug resistance that the virus develops against lamivudine makes the virus reproduce at a slower rate. This drug resistance can also improve the antiviral activity of Retrovir (zidovudine) and Viread (tenofovir), and for that reason, some providers continue Epivir treatment in combination with other antiretrovirals after resistance develops. Lamivudine is also available in several combination products: Cimduo (with tenofovir DF), Combivir (with zidovudine), Epzicom (with abacavir), Trizivir (with zidovudine and abacavir), Symfi and Symfi Lo (with tenofovir DF and efavirenz), Delstrigo (with tenofovir DF and doravirine), and Triumeq (with dolutegravir and abacavir). Epivir as part of the combination tablet Combivir is recommended as an alternative NRTI combination component of an ART regimen during pregnancy. Epivir is available as generic lamivudine, which should be as effective and well tolerated 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, AZT) 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 Genvoya or Triumeq, might be restricted to patients who can't physically tolerate generic regimens.

DR. DAVID HARDY SAYS: Epivir was approved in 1995 as the fourth antiretroviral medication and nuke. Due to its high potency and excellent tolerability (it has virtually no side effects), it has survived for 23 years as a commonly used antiretroviral as most other antiretrovirals approved during that time have fallen by the wayside due to toxicity. It has been available as generic lamivudine since 2011. As mentioned on the Emtriva page, due to their almost identical properties Emtriva and Epivir are almost interchangeable, including their high susceptibility to the very common M184V mutation in the virus. In a 2-drug regimen with Tivicay (see dolutegravir/3TC), Epivir was recently shown to be part of a successful 2-drug, non-protease inhibitor regimen for first-line therapy.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Epivir, or lamivudine, is the oldest antiretroviral still in use today. It is well tolerated, very effective, and has no drug-drug interactions. It has been used in combination with other NRTIs like zidovudine (Combivir) and abacavir (Epzicom) and is a component of the single-tablet regimen Triumeq. It is used to treat individuals co-infected with HIV and HBV. It seems to work best in combination with other nukes as the backbone of a regimen. The only downside is its resistance profile. One mutation (M184V) can reduce its effectiveness.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Epivir 300 mg tablets, 30 tablets: **$498.89**/month
generic lamivudine 300 mg tablets, 30 tablets: **$429.19**/month

GENERIC IS AVAILABLE.

Viread tenofovir disoproxil fumarate (TDF)

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE

STANDARD DOSE

One 300 mg tablet once daily, without regard to food in adults and children at least 2 years old weighing at least 21 pounds (10 kg). Viread tablets are also available in the following dosages: 150 mg, 200 mg, 250 mg tablets, and oral powder (40 mg/g in 60 g packets). Viread tablets can be disintegrated in water, grape juice, or orange juice with minor stirring and pressure from a spoon. In children, Viread is dosed based on body weight. See package insert for specific weight-based dosing. Must be taken in combination with another antiretroviral(s) which does not contain the medication in this drug.

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. Dosing frequency needs to be adjusted for adults and children with decreased kidney function (for creatinine clearance, or CrCl, less than 50 mL/min). See package insert for guidance on dosing in the setting of kidney impairment. FDA approved for chronic HBV in patients 12 years and older weighing at least 77 pounds (35 kg).

➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Generally well tolerated, but some may experience nausea, diarrhea, vomiting, 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. Viread may cause kidney toxicities. Creatinine clearance (CrCl) should be assessed before initiating treatment. In addition to CrCl, glucose and protein in the urine and serum phosphorus should be monitored more often in patients at risk for kidney problems. Tell your provider about any pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits, as these could be signs of kidney problems. If you have HIV and HBV, guidelines recommend treatment for both viruses. Viread can treat both HIV and HBV, but must be used in combination with another hep B drug (such as Emtriva) to treat the hep B. If you are co-infected with HBV and HIV, you should not stop Viread without medical supervision because it can cause your HBV to flare and cause you to experience signs and symptoms of acute hepatitis. HBV should be closely monitored by your provider. The Viread formulation contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

POTENTIAL DRUG INTERACTIONS

Viread decreases the 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/Norvir, and Reyataz/Norvir increase Viread levels, but there is no dose adjustment needed. Patients taking Kaletra, Prezista/Norvir, or Reyataz/Norvir with TDF should be monitored for Viread side effects (including kidney disorders) due to the higher TDF levels. Do not take Viread with adefovir. Avoid taking Viread with drugs that negatively affect the kidneys, including chronic use or high doses of NSAIDS (non-steroidal anti-inflammatory drugs for pain, such as Advil or Motrin (ibuprofen) and Aleve (naproxen). Viread may be used with hepatitis C drugs such as Daklinza, Harvoni, Olysio, Sovaldi, Viekira Pak, or Zepatier, depending on the other components in the HIV regimen. Monitor for tenofovir toxicities if used with Epclusa. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

TDF with emtricitabine, as Truvada, is a recommended NRTI combination by DHHS HIV treatment guidelines for first-time therapy. A new version of tenofovir, called tenofovir alafenamide (TAF), replaced TDF in certain fixed-dose combinations. Biktarvy, Genvoya, and Odefsey are three single-tablet regimens containing TAF instead of TDF. Descovy is another version of Truvada, combining emtricitabine with TAF instead of TDF. In clinical trials, TAF had fewer kidney and bone issues than TDF. The NIH reported last year that infants exposed in the womb to TDF may have lower bone mineral content than those exposed to other antivirals. Tenofovir DF was approved in 2012 as part of Truvada for HIV prevention as PrEP (pre-exposure prophylaxis; see Truvada for PrEP page). TDF is part of the single-tablet regimens Atripla, Symfi, Symfi Lo, Complera, Delstrigo, and Stribild as well as the fixed-dose combination tablets Cimduo and Temixys. Viread as part of the combination tablet Truvada is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen in pregnancy.

DR. DAVID HARDY SAYS: Viread was approved in 2001 as the sixth nuke. Because of its different HIV resistance mutation pattern, it continued to be potent when other nukes had failed and thus became a common part of most ART regimens from 2001 to 2015. Its most common short-term side effects are mild nausea, queasiness, and mild diarrhea; on a long-term basis it can cause kidney damage and weakening of bones (osteoporosis or bone demineralization) in a small percentage of PLWH. It is increasingly being replaced by TAF-containing regimens. A generic form of Viread became available in the U.S. in December 2017.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Viread, or tenofovir disoproxil fumarate (TDF), is potent, well tolerated, and has a long half-life. Monitoring kidney function is important while taking TDF. It has been shown to cause kidney toxicity as well as loss of bone density. These side effects tend to disappear when discontinued. It is a component of the single-tablet regimens Complera and Stribild, as well as Truvada, a widely used fixed-dose combination as a nuke backbone, and as a prophylaxis for HIV infection. Its manufacturer has developed an improved version of TDF known as TAF (tenofovir alafenamide fumarate). TAF is a component of the single-tablet regimen Genvoya and is replacing TDF in many fixed-dose combination and single-tablet regimens.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

300 mg tablets:
$1,368.26/month
generic 300 mg tablets:
$1215.94/month

GENERIC IS AVAILABLE.

Ziagen abacavir (ABC)

NRTI NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NUCLEOSIDE, OR "NUKE")

★ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN FOR MOST PEOPLE WHEN USED IN COMBINATION WITH DOLUTEGRAVIR AND LAMIVUDINE (AS TRIUMEQ)

STANDARD DOSE

Two 300 mg tablets once daily (or one 300 mg tablet twice daily), without regard to food.

For adults and children at least 3 months of age and older. In children Ziagen is dosed based on body weight. See the package insert for weight-based dosing. Tablets may be crushed or split and added to a small amount of semi-solid food or liquid. Ziagen is also available as an oral solution (20 mg/mL) (strawberry-banana flavor) for children and adults who are not able to swallow the tablets. Must be taken in combination with another antiretroviral(s) which does not contain the medication in this drug.

Dose adjustment is not needed for people with kidney impairment. Dose adjustment is needed for people with mild liver impairment (200 mg twice daily). Ziagen should not be used in people with moderate or severe liver disease.

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.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The length of this section is meant to be informative, not scary. The most common side effects with an incidence greater than 10% were nausea, headache, malaise (general ill feeling), fatigue, vomiting, and dreams/sleep disorders. In pediatric patients, the more common side effects were fever and/or chills, nausea and vomiting, skin rashes, and ear/nose/throat infections.

Approximately 8% of people who took abacavir in clinical trials (where screening for HLA-B*5701, a genetic marker associated with abacavir hypersensitivity, was not performed) experienced hypersensitivity reaction (HSR), an allergic-like reaction. To minimize the risk for HSR, a blood test for HLA-B*5701 should be done prior to starting an HIV regimen containing abacavir to identify patients at higher risk for this reaction. This test is covered by most insurance and also by LabCorp/ViiV (go to viivconnect.com). If the HLA-B*5701 test is positive, you are at an increased risk for HSR and you should not take abacavir. An allergy to it should be entered in your medical record. A negative HLA-B*5701 test does not mean you won't have HSR, but the risk is very low (1% from clinical studies). 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, and 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 usually resolve after permanent discontinuation. If you develop HSR, abacavir should be stopped and you can never take abacavir or any product containing abacavir (Epzicom, Trizivir, Ziagen, or Triumeq) again (starting again is called rechallenging). Rechallenging can cause a rare life-threatening reaction. This does not apply to a missed dose when there is no HSR, but talk with your healthcare provider and watch for symptoms if you've stopped the drug for a few days, preferably under the observation of others who can call for medical help if you develop symptoms. An HSR can technically occur at any time, regardless of how long you have been taking the medication, however, it is much more likely to occur when you start (or re-start) the medication (90% occur within the first 6 weeks of treatment).

Some large observational studies suggest abacavir may increase the risk of cardiovascular events, including myocardial infarction (MI, or heart attack), in people with risk factors (such as older age, smoking, diabetes, high blood pressure, high cholesterol, family history of heart disease, and drug use), especially within the first 6 months of therapy. However, other studies, including a large meta-analysis, have shown no increase in cardiovascular risk. To date, no consensus has been reached on the association of abacavir with cardiac risk or a possible mechanism for the association. People who are at high risk for heart disease should discuss risks with their provider and they should be monitored more closely.

POTENTIAL DRUG INTERACTIONS

Alcohol can increase abacavir levels and therefore can increase the possibility of side effects. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

DR. DAVID HARDY SAYS: Ziagen was approved in 1998 as the fifth nuke at a time when HIV resistance to antiretrovirals and treatment failure was very common. It provided a new option for treatment at the time it was approved. From the beginning, this medication has had its challenges. As the drug was being studied in the late 1990s, a severe and possibly fatal allergic reaction (hypersensitivity) was discovered. Super elegant (cool) pharmacogenetic studies linked the occurrence of this side effect to a specific gene (HLA-B*5701). A simple blood or mouth swab can be used to detect this gene and determine if a PLWH can take the medication safely. Next, a European cohort study linked Ziagen to heart attacks, and a U.S. study showed it to be less potent than Viread. Despite these challenges, Ziagen has survived, a bit tattered, as a nuke still used today, almost exclusively in the STR Triumeq. A generic form of Ziagen has been available in the U.S. since 2012.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Abacavir is a nucleoside reverse transcriptase inhibitor drug used for the treatment of HIV infection in combination with other HIV medicines. Serious side effects of abacavir include allergic reactions, a build-up of acid in the blood (lactic acidosis), and liver problems. If when taking abacavir you find yourself having an allergic reaction, stop the drug immediately and call your doctor. This hypersensitivity reaction can cause death. Your risk for this reaction is high if you have a specific gene variation, which can be determined by a blood test prescribed by a doctor.

MORE INFORMATION

The ACTG A5202 study found that abacavir/lamivudine (Epzicom) was inferior to tenofovir/emtricitabine (Truvada) in getting people undetectable when their pre-treatment viral load was over 100,000 copies/mL. However, when combined with Tivicay (dolutegravir), Epzicom performed just as well as Truvada in people with high viral loads (over 100,000 copies/mL). Hence, Triumeq is the only abacavir-containing regimen recommended by DHHS as initial therapy for most HLA-B*5701 negative people. 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. But again, a simple test reveals whether you are at high risk for the allergic reaction. FDA researchers reported finding a mechanism for autoimmune drug reactions, including abacavir HSR, and hope it helps improve drug safety in the future. Ziagen as part of the combination tablet Epzicom is recommended by DHHS as one of the preferred NRTI combination components of an ART regimen during pregnancy.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Ziagen
300 mg tablet, 60 tablets: **$670.37**/month
generic abacavir
300 mg tablet, 60 tablets: **$602.71**/month

Edurant rilpivirine (RPV)

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS IN COMBINATION WITH DESCOVY OR TRUVADA (AS ODEFSEY OR COMPLERA)

STANDARD DOSE

One 25 mg tablet once daily with a standard meal (more than 390 calories). For adults and children 12 years of age and older weighing at least 77 pounds (35 kg). Must be taken in combination with another antiretroviral(s) which does not contain the medication in this drug or medication from the same drug class. No dose adjustment needed for pregnant patients with undetectable viral load on a stable rilpivirine-based regimen, but monitor viral load closely because lower rilpivirine drug exposure has been seen during pregnancy.

Viral load (HIV RNA) must be less than 100,000 copies/mL and CD4 T-cell count must be above 200 cells/mm^3 before starting Edurant due to higher rates of virologic failure in these patients.

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

Must be taken with a meal that you chew—not just nutritional drinks or protein shakes. Taking rilpivirine without food could result in a 40% decrease in drug absorption and may lead to resistance.

➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Moderate to severe side effects are uncommon. Most common side effects occurring in 3–5% of study subjects were insomnia, headache, rash, and depressive disorders. Tell your doctor right away if you experience feelings of sadness, hopelessness, anxiety or restlessness, or have suicidal thoughts or actions. A small study showed a higher rate of depressive disorders in adolescents (19.4%—seven out of 36 youths—vs. 9% for adults), which may or may not have been related to Edurant. Two different studies comparing Edurant to Sustiva showed that Edurant was slightly better tolerated. Edurant also has minimal negative effects on LDL ("bad") cholesterol, total cholesterol, and triglycerides when compared to Sustiva. Edurant improved HDL ("good") cholesterol slightly less than Sustiva. Liver problems can occur with Edurant (even in patients without a history of liver disease). Edurant can cause a small, reversible increase in kidney function test (serum creatinine) within the first few weeks of treatment without affecting actual kidney function.

POTENTIAL DRUG INTERACTIONS

Edurant cannot be taken with the anti-seizure medications carbamazepine, oxcarbazepine, phenobarbital, or phenytoin; the anti-TB drugs rifampin and rifapentine; proton pump inhibitors (Aciphex, Dexilant, Nexium, Prevacid, Protonix, and Prilosec); or the herb St. John's wort. Do not take with more than one systemic dose of the steroid dexamethasone. 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. If administered with rifabutin, the dose of Edurant 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. Monitor for worsening of any fungal infections when Edurant is used with antifungal 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 other medications with a known risk of torsades de pointes or QT prolongation (these abnormal heart rhythms can make the heart stop). No dose adjustment needed with hepatitis C medications Daklinza, Epclusa, Harvoni, Olysio, Sovaldi, or Zepatier. Cannot be taken with Viekira Pak. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

A new medication combining rilpivirine with dolutegravir was approved by the FDA in late 2017; see Juluca. Edurant is not recommended for treatment-naïve patients with a pre-treatment viral load greater than 100,000 copies/mL or CD4 less than 200 cells/mm^3. A rilpivirine-based regimen may be advantageous in people with high risk for heart disease due to its relatively low impact on lipid profile. While its tolerability and safety profiles are advantages for Edurant, the greater potential for virologic failure in patients with high viral loads or low CD4 counts, food restrictions, and cross-resistance to the other NNRTIs puts Edurant at a disadvantage for first-time treatment—people may not be able to switch to another NNRTI if their HIV develops NNRTI resistant mutations to Edurant. Data for use of rilpivirine in combination with an abacavir/lamivudine background are insufficient to recommend at this time. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Edurant can be used during pregnancy, and is listed as a DHHS alternative NNRTI to use in pregnancy in combination with a two-NRTI backbone. According to the FDA, lower exposures of rilpivirine were observed during pregnancy, therefore, viral load should be monitored closely.

DR. DAVID HARDY SAYS: Edurant was approved in 2011 as the second "second generation" NNRTI to be used as an ART regimen in treatment-naïve PLWH. Its upside is its excellent tolerability (side effects occur uncommonly); its downside is that it lacks potency for PLWH with high viral loads (greater than 100,000 copies/ml). Edurant has been used in three STRs, Complera, Juluca, and Odefsey (see those pages). Due to its potency concerns, it has never been considered the best choice for all PLWH starting their first ART regimens, but only those with lower viral loads (less than 100,000 copies/mL).

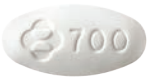
ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Rilpivirine is an NNRTI shown not to be inferior to efavirenz in individuals with a viral load less than 100,000. It was first approved as a single agent but nowadays it is used in various single-tablet regimens: Complera, Odefsey, and Juluca. The resistance profile of this drug is complicated. If resistance to rilpivirine develops, cross-resistance to Intelence (etravirine) occurs. It is well tolerated and needs to be taken with food. It works well when used to switch regimens in individuals who have an undetectable viral load. It is important to know the drug-drug interactions of rilpivirine. It should not be taken with antacids because it will affect drug absorption. Rilpivirine plus cabotegravir is under investigation as a once-a-month long-acting fixed-dose HIV treatment.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,338.13/month



Pifeltro doravirine (DOR)

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ RECOMMENDED AS COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS

STANDARD DOSE

One tablet once daily without regard to food. Tablet contains 100 mg of doravirine. Must be taken in combination with another antiretroviral(s) which does not contain the medication in this drug or medication from the same drug class.

Approved only for adults at this time. 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. No dosage adjustment necessary for mild, moderate, or severe kidney impairment or for mild or moderate liver impairment. Pifeltro has not been studied in patients with severe liver impairment.

➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Most common side effects (at least 5% of people taking it) observed with Pifeltro in studies were nausea (7%), dizziness (7%), headache (6%), fatigue (6%), diarrhea (5%), abdominal pain (5%), abnormal dreams (1%), and increased bilirubin (5%). Rash, which is a common side effect of the NNRTIs, was reported in up to 2% of the studied population. In one study (DRIVE-AHEAD), an in-depth analysis was conducted of the incidence of neuropsychiatric adverse events associated with a doravirine-containing regimen (Delstrigo) compared to Atripla. Neuropsychiatric events, such as depression, sleep disturbances, and dizziness, are another common side effect of the NNRTI class. See data online. Doravirine did not appear to negatively affect cholesterol in studied populations.

POTENTIAL DRUG INTERACTIONS

New interactions continue to be discovered after drug approval. When using with the antibiotic drug rifabutin (used for TB and MAC treatment), increase the Pifeltro dose to one tablet twice a day, approximately every 12 hours. The following are among the medications that may lower the blood levels of Pifeltro, and therefore may decrease its effectiveness, and should not be used with Pifeltro: the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent (cancer drug) mitotane; and the herbal St. John's wort. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Received FDA approval in 2018. Doravirine may be an option for patients who have developed drug resistance to other NNRTIs. A single-tablet regimen (STR) containing doravirine was also approved last year; see Delstrigo page. Delstrigo, however, contains the older version of tenofovir, tenofovir DF. The stand-alone Pifeltro allows people to take it with the newer and less toxic tenofovir alafenamide, or TAF (found in Descovy). On the other hand, of course, the use of Pifeltro means the necessity for an extra pill of Descovy, or maybe more than one extra pill, depending on the regimen being used. Merck has applied to the FDA for a switch indication, so that people with undetectable viral load on their current treatment can switch to a Pifeltro-based regimen. Pifeltro was found to be non-inferior to boosted darunavir (Prezista) as well as efavirenz (Sustiva) at 48 weeks. Doravirine was superior to boosted darunavir at week 96 in terms of virologic suppression, but it should be noted there was a higher rate of study discontinuation in the boosted darunavir group. Doravirine is a non-nucleoside medication, and it should be noted that this class of drugs typically has a lower barrier to resistance as well as have extensive cross-resistance. Additionally, the emergence of resistance at the time of virologic failure has been reported with doravirine. Despite the side effects listed above, doravirine has tolerability advantages over efavirenz and has relatively favorable lipid effects when compared with both boosted darunavir and efavirenz. It also has fewer potential drug interactions than efavirenz or rilpivirine, and, unlike rilpivirine, virologic efficacy is not compromised in those with high baseline viral loads or low CD4 counts. Doravirine has not been directly compared to integrase inhibitor-based regimens in clinical trials yet. Because there were significantly fewer people who received doravirine + Epzicom compared to those who received Truvada, the guidelines consider Pifeltro plus Epzicom to be an option for initial therapy but the guidelines panel has less confidence in this regimen than in the other doravirine-containing regimens. There is no data on the safety of doravirine use in pregnancy. In the DRIVE-FORWARD study, comparing doravirine to darunavir, the treatment-naïve individuals in the study were 80% (darunavir group) and 84% (doravirine group) undetectable (less than 50 copies viral load). That's a lower success rate than is expected in HIV treatment today, but was thought to be affected by the number of people who quickly dropped out of the study when they saw how many pills they had to take. Those drop-outs were counted as virologic failures. Only 1 of 364 doravirine-treated patients developed drug resistance, a low number for an NNRTI; there was no resistance noted in the boosted darunavir group. See more data online. Merck has applied to the FDA for a switch indication, so that people with undetectable viral load on their current treatment can switch to a Pifeltro-based regimen.

DR. DAVID HARDY SAYS: Pifeltro was FDA approved in August 2018 and is also considered to be a "second generation" NNRTI due to its enhanced resistance profile compared to Sustiva and other older "first generation" NNRTIs. In fact, lab studies predict that it may be effective after a first generation NNRTI has failed and left HIV resistance mutations. To date, data from two large clinical trials comparing doravirine to Sustiva and to Prezista/Norvir have shown that Pilfeltro has similar anti-HIV potency as those two known potent medications and fewer side effects. Pifeltro is also approved (August 2018) as an STR combining it with generic tenofovir DF and lamivudine (see Delstrigo).

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Pifeltro is the new Merck once-a-day stand-alone non-nucleoside reverse transcriptase inhibitor used to treat HIV in combination with other HIV medicines. Pifeltro is contained in the single-tablet regimen Delstrigo. This treatment is contraindicated with medications that are metabolized by the P450 enzyme inducer. This enzyme causes a significant decrease in doravirine plasma levels and low plasma levels decrease its effectiveness.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

$1,656.00/month

GENERIC IS AVAILABLE.

Sustiva efavirenz (EFV)

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ RECOMMENDED AS A COMPONENT OF INITIAL REGIMEN IN CERTAIN CLINICAL SITUATIONS (AS A COMPONENT OF ATRIPLA, SYMFI, OR SYMFI LO, OR IN COMBINATION WITH DESCOVY OR TRUVADA)

STANDARD DOSE

One 600 mg tablet once daily, preferably on an empty stomach at bedtime. Must be taken in combination with another antiretroviral(s) which does not contain the medication in this drug or medication from the same drug class.

Approved for adults and children 3 months and older weighing at least 7.7 pounds (3.5 kg). For children weighing less than 88 pounds (40 kg), the dose is based on weight. See the package insert for specific weight-based dosing. For children weighing at least 88 pounds, use the standard adult dose. 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.

Take missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose. Also available in 50 mg and 200 mg capsules.

Use with caution in mild liver impairment; not recommended with moderate or severe liver impairment.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

Central nervous system (CNS) symptoms (dizziness, insomnia, impaired concentration, abnormal or vivid dreams, and hallucinations) are most common at the start of treatment and usually diminish in two to four weeks. Bedtime dosing on an empty stomach can help reduce symptoms. Less common psychiatric symptoms (catatonia, depression, suicidal thoughts or actions, aggression, paranoid/manic reactions) may also occur. A 2014 study reviewed four previously published AIDS Clinical Trials Group (ACTG) studies regarding efavirenz and suicidal ideation and re-emphasized the fact that efavirenz has an association with suicidality (reported suicidal ideation or attempted or completed suicide), and should be used with caution in patients with severe or uncontrolled depression and/or a history of suicidality. It is recommended for anyone on a regimen containing efavirenz to be screened for depression and suicidality. Additional 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. Efavirenz can cause a false positive for marijuana on certain drug tests. A more specific confirmatory test can be done. A link to birth defects in humans has not been supported in meta-analyses. The pregnancy recommendation is that women in their first trimester continue taking efavirenz 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. Because of the association with suicidality and neuropsychiatric effects, it is also recommended to screen for antenatal and postpartum depression in women with HIV who are taking a regimen containing efavirenz. Regular monitoring for increased liver enzyme levels is recommended initially and during treatment for people with hepatitis B/C or liver disease.

POTENTIAL DRUG INTERACTIONS

Tell your provider or pharmacist about all medications, herbals, supplements, and over-the-counter products you are taking or thinking of taking, prescribed or not, as there are other drug interactions not listed here. Do not take with midazolam, pimozide, ergot derivatives, St. John's wort, or triazolam. May affect warfarin levels. Can decrease levels of buprenorphine and methadone—monitor for withdrawal. Increase Kaletra to two 200/50 mg tablets plus one 100/25 mg tablet twice daily (total 500/125 mg twice daily) with food when taken with Sustiva. Kaletra cannot be taken once daily with Sustiva. 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 1,400 mg with 300 mg Norvir. No change in the ritonavir dose is required when efavirenz is administered with Lexiva plus ritonavir twice daily. Increase Selzentry to 600 mg twice daily. Increase the Sustiva dose to 800 mg once daily with rifampin for people weighing 110 pounds (50 kg) or more. Rifabutin can be used as an alternative, but dose adjustment is needed. When taken with 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 posaconazole (avoid unless benefit outweighs potential risk) and itraconazole. 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 using azithromycin instead. Levels of immunosuppressants should be monitored when starting or stopping Sustiva. Cardizem, Lipitor, Pravachol, and Zocor doses may need to be adjusted. Titrate dose of bupropion and sertraline based on clinical response. Should not be taken with other medications that prolong QT interval or medications with a known risk of torsades de pointes. No dose adjustment with Harvoni or Sovaldi. Increase Daklinza dose to 90 mg with Sustiva. Don't take with Epclusa, Olysio, Viekira Pak, or Zepatier. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

If you can't sleep, ask your doctor about gradually adjusting the timing of your dose until it's taken during the day. A rare genetic trait affecting drug metabolism of Sustiva, leading to a higher rate of side effects, occurs more in African Americans. In pediatric HIV guidelines, Sustiva was downgraded in 2017 from "preferred" to an "alternative" component of an initial regimen for children ages 3–12 years. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs. Efavirenz is found in the single-tablet regimens Atripla, Symfi, and Symfi Lo; see those pages.

DR. DAVID HARDY SAYS: Approved in 1998, Sustiva was the "queen bee" of antiretrovirals as the "kinder and gentler" alternative to the highly potent but difficult to tolerate protease inhibitors until the appearance of the integrase inhibitors in 2007. Although highly potent against HIV and taken just once daily, the unique side effects of grogginess, dizziness, and vivid dreams were often treatment-limiting side effects for many PLWH. It was thought that these side effects would go away over time, but long-term studies with Sustiva (up to 5 years) showed that they never improve for some PLWH. Worsening of mental health conditions and increased suicidal thoughts and attempts have limited Sustiva's use. It is still the most commonly prescribed antiretroviral in the world, although this is starting to change.

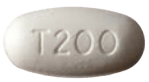
ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Efavirenz is a very potent and long-acting antiviral. Sustiva is the anchor drug of Atripla, the first and most widely used single-tablet regimen for the last 11 years. Sustiva's central nervous system side effects are challenging. Dizziness, weird dreams, depression, and feeling tired constantly are some of the side effects reported. Some individuals tolerate it well and others manage to overcome them after three months. Other NNRTIs and INSTIs with no CNS side effects, as effective and way more tolerable have been developed.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

600 mg tablets:
$1,176.74/month
generic: **$1,117.90**/month



Intelence etravirine (ETR)

NNRTI NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NON-NUCLEOSIDE, OR "NON-NUKE")

✔ FOR TREATMENT-EXPERIENCED PATIENTS WITH VIRAL STRAINS RESISTANT TO AN NNRTI AND OTHER ANTIRETROVIRAL DRUGS ONLY

STANDARD DOSE

One 200 mg tablet, twice daily with food. Approved for adults and children 2 years and older weighing at least 22 pounds (10 kg). See the package insert for specific weight-based dosing in children. Also available in 25 mg and 100 mg tablets. Must be taken in combination with another antiretroviral(s) which does not contain medication from the same drug class.

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. People unable to swallow pills (Intelence tablets are "chalky") can dissolve tablets in 1 teaspoon (5 mL) of water or at least enough liquid to cover the medication, stir well until the water turns milky, add more water if desired—use orange juice or milk as an alternative, always placing tablets in water first. Avoid warm (over 104° F) or carbonated beverages. Drink 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. Taking Intelence without food could result in a 50% decrease in the drug absorption and may lead to HIV drug resistance

- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.
- **TELL YOUR PROVIDER OR PHARMACIST** about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

POTENTIAL SIDE EFFECTS AND TOXICITY

Generally well tolerated, but most common side effects include rash as well as numbness, tingling, or pain in the hands or feet. Rare side effects include severe rash and peripheral neuropathy. 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, general malaise [general ill feeling], fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial edema, hepatitis, eosinophilia, or angioedema). 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.

POTENTIAL DRUG INTERACTIONS

If Intelence is taken in combination with a protease inhibitor, the PI must be boosted with low-dose Norvir. Avoid Intelence with boosted Aptivus or Lexiva. It 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 and 150 mg twice daily when used with a boosted PI. Do not take Intelence with Tegretol, Luminal, Dilantin, Priftin, Rifadin, or the herb St. John's wort. Use with caution when combined with the antifungals Diflucan and Vfend. Dose adjustments of the antifungals ketoconazole, itraconazole, and posaconazole may be needed. 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 also taking a boosted PI. Intelence can be safely combined with methadone or buprenorphine with additional monitoring for potential signs of withdrawal. Intelence can also be safely combined with Viagra, Cialis, and Levitra, though a dosage adjustment of Viagra may be necessary. Can be taken with Daklinza (increase Daklinza dose to 90 mg). Interactions with Sovaldi and Harvoni have not been studied; but based on the metabolism, a clinically significant interaction is not expected. Taking with Olysio, Viekira Pak, or Zepatier is not recommended.

DR. DAVID HARDY SAYS: Approved in 2008 as the first "second generation" NNRTI due to its improved resistance profile, Intelence has generally been used only for PLWH whose HIV has a significant amount of resistance to other antiretroviral medications. It is approved to be given only on a twice-daily basis and generally best with boosted Prezista with or without an integrase inhibitor. It is not approved to be used in a first-time ART regimen, although a couple of small studies have shown that it can work.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Etravirine is a second-generation NNRTI that has shown significant viral load reduction in individuals who developed resistance to the first generation of NNRTIs (efavirenz and nevirapine). Like other NNRTIs, etravirine's drug-drug interactions are many and complicated. It is important to understand the interactions and inform the doctor of all over-the-counter medications, supplements, and herbals. They might affect the absorption of etravirine. It is well tolerated but may cause some rare side effects like rash or increased cholesterol. It is a good second-line alternative for treatment-experienced people. The size of the pill makes it hard to swallow and it leaves a chalky taste in the mouth. There is the option of dissolving it in water.

MORE INFORMATION

For patients who have had virologic failure on an NNRTI-containing regimen, do not use Intelence in combination with a nucleoside backbone alone. Although taking once daily is 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. In Europe, it is approved as a once-daily medication. The once-daily dosing may improve patient adherence. The TRIO study reported the combination of Intelence with Prezista/Norvir and Isentress in highly treatment-experienced patients was successful in getting many patients to undetectable. Some patients complain of hard-to-swallow, large chalky pills; see dissolving instructions in dose section or package insert. For individuals with HIV-2, commonly found in some other countries, an NNRTI would not be recommended as HIV-2 is inherently resistant to NNRTIs.

MANUFACTURER

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

AVERAGE WHOLESALE PRICE

200 mg tablets,
60 tablets: **$1,628.03**/month

Selzentry maraviroc (MVC)

EI ENTRY/ATTACHMENT INHIBITOR: ENTRY INHIBITOR: CCR5 ANTAGONIST

▼ NOT RECOMMENDED AS COMPONENT OF AN INITIAL REGIMEN

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). Approved for adults and children at least two years old weighing at least 22 pounds (10 kg) and having a creatinine clearance of at least 30mL/min (measurement of kidney function); dose depends on weight. Available in a 20 mg/mL oral solution as well as 25 mg and 75 mg tablets. The oral solution should be administered using the included press-in bottle adapter and oral dosing syringe. Can be taken without regard to food. Must be taken in combination with another antiretroviral(s).

Take missed dose as soon as possible, unless it is closer in time to your next dose. Do not double up on your next dose. Before you start Selzentry, you will need a specific blood test called a Trofile to determine if this medication will work for you.

➤ SEE PACKAGE INSERT for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common side effects occurring in greater than 8% of studied patients include cough, upper respiratory tract infections, bronchitis, fever, rash, muscle and joint pain, flatulence, bloating and distention, abdominal pain, dizziness, and trouble sleeping. Other less common 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 by 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 up to five years of follow-up, and some data indicate it may be beneficial in cancer or for preventing metastasis (the spread of cancer to other parts of the body).

POTENTIAL DRUG INTERACTIONS

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 boosted protease inhibitors (except for Aptivus), Stribild, Genvoya, Tybost, Rescriptor, clarithromycin, and itraconazole; 300 mg twice daily if taken with Aptivus, Viramune, Isentress, Tivicay, Triumeq, 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 Atripla, Sustiva, Intelence, rifampin, and some anti-convulsants such as carbamazepine (Tegretol), phenobarbital, and phenytoin (Dilantin). Likely dose with rifapentine is 600 mg twice daily, but use with caution. Not recommended with St. John's wort. Selzentry may be co-administered with the hepatitis C medications Sovaldi, Olysio, Harvoni, and Daklinza at a dose of 300 mg twice daily; however, ledipasvir (in Harvoni) may have potential to increase Selzentry levels. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Not recommended by DHHS as a component of an initial regimen due to requirement of CCR5 tropism prior to initiation of therapy, lack of virologic benefit when compared to other recommended regimens, and because it requires twice-daily dosing.

Selzentry is generally recommended only when other HIV medications from other classes cannot be used or when a new class of medication is needed to construct a complete and durable treatment regimen for patients who have drug resistance. Complex dosing, the need for a tropism test, and competition from newer drugs have dimmed some of the initial enthusiasm for this drug. Selzentry appears to be synergistic with Trogarzo for people with extensive HIV drug resistance. See ibalizumab page. A tropism assay (Trofile, Trofile DNA, or HIV-1 Coreceptor Tropism with Reflex to UDS) is needed 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 to complete. Genotypic tests are also available and may provide a faster and less expensive alternative. Selzentry only works for those people with CCR5-tropic virus. Viral tropism refers to the types of HIV that a person can have, CCR5 (R5), CXCR4 (X4), or Dual-Mix Tropic (R5 and X4). Selzentry blocks CCR5, a receptor on the outside of a CD4 cell, and shuts down this point of entry for the virus. Most people are infected with R5 virus initially, and then over time, X4 and mixed viruses may predominate. Blocking R5 with Selzentry does not cause a shift to X4 or negatively affect disease progression or CD4 count in people whose virus can use dual-mix. The tropism test needed is now generally paid for by public health departments, Medicare, and private insurances. ViiV may cover the payment for the Trofile test under certain circumstances. Selzentry seems to have minimal impact on lipid levels. Not recommended for pregnant women on initial HIV medication.

DR. DAVID HARDY SAYS: Selzentry was approved in 2007 for PLWH with highly drug-resistant HIV and for first-time ART treatment in PLWH in 2009. Selzentry was the second antiretroviral in the entry inhibitor class to be approved (the first was Fuzeon in 2003). Selzentry works uniquely by blocking the CCR5 receptor on the surface of CD4+ T cells to which HIV must attach to infect these cells. It stops HIV infection before it enters the cell. Despite favorable study results, primarily in treatment-experienced PLWH, and an excellent safety profile, Selzentry use has been limited in the U.S. due to a costly and slow turn-around blood test which must be used to check for susceptibility to the drug and poor results in subsequent clinical trials in PLWH starting first-line treatment. It is being studied as a possible treatment for HIV Associate Neurocognitive Disease (HAND).

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Selzentry, or maraviroc, is an entry inhibitor. It is a CCR5 antagonist that blocks one of the two receptors (CCR5) on the outside of the CD4 used by the virus to enter and infect the cell. People living with HIV need to have a tropism test that will determine if the CCR5 receptor is active. In treatment-experienced patients HIV may adapt to target CXCR4. When this occurs, individuals are unable to benefit from a CCR5 inhibitor. Even though it is not as popular as expected, it has become an important option for those who need add extra help to create an HIV regimen.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
selzentry.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

300 mg tablets, 60 tablets: **$1,874.44**/month

Trogarzo ibalizumab-uiyk (IBA)

AI ENTRY/ATTACHMENT INHIBITOR: CD4 POST-ATTACHMENT INHIBITOR

▼ FOR PEOPLE LACKING SUFFICIENT TREATMENT OPTIONS; SEE 'MORE INFORMATION SECTION' BELOW

DOSE USED IN STUDIES

Administered once every two weeks via intravenous infusion. Treatment begins with an IV loading (starting) dose of 2,000 mg, followed by an 800 mg IV infusion maintenance dose given every two weeks thereafter. Must be taken in combination with another antiretroviral(s).

The first infusion takes at least 30 minutes. If no infusion-related adverse events occur, subsequent infusions take 15 minutes. Doses may be administered every two weeks at an inpatient and/or outpatient setting, including at-home infusion, if desired. All patients should be observed for 1 hour after completing first infusion. If no infusion-associated adverse reaction is noted, the post-infusion observation time can be reduced to 15 minutes. Must be given with an optimized background regimen (OBR). An OBR consists of the best antiretroviral therapy that can be made for each patient based on the patterns of HIV drug resistance in their virus. Dose modifications of Trogarzo are not required when administered with any other antiretroviral or any other treatments.

If a maintenance dose of Trogarzo is missed by 3 days or longer beyond the scheduled dosing day, a loading dose (2,000 mg) should be administered as early as possible. Then resume maintenance dosing (800 mg) every 14 days thereafter.

➤ **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

The most common adverse reactions observed in clinical studies were diarrhea (8%), dizziness (8%), nausea (5%), and rash (5%). Additionally, selected lab abnormalities noted to occur in at least 5% of studied patients were increased bilirubin (greater than 2.6 times ULN—upper limit of normal) (5%), increased creatinine (greater than1.8 times ULN or 1.5x baseline) (10%), increased lipase (greater than 3 times ULN) (5%), decreased leucocytes (5%), and decreased neutrophils (5%). Most (90%) of the adverse reactions reported were mild or moderate in severity. No formal studies were conducted to examine the effects of either renal or hepatic impairment on the pharmacokinetics of ibalizumab. Renal impairment is not anticipated to impact the pharmacokinetics of ibalizumab.

POTENTIAL DRUG INTERACTIONS

Based on Trogarzo's mechanism of action and pharmacokinetic profile, drug-drug interactions are not expected. No drug interaction studies have been conducted with Trogarzo. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

Essentially, this drug's niche is deep salvage therapy for heavily treatment-experienced people with multi-drug resistance, along with an optimized background regimen (OBR). A key point is that people must still take other HIV medications that have some activity—there has to be at least one HIV drug to which their virus is sensitive included in their OBR. U.S. HIV treatment guidelines list Trogarzo this way: "Patients with ongoing detectable viremia [detectable viral load] who lack sufficient treatment options to construct a fully suppressive regimen [get to undetectable viral load] may be candidates for the recently approved CD4 post-attachment inhibitor ibalizumab." Ibalizumab is a shiny brand new option, but it doesn't come without some rules. It is expensive because the cost of the drug will be added to other expenses such as the time at the infusion center and qualified individuals to administer and handle the medication, although there may be an option for patients to receive their infusion at home. Non-adherence won't be an option—people won't be able to just show up whenever they want or be late to appointments when going to an infusion center. It will be like chemotherapy or dialysis. Patients must be on time.

Trogarzo is new and works differently than any other available HIV medication. Ibalizumab is the first HIV drug that is not taken every day. Still, because it must be used with other HIV medications, antiviral treatment will still be required to be taken daily. Ibalizumab is also the first HIV orphan drug—one that is produced for a relatively small population of patients (fewer than 200,000). It was produced for people with multi-drug resistant HIV, estimated to be fewer than 40,000 in the U.S.; the company estimates that there are fewer than 25,000. These are heavily treatment-experienced people who have multi-drug resistance, and have therefore, usually, limited treatment options. Ibalizumab has been shown to work against highly drug-resistant virus, when combined with an OBR.

Ibalizumab was studied in a relatively small (only 40 patients!) Phase 3 study. Individuals with advanced disease and limited treatment options receiving Trogarzo noted significant improvements in viral load reduction and T cell increases. After the initial loading dose, 83% of participants achieved a clinically significant decrease in viral load.

As a biologic, IBA is the first HIV medication made from cells rather than from chemicals. This does not make ibalizumab better, just different. All monoclonal antibodies (or mAbs, hence the last syllable of "ibalizumab"), are made this way, including biologics used to treat rheumatoid arthritis and psoriasis. Ibalizumab works differently from any other HIV drug currently on the market. It binds to a domain (location) of the CD4 receptor (in this case, domain 2), blocking viral entry into the CD4 cell. Ibalizumab works against both CCR5 and CXCR4 virus, and appears to be synergistic with all other classes of antiretrovirals. Resistance test results revealed no evidence of cross-resistance between Trogarzo and any of the approved classes of HIV drugs. Ibalizumab is widely considered to be an HIV entry inhibitor medication. IBA is neither metabolized in the liver nor eliminated by the kidneys. No adequate human data are available to establish whether or not Trogarzo poses a risk to pregnancy outcomes. Monoclonal antibodies such as ibalizumab are transported across the placenta as pregnancy progresses; therefore, ibalizumab has the potential to be transmitted from the mother to the developing fetus. The safety and effectiveness of Trogarzo in pediatric patients have not been established.

DR. DAVID HARDY SAYS: Trogarzo was approved by the FDA in March 2018 and is the first antiretroviral given exclusively as an intravenous (IV) infusion. Trogarzo is the first monoclonal (synthetically produced) antibody that prevents HIV from attaching to the CD4+ receptor on the surface of CD4+ T cells. Due to this specific inhibition process, HIV cannot grab onto and get inside of a PLWH's CD4+ T cells and cause infection of that cell. A small but conclusive study showed that Trogarzo significantly dropped viral loads in PLWH with highly drug-resistant HIV when the drug was infused by vein into these persons every 2 to 4 weeks along with other antiretrovirals. The side effects of this monoclonal antibody treatment are minimal and well tolerated. It is notable that in this study, 43% (17 of 40) of PLWH also received fostemsavir as one of the active agents in an optimized treatment regimen. Also notable is the cost of Trogarzo; its monthly wholesale acquisition cost (WAC) is $9,089, or $108,960 per year.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Ibalizumab is a new drug in the entry inhibitor drug class. The way it works is different from all the other antivirals. It blocks viral entry into cells by attaching to a different domain on CD4 cells. Ibalizumab works against both CCR5 and CXCR4 virus. It is not metabolized in the liver or eliminated by the kidneys. Ibalizumab is what is known as a humanized monoclonal antibody. It is the first medication to treat HIV that is not taken daily. It must be used in combination with other HIV medicines. This is what we know as a salvage therapy, meaning it is for people with multi-drug resistant HIV who cannot achieve undetectable levels of HIV. It is administrated by IV infusion.

MANUFACTURER

TaiMed USA
DISTRIBUTED BY
Theratechnologies Inc.
theratech.com
trogarzo.com

AVERAGE WHOLESALE PRICE

$2,724.00 per vial;
10 vials for loading dose and two vials for continuing dose (every two weeks)

INVESTIGATIONAL DRUG AT PRESS TIME.

PHOTO UNAVAILABLE

fostemsavir (FTR)

AI ENTRY/ATTACHMENT INHIBITOR: gp120 ATTACHMENT INHIBITOR

● DHHS RECOMMENDATION NOT YET ESTABLISHED

STANDARD DOSE

In clinical trials, the investigational dose taken forward for further study was 600 mg, sometimes once daily and sometimes twice daily. Doses were taken after eating. Must be taken in combination with another antiretroviral(s).

Recommended for heavily treatment-experienced patients with history of 3-class antiretroviral resistance in addition to an optimized background regimen of other active antiretroviral drugs. Not studied in treatment-naïve patients at this time. No data in pregnant women or pediatric patients under age 18 years.

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

➤ SEE PACKAGE INSERT when available for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

In the Phase 3 BRIGHTE study results out to one year (48 weeks), a third of participants experienced one or more serious adverse event (SAE), mostly infections (of which pneumonia was most common). Three percent of the SAEs were related to fostemsavir. A high rate of SAEs in the study population is not unexpected, given the heavily HIV treatment-experienced background of participants, and likely their advanced disease. In a week 24 BRIGHTE safety report, 91% of participants had experienced at least one adverse event, mostly Grade 1 or 2 (mild to moderate). Grade 2 to 4 adverse events (moderate to serious) occurring in a total 18% of participants included nausea (4%), diarrhea (2%), headache (2%), vomiting (2%), fatigue (1%), and asthenia (muscle weakness) (1%). Remember, most of the participants were also taking at least one other new drug. Seventeen participants (5%) died, due to AIDS-related causes or IRIS (immune reconstitution inflammatory syndrome, in which the body begins to wake up "sleeping" illnesses as the immune system improves). Again, this is not unexpected in patients with advanced disease. Six percent of study participants overall discontinued the study due to an adverse event.

POTENTIAL DRUG INTERACTIONS

New interactions continue to be discovered after drug approval. Dose modification of fostemsavir is not required when co-administering with tenofovir DF, ritonavir-boosted atazanavir, ritonavir-boosted darunavir with or without etravirine, etravirine alone, ritonavir alone, or raltegravir + tenofovir DF. Dose modification is also not required when co-administering with rifabutin (with or without ritonavir). It is not recommended to co-administer with rifampin due to significantly reduced levels of fostemsavir. Based on fostemsavir's metabolism, a theoretical interaction likely exists with statins (drugs used to treat high cholesterol). This may require a dose reduction or adjustment of certain statins when co-administered with fostemsavir. No dose modification necessary when co-administered with methadone or buprenorphine. Fostemsavir could affect oral contraceptive concentrations, especially those containing ethinyl estradiol. If a booster is not given in the regimen with fostemsavir, it may be co-administered with a combined oral contraceptive containing norethindrone and 30 mcg or less of ethinyl estradiol. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not, as there are other drug interactions which are not listed here.

MORE INFORMATION

May be FDA approved this year. Fostemsavir is the first HIV drug of its type to get this far in development. It's a gp120 attachment inhibitor. (That's under the drug class of HIV entry inhibitors.) Watch a video of its mechanism of action at youtu.be/WnreXE-TVi8. Fostemsavir works on the gp120 protein that lays on the surface of human immune cells. It's a necessary part of getting the virus to enter the cell. Fostemsavir prevents attachment to the CD4 immune cell by binding to the CD4 receptor binding sites on gp120 on the virus. This causes the virus to accumulate in extracellular space and is subsequently removed by the body's immune system. Very cool. Fostemsavir is likely to be approved as an oral twice-daily drug, making it unlikely to be used in treatment-naïve individuals. The drug is designed to be used in HIV treatment-experienced people, who typically have fewer options for HIV treatment than those just beginning antiretroviral therapy. An option for treatment-experienced individuals is a good thing. "Even in the era of modern HAART [highly active antiretroviral therapy], antiretroviral (ARV) failure and resistance is still a problem worldwide," wrote HIV specialist Dr. Pedro Cahn and colleagues in *Current Opinion in HIV and AIDS* published last July. Dr. Cahn worked on fostemsavir research. See more data online.

MANUFACTURER

ViiV Healthcare
viivhealthcare.com
(877) 844-8872

AVERAGE WHOLESALE PRICE

Not yet established.

DR. DAVID HARDY SAYS: Fostemsavir is a prodrug that is metabolized to the active compound temsavir, an attachment inhibitor that binds to glycoprotein 120 (gp120) on the envelope of HIV's surface. It works by locking HIV gp120 in a conformational state that inhibits the necessary binding between the virus and the CD4+ protein on human T cells, and prevents viral attachment and entry into these cells. Because of its unique mechanism of action, there is no known cross-resistance with other classes of antiretrovirals which may help PLWH whose viruses have become resistant to most other medications. While the BRIGHTE study data has been submitted to the FDA for review, fostemsavir's approval has been delayed due to manufacturing limitations. It is expected that fostemsavir will be approved and available in 2019. It is given as a tablet twice daily along with other antiretrovirals. The BRIGHTE study (NCT02362503) is a two-cohort (randomized and open-label), Phase 3 clinical trial evaluating the safety and efficacy of fostemsavir in 371 heavily treatment-experienced PLWH. All had documented resistance, intolerability, and/or contraindication to all antiretrovirals in at least four of the six available ART classes. PLWH in the randomized cohort had to have one, but no more than two, fully active antiretroviral classes remaining at baseline, but were unable to construct an effective regimen from their remaining antiretrovirals. These PLWH were randomized 3:1 to add blinded fostemsavir or blinded placebo (n=272) to their current failing regimen for eight days of functional monotherapy. Patients without any remaining fully active approved antiretrovirals (n=99) were assigned to the open-label cohort and received fostemsavir plus other optimized antiretrovirals. The primary endpoint of the study was mean change in viral load between Day 1 and Day 8 for the randomized cohort. After the 8-day blinded period, all patients in the randomized cohort received open-label fostemsavir plus an optimized ART regimen. By Day 8, those PLWH who received fostemsavir saw their viral loads drop by 0.8 $\log^{10}$, or about 6.5-fold, compared with a 0.2 $\log^{10}$ drop among those who received placebo, thus confirming fostemsavir's anti-HIV activity in highly treatment-experienced PLWH. After 48 weeks, 62% of PLWH in the randomized group had undetectable viral loads (less than 40 copies/mL) and 86% had viral loads below 400 copies/mL. Among PLWH in the initial open-label group, 48% had viral loads less than 40 copies/mL and 55% had viral loads less than 400 copies/mL. PLWH in the randomized group experienced an average rise in CD4+ T cells of 139/mm^3, while those in the initial open-label group gained an average of 64 CD4+ T cells/mm^3.

ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: Fostemsavir is developed to be used in PLWH with multi-drug resistance. Fostemsavir is a prodrug. When the drug is taken, it metabolizes to the active compound, temsavir, which inhibits the binding of HIV to CD4+ T cells through blocking the HIV gp120 receptor. Since this is a highly conserved protein between HIV strains, fostemsavir has a high genetic barrier to resistance, and its novel method of action provides an alternative option for patients with highly resistant viral HIV strains.

Egrifta tesamorelin for injection

NON-HIV INJECTABLE FOR TREATING HIV-RELATED EXCESS BELLY FAT (LIPOHYPERTROPHY)

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 and this page for more information).

A potential complication of HIV, antiretroviral therapy, or both may be changes in the distribution of adipose tissue (fat), otherwise known as lipodystrophy; previous reports of prevalence in the U.S. varied 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. This is different from subcutaneous fat. 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. Egrifta reduces VAT while preserving subcutaneous fat. 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. In the Phase 3 clinical studies, 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. 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.

CAP & PAP INFO

Co-pay covers up to $6,000 per year. If someone is having difficulty paying for Egrifta, there are several programs available through Thera patient support at (833) 23-THERA (833-238-4372), Monday–Friday, 8 a.m.–8 p.m., EST or at egrifta.com.

MANUFACTURER

Theratechnologies, Inc.
egrifta.com
Thera Patient Support:
(833) 23-THERA
(833-238-4372)
therapatientsupport.com

AVERAGE WHOLESALE PRICE

$5,850.00/month

Mytesi crofelemer

NON-HIV ANTI-DIARRHEAL APPROVED FOR USE IN THOSE WITH HIV/AIDS AND ON ANTIRETROVIRAL THERAPY

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.

Mytesi (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.

Mytesi approval was based on a randomized, placebo-controlled study of 374 HIV-positive patients who had about 3 watery stools per day and were 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 Mytesi-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. Mytesi 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). Mytesi was less effective in African Americans in this clinical study.

An infectious cause should be ruled out prior to initiating Mytesi. 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 (Mytesi, 3.8% of patients vs. placebo, 2.9%). Other reported side effects included bronchitis, cough, flatulence (gas), and increased bilirubin. Based on animal data, Mytesi may cause fetal harm. Mytesi 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 in *Expert Review of Clinical Pharmacology* published in 2015 by Castro *et al.*, the use of Mytesi is recommended as a reasonable choice in patients not responding to over-the-counter psyllium and loperamide. Patients should be informed that the benefits of Mytesi are not immediate, possibly taking about four weeks, and if an inadequate response is seen after three months, Mytesi should be discontinued.

CAP & PAP INFO

Co-pay program:
(877) 336-4397
Pay no more than $25, maximum benefit of $100 on each prescription.
PAP: (888) 527-6276;
mytesi.com

MANUFACTURER

Napo Pharmaceuticals
mytesi.com
(844) 722-8256

AVERAGE WHOLESALE PRICE

$802.22/60 tablets

Serostim somatropin for injection

NON-HIV INJECTABLE HUMAN GROWTH HORMONE USED FOR TREATING HIV-ASSOCIATED WASTING IN THOSE ON ART

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.

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 birthmarks 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. An injection training program is available; see the website or call the toll-free number. 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.

CAP & PAP INFO

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 the Co-Pay Assistance Program (CAP). To find out more about these programs, call (877) 714-2947.

This year, the co-pay card is frontloaded. $0 initial fill (rebate form provided if you need to pay up front and are eligible), and up to $1,500 for each additional monthly fill, not to exceed $18,000/year. PAP also available if you qualify. Call AXIS Center (877) 714-AXIS (2947).

Go to serostim.com for additional information.

MANUFACTURER

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

AWP

6 mg: 7 injections (usually a one week supply)
$4,375.43

Truvada for PrEP

emtricitabine/tenofovir DF **(FTC/TDF)**

PrEP (PRE-EXPOSURE PROPHYLAXIS) ★ CDC RECOMMENDED FOR PREVENTION OF HIV

STANDARD DOSE

For HIV-negative adults and adolescents weighing at least 77 pounds (35 kg), one tablet once daily, without regard to food. The tablet contains 200 mg emtricitabine and 300 mg tenofovir disoproxil fumarate.

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. Truvada should not be used for prevention if eCrCl or eGFR (measures of kidney function) is less than 60 mL/min.

- **SEE THE INDIVIDUAL DRUGS CONTAINED IN TRUVADA:** Viread and Emtriva
- **SEE PACKAGE INSERT** for more complete information on potential side effects and interactions.

POTENTIAL SIDE EFFECTS AND TOXICITY

No new serious side effects were seen when Truvada was studied for HIV prevention in clinical trials. Some patients may experience nausea, headache, stomach pain, or weight loss. Risk compensation (when people put themselves at greater risk for infection, such as anonymous or multiple sex partners, because they think PrEP will protect them) was not observed in clinical trials. The tenofovir DF (Viread) in Truvada is associated with long-term decreases in bone mineral density (BMD). BMD monitoring should be considered in people who have a history of bone fracture due to a disease or are at risk for osteopenia or osteoporosis. Truvada can cause kidney toxicities. In prevention studies, decreases in BMD and creatinine clearance or eGFR (a marker of kidney function) were rare, mild, and reversible upon stopping Truvada. Tell your provider about pain in extremities, persistent or worsening bone pain and fractures, with or without muscular pain or weakness, as well as any concerning changes in urinary habits as these could be signs of kidney or bone problems. If Truvada is discontinued abruptly in people with hepatitis B virus (HBV), flare-up of hepatitis may occur—talk to your provider before discontinuing. In studies, there were cases of people who had unidentified HIV infection when starting Truvada for PrEP and subsequently developed drug resistance. A negative HIV test must be confirmed immediately prior to starting Truvada for PrEP. Truvada alone is not a complete regimen to treat HIV. Continuing only with Truvada after acquiring HIV may lead to drug resistance and limit future antiviral options. Truvada contains lactose, which can cause some abdominal discomfort, especially in patients sensitive to lactose.

POTENTIAL DRUG INTERACTIONS

Do not take with any other HIV or HBV drugs when used for PrEP. Avoid taking Truvada with drugs that negatively affect the kidneys, including chronic use or high doses of anti-inflammatory drugs for pain like Advil or Motrin (ibuprofen) and Aleve (naproxen). Truvada for PreP can be used with the hepatitis C drugs Daklinza, Harvoni, Sovaldi, Olysio, Viekira Pak, or Zepatier. Monitor for tenofovir toxicities if used with Epclusa. Tell your provider or pharmacist about all medications, herbals, and supplements you are taking or thinking of taking, prescribed or not.

MORE INFORMATION

Let's be clear: Truvada for PrEP is almost 100% effective in preventing HIV—this is a done deal. Why aren't more people using it to help end the epidemic? Stigma and lack of access to health care continue to fuel HIV infections. Remember, risk depends on the situation—including where you live or how much money your friends have or some such. Stigma—not sex—is the real shame. Other problems include not knowing about PrEP and inability to perceive a need for it (not realizing one may be vulnerable at all). Altogether, even doctors continue to avoid prescribing PrEP. Although PrEP should become medically routine, like HIV tests for pregnant women, until it is, we'll tell you again: seeing an HIV specialist is the best way to obtain PrEP. They get it. It's not about being a whore. And better yet, they care. Fortunately, new avenues for PrEP—many without HIV specialty—are opening up: pharmacist-led PrEP clinics, tele-PrEP (via video consultation), use of ERs and STD clinics, and so on. As for "just use a condom," there are many reasons why condoms are not enough. So can we move on?

Truvada, a widely-used medication for the treatment of HIV, was approved in July 2012 by the Food and Drug Administration (FDA) to reduce the risk of HIV infection in HIV-negative individuals "at risk" for HIV acquisition (according to the drug label – in reality, people rarely realize that they're at risk for HIV at all). Although the drug label specifies sexually-acquired infection, U.S. HIV guidelines also recommend use for protecting against infection through injection drug use (reducing the risk of HIV by more than 70%, according to the CDC). This approach to HIV prevention is called pre-exposure prophylaxis, or PrEP ("prophylaxis" means something that prevents disease, such as a condom or a vaccine). The U.S. Public Health Service (USPHS) has issued updated guidelines for the use of Truvada for PrEP. Go to cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Truvada is currently the only drug approved for PrEP.

There are many considerations regarding Truvada for PrEP. Proper use is crucial. It is vital that people test HIV-negative right before being given a prescription (the label says "immediately," the CDC says within 7 days). Patients should also be re-tested for HIV infection at least every three months while taking Truvada for PrEP. People who are already unknowingly HIV infected when starting PrEP risk developing drug-resistant virus because Truvada alone is not adequate for the treatment of HIV. Drug resistance can only occur in HIV-positive individuals. Truvada for PrEP should not be given to people with symptoms of recent (acute) infection, such as fever, fatigue, sweating a lot (especially at night), rash, vomiting, diarrhea, joint or muscle aches, headache, sore throat, or enlarged lymph nodes (especially in the neck or groin). PrEP should not be started (or re-started) if any of these symptoms appear after a potential exposure to HIV unless evaluated by a doctor and possibly re-tested for HIV. People on PrEP who have these symptoms after a potential exposure to HIV should let their provider know immediately.

Truvada for PrEP is not a "morning-after pill" or a weekend medication. It must be taken every day to be maximally effective. In studies, greater protection was seen with greater adherence. Truvada for PrEP works if you take it as prescribed. On the other hand, there have been good results with using it around the time of sex (kudos to the IPERGAY study)—the research continues. **Unlike HIV therapy,** which is long-term, PrEP may be used just for periods of time when HIV-negative individuals are most vulnerable to infection.

While some people may use PrEP as their only prevention method, it was studied and approved as part of a more comprehensive HIV prevention strategy that includes the use of condoms and risk reduction counseling. That said, the CDC has changed the definition of protected sex to include sex without condoms, given new modalities such as PrEP. Although consistent condom use is an important part of a prevention plan for all people prescribed PrEP, lack of use of a barrier protection is not a reason to withhold PrEP. On the contrary, the PrEP label lists people who are unwilling or unable to use condoms as at-risk candidates for whom the drug is indicated. PrEP does not protect against other sexually transmitted infections (STDs) including hepatitis C or against pregnancy.

Other screening and monitoring requirements include measuring kidney function and checking for STIs and hepatitis B and C, treatment for STIs, and vaccination for HBV if warranted.

Although a PrEP prescription can be given to a wide range of people, the Truvada PrEP drug label states that it is indicated for those considered "at risk" for infection. The label notes that people at risk include those who engage in sexual activity in a high-prevalence area or social network and have one or more of the following: (a) inconsistent or no condom use, (b) diagnosis of sexually transmitted infections (STIs), (c) exchange of sex for commodities (money, food, shelter, or drugs), (d) use of illicit drugs or alcohol dependence, (e) history of incarceration, or (f) sexual partners of unknown HIV status with any of the above risk factors. U.S. HIV treatment guidelines state that, "Truvada has been shown to be safe and effective at preventing HIV in healthy adults who meet

recommended criteria in the following populations: MSM [men who have sex with men], heterosexually active men and women, and IV drug users."

Individuals who have used post-exposure prophylaxis (PEP) multiple times are also good candidates for PrEP because of their continuing risk for HIV. PEP is a course of HIV medications taken for 28 days after exposure to HIV to prevent infection; it must be started as soon as possible but no later than 72 hours after exposure.

Although pregnant women were not enrolled in PrEP studies, there is hope for PrEP to help serodiscordant couples (where one partner is positive and one is negative) conceive without transmitting the virus. Last year, the DHHS perinatal HIV guidelines added a section on the use of PrEP and HIV therapy to prevent transmission in sero-different couples trying to conceive; go to aidsinfo.nih.gov. The Bay Area Perinatal AIDS Center (BAPAC) is leading the charge for safer conception options, including MSM, plus a new providers list at pleaseprepme.org; go to hiveonline.org.

According to the World Health Organization, it takes Truvada for PrEP 7 days to reach protective levels, whether exposure is rectal or vaginal. The CDC notes time to steady state, or maximum intracellular concentrations of tenofovir diphospate (TFV-DP), of 7 days for the rectal tract and about 20 days for vaginal tissue. Protective levels, however, are reached much earlier, based on pharmacokinetic (PK) models.

The two studies that led to Truvada's approval for PrEP, iPrEx (in high-risk MSM and transgender women) and Partners PrEP (in serodiscordant couples, most of them heterosexual), showed efficacy rates between 90%–92% when participants take their meds. PrEP with Truvada has also been studied in other patient populations, including younger single men and women, injection drug users, and women. In all the studies, the common theme is that PrEP is effective if you take it every day. Other drugs are being studied for use as HIV PrEP, including long-acting injection formulations requiring only one injection every 4–8 weeks.

Some providers not working in HIV are still learning about PrEP, and some continue to be reluctant to prescribe it. Read the PDF of the CDC brochure "Talk to Your Doctor about PrEP." The brochure includes resources for providers. HIV specialists may be best for a PEP or PrEP prescription, as they are familiar with the medications and more supportive of PrEP; find providers at hivma.org and aahivm.org, as well as pleaseprepme.org. HIV specialists are generally in high demand, however, and advocates are looking to make Truvada for PrEP much more accessible. There is also a complex set of standards to use in prescribing PrEP that may cause many providers to turn away, including a call for safer sex counseling. Requirements for a PrEP prescription can be burdensome. Truvada for PrEP has a Risk Evaluation and Mitigation Strategy (REMS) program which providers can access to ensure safe prescribing. The National Alliance of State and Territorial AIDS Directors (NASTAD) developed a guide to help providers bill for PrEP services available at nastad.org/resource/billing-coding-guide-hiv-prevention. Two excellent websites for finding a PrEP provider are preplocator.org and aidsvu.org. All you need to do is enter your ZIP code, and a list of providers who prescribe Truvada for PrEP will appear.

Greater PrEP acceptance and use, however, appears to be increasing among communities most vulnerable to HIV. Health departments across the country are promoting PrEP as part of a strategy to end the HIV epidemic. In addition, prevention efforts are also focusing on U=U (Undetectable equals Untransmittable), promoting the awareness that people living with HIV who have undetectable viral loads do not transmit the virus to sexual partners. Go to preventionaccess.org.

Providers are reporting widespread acceptance of PrEP prescriptions by insurers. Gilead Sciences helps patients work with their insurance, including pre-authorizations, as well as provides free PrEP to uninsured patients who are eligible and co-pay assistance up to $4,800 a year; contact the patient assistance hotline at (855) 330-5479, or go to gileadadvancingaccess.com. Patients may also need to advocate on their own behalf; keeping good notes of conversations and other communication is a good idea. Also, check out prep4love.com.

PrEP Facts: Rethinking HIV Prevention and Sex is a closed Facebook group for people interested in or currently on PrEP, and their allies. Demonstration projects providing free PrEP to study its use in the real world can be found at PrEPWatch.org from AVAC and projectinform.org/prep. Providers can use V107 as a medical billing code for PrEP (exposure to infectious disease, including HIV).

Other information sources:

- cdc.gov/hiv/basics/prep
- nccc.ucsf.edu/clinical-resources/pep-resources/prep
- whatisprep.org
- truvadapreprems.com
- hivinsite.com

Robert Grant, MD, principal investigator for the iPrEx study, wrote in an article for POSITIVELY AWARE, "The combination of highly active antiretroviral interventions for both HIV prevention and treatment has led to unprecedented optimism about the prospect of ending AIDS."

Read POSITIVELY AWARE's special issues on PrEP: positivelyaware.com/issues/prep-issue-summer-2015.

DR. DAVID HARDY SAYS: Truvada was FDA approved as the first antiretroviral for pre-exposure prophylaxis (PrEP) for HIV in July 2012 based upon a very robust package of placebo-controlled randomized clinical trials among MSM and TGW (iPrEX study); serodiscordant, heterosexual couples (Partners PrEP study); single, heterosexual couples (TDF-2 study); and male and female injection drug users (Bangkok Tenofovir study). While its uptake was initially slow in the U.S., a significant increase in Truvada for PrEP prescriptions has been seen since 2016 with an estimated 220,000 to 250,000 persons receiving PrEP in the U.S. (PrEPWatch, August 2018; prepwatch.org/country/united-states, accessed January 14, 2019). However, several reports from HIV conferences have focused on the disproportionate high uptake among white MSM but low uptake among black and Hispanic MSM, and cis-gender, heterosexual, and transgender women (natap.org/2018/CROI/croi_196.htm). A report at the IAS 2018 conference from the CDC, Emory University, and Gilead showed a significant decline in newly diagnosed PLWH in areas of the U.S. where PrEP uptake was the highest (poz.com/article/rising-prep-use-associated-declining-hiv-diagnoses-united-states). Also, of note, the approval of Truvada for PrEP was extended to smaller and (most likely) younger persons at-risk for HIV as the FDA approved the use of Truvada for PrEP in persons weighing at least 35 kilograms or 77 pounds in May of 2018. With the availability of the generic, near-equivalent, and less costly Cimduo (tenfovir DF/lamivudine; see that page), the use of this antiretroviral for PrEP is a growing possibility. Regulatory-wise and according to the FDA, Cimduo is not officially approved for PrEP, only for treatment of HIV. Will this distinction matter when it comes time to spend less money and increase access to PrEP?

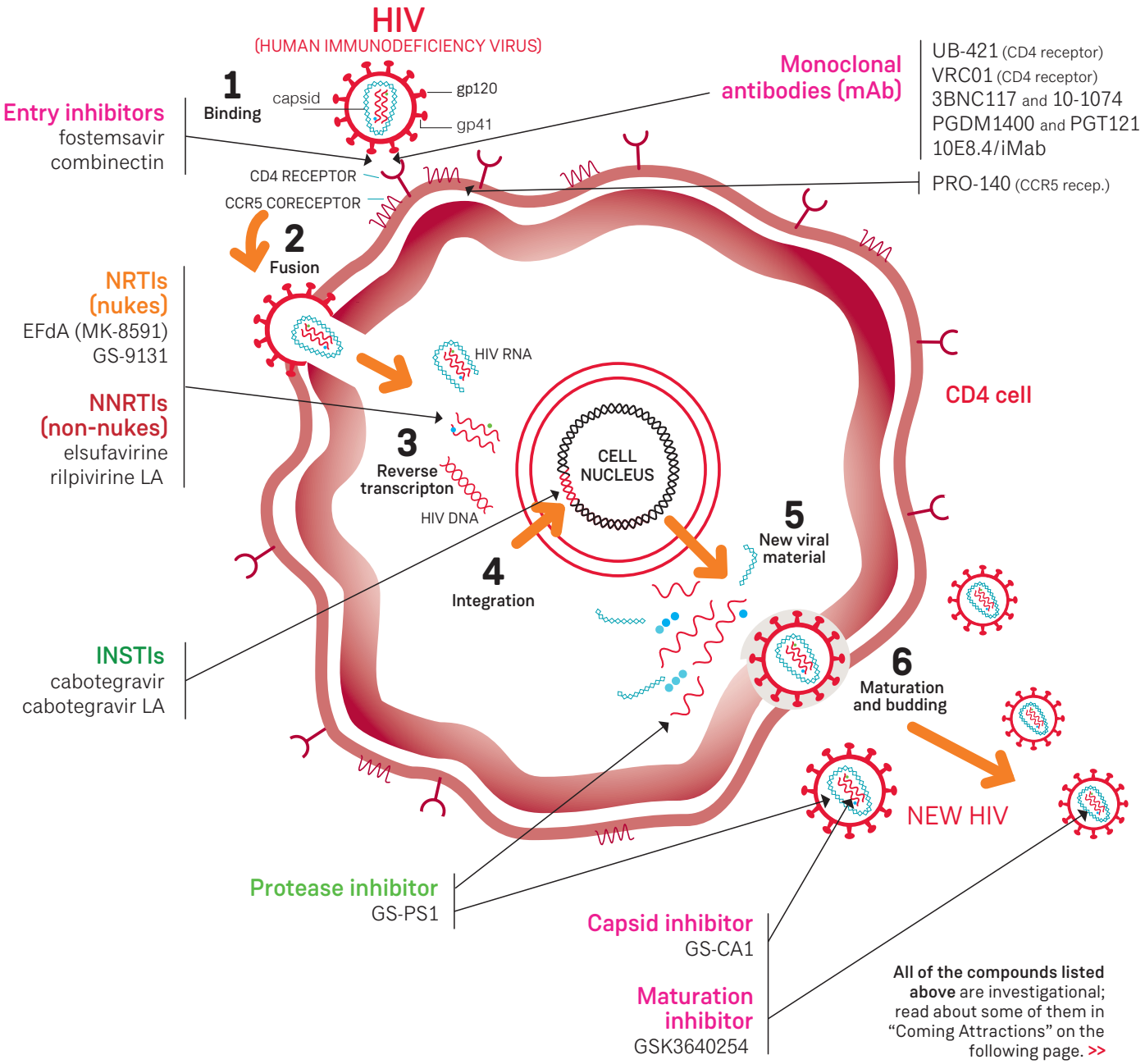
ACTIVIST MOISÉS AGOSTO-ROSARIO SAYS: PrEP is short for pre-exposure prophylaxis, which means protecting yourself from exposure to the HIV virus. Truvada is an HIV drug that has proven to reduce the risk of getting infected with HIV through sex. It is prescribed to be taken once a day, every day. Adherence is very important for PrEP to work. You have to be tested before using Truvada for PrEP and every three months see your health care provider who will test you for HIV and other sexually transmitted diseases (STDs). Truvada for PrEP does not reduce the risk for contracting STDs; that's why it is strongly recommended to practice safer sex practices even if you take Truvada for PrEP. Truvada can cause serious adverse events like kidney damage and bone density loss. You should be monitored for both. Liver damage might occur, so it is important to check your liver enzymes.

MANUFACTURER
Gilead Sciences, Inc.
gilead.com
truvada.com
cdc.gov/hiv/basics/prep.html
(800) GILEAD-5
(445-3235)

AVERAGE WHOLESALE PRICE
$2,010.95/month

An ensemble cast

How different drug classes play their part—and a look at some of the new players



All of the compounds listed above are investigational; read about some of them in "Coming Attractions" on the following page. >>

STAGES OF THE HIV LIFE CYCLE

1. BINDING
HIV attaches to a CD4 cell.

2. FUSION
HIV enters a CD4 cell and HIV proteins and enzymes are released into the cell.

3. REVERSE TRANSCRIPTION
Reverse transcriptase makes double strand HIV.

4. INTEGRATION
Integrase enables HIV to join the cell DNA.

5. REPLICATION
Protease cuts and reassembles new HIV.

6. MATURATION AND BUDDING
Each cell produces hundreds of new virions.

SOURCE: HIV i-Base (www.i-Base.info)

Coming attractions

A sneak peak at some of the new drugs coming soon

COMPLETED PHASE 3 STUDY OR SUBMITTED FOR APPROVAL

dolutegravir/3TC

Single-tablet regimen comprised of an INSTI and an NRTI. Phase 3 Gemini studies as initial ART complete; TANGO switch study ongoing; regulatory decision expected third quarter of 2019. From ViiV.
SEE DRUG PAGE IN THIS GUIDE.

fostemsavir (GSK3684934)

An ap120 attachment inhibitor. 48-week results from the Phase 3 BRIGHTE study in heavily treatment-experienced with extensive drug resistance; not yet submitted. From ViiV.
SEE DRUG PAGE IN THIS GUIDE.

PHASE 3

cabotegravir

Oral formulation of an integrase inhibitor mainly used for lead-in dose before long-acting formulation. From ViiV.

cabotegravir LA/rilpivirine LA

An INSTI/NNRTI injection with very long half-life—detectable after more than one year following single injection. Studied as both treatment with rilpivirine CAB LAstudied as both treatment with rilpivirine LA and prevention as single INSTI injection. From ViiV.
SEE DRUG PAGE IN THIS GUIDE.

PRO 140

Monoclonal antibody CCR5 target. Once-weekly (350 mg) subcutaneous injection being studied in addition to ART for multi-drug resistance and as monotherapy maintenance therapy (without ART). From CytoDyn.

UB-421

Monoclonal antibody CD4 binding. Infusion dosed either weekly or every two weeks as alternative to ART during treatment interruption. From United BioPharma.

PHASE 1–2

MK-8591 (EFdA)

A new NRTI, highly potent, low dose, active against NRTI resistance. Long half-life, potential as oral (weekly dose) and implant (annual implant for PrEP). From Merck.

MK-8591/3TC/doravirine

Fixed-dose combination of an NNRTI + 2 NRTIs. Fixed-dose combination with NNRTI doravirine plus generic 3TC and new NRTI MK-8591 (EFdA). From Merck.

GS-9131

A new NRTI active against NRTI resistance. Synergy reported with AZT, FTC, abacavir, efavirenz, bictegravir, dolutegravir and lopinavir; additive activity with TDF and TAF. Will be co-formulated with other Gilead drugs. Phase 2 dose-finding study in Ugandan women. From Gilead.

GSK3640254

A maturation inhibitor acquired by ViiV from BMS.

3BNC117 and 10-1074

Monoclonal antibodies. Phase 1 open-label dose-ranging studies include studying these two antibodies in HIV-positive and HIV-negative participants. Both also have longer-acting (LA) formulations. From Rockefeller University.

PGDM1400 and PGT121

Another dual monoclonal antibody combination in a Phase 1 study with the potential for both treatment and prevention. From the Ragon Institute and IAVI.

SELECTED PRE-CLINICAL COMPOUNDS NOT IN HUMAN STUDIES

Combinectin (GSK3732394)

A gp41 / CD4 entry inhibitor. Combined adnectin/fusion inhibitor that stops viral entry by targeting multiple sites of action; potential for self-administered once-weekly injections. From ViiV.

GS-PS1

New once-daily unboosted protease inhibitor; high potency, long half-life, potential for fixed-dose combination single-tablet regimen. From Gilead.

GS-CA1

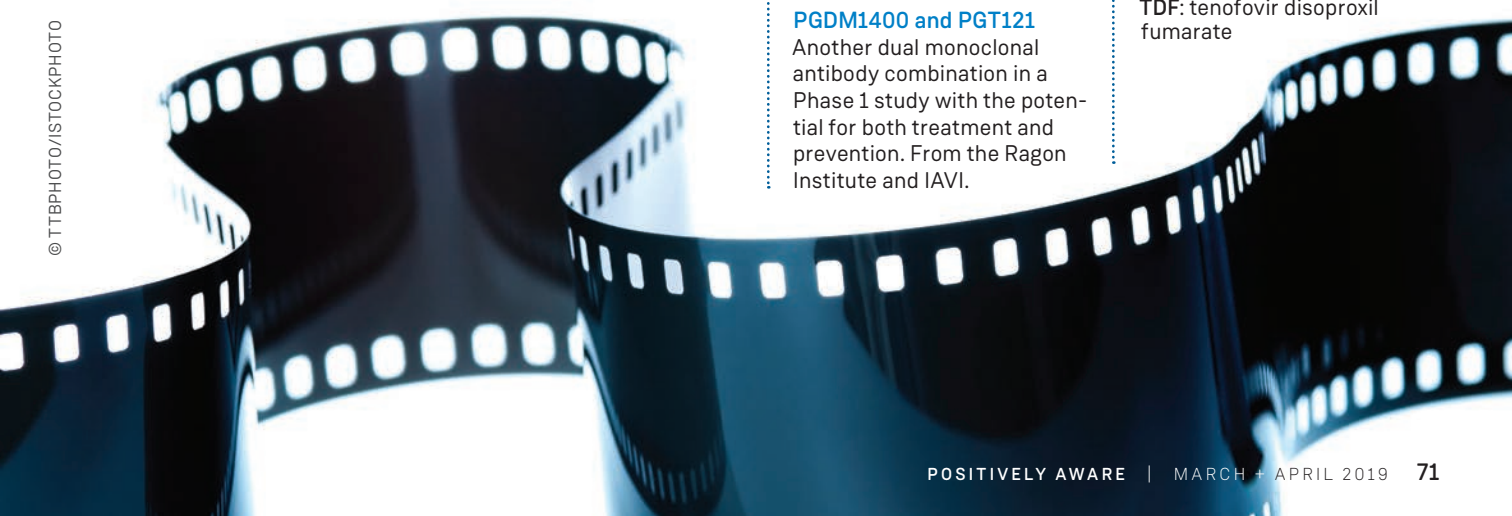
Early stage for a new drug class with activity at multiple stages of viral lifecycle. Subcutaneous injection with monthly or less frequent dosing. From Gilead.

ABBREVIATIONS

3TC: lamivudine
AZT: zidovudine
FDC: fixed-dose combination
FTC: emtricitabine
INSTI: integrase inhibitor
mAb: monoclonal antibody
NNRTI: non-nucleoside reverse transcriptase inhibitor
NRTI: nucleoside reverse transcriptase inhibitor
PI: protease inhibitor
STR: single-tablet regimen
TAF: tenofovir alafenamide
TDF: tenofovir disoproxil fumarate

ADAPTED FROM

HIV Pipeline 2018: New Drugs in Development, published by HIV i-Base, July 2018. For the full report, go to http://i-base.info/htb/34488.



Positively Aging: BEGINNINGS

New collaboration focuses on **practical solutions for long-term survivors** and older adults living with HIV

BY **JEFF BERRY**

Launched this year, Positively Aging is a new collaboration between The Reunion Project and TPAN, the publisher of POSITIVELY AWARE. This joint venture seeks to strengthen an already-existing national network of long-term survivors and create a new program in Chicago for older adults living with HIV, all the while elevating all our stories through profiles, opinion pieces, and interviews in this new regular column appearing in PA.

We need to improve the quality of life of people living with HIV over age 50, and achieve health equity for all groups of people living with the virus.

Nationally, over 50% of people living with HIV (PLWH) are over the age of 50. But in Chicago, where TPAN provides direct services to the community, over 73% of PLWH are over 50. People are living longer, and that's a good thing—it means we're doing our part to get people tested, into care, and keeping them there. Getting them on effective treatment to keep their virus suppressed, and working to prevent transmission from happening in the first place.

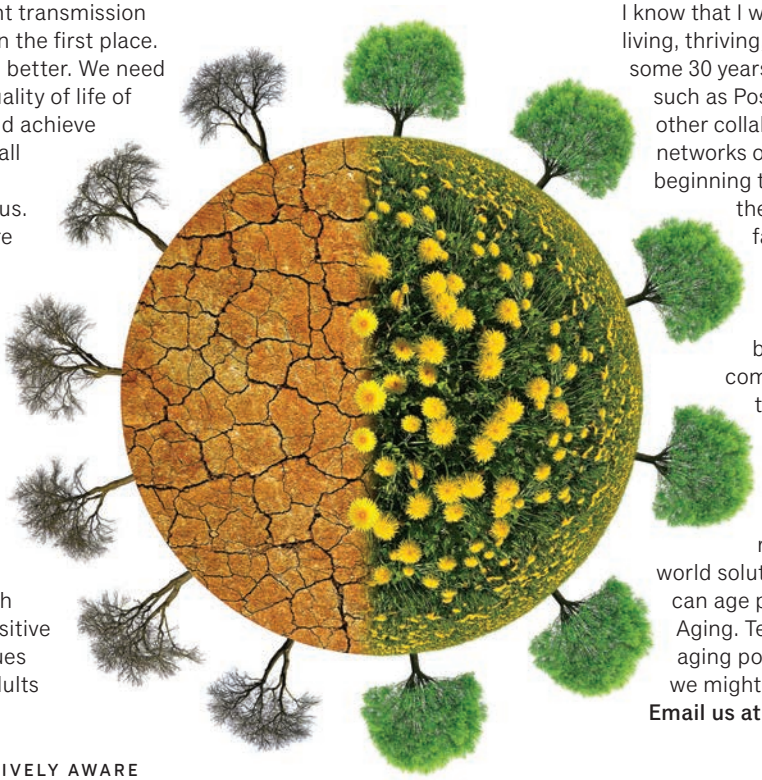
But we can do better. We need to improve the quality of life of PLWH over 50, and achieve health equity for all groups of people living with the virus. We need to ensure access to mental health services for PLWH over 50 that are better targeted and designed to address issues such as trauma, PTSD, isolation, and depression. We also need to make sure that mental health providers are sensitive to the unique issues affecting older adults living with HIV.

The Positively Aging collaboration seeks to address some of these issues. In Chicago, TPAN will implement Positively Aging through the delivery of services tailored to the needs of older adults. Comprehensive mental health services and case management will be integrated with access to on-site primary medical care (provided by TPAN's existing on-site collaborator, Howard Brown Health). In addition, the program will incorporate group social activities to address the isolation known to impede access to care for older adults.

Nationally, Positively Aging will enable The Reunion Project to expand its outreach to and engagement with long-term survivors and other older individuals affected by HIV. In cities across the country, The Reunion Project will expand its schedule of local town halls to deliver vital access to peer support and education. The Reunion Project will also expand its online and digital presence.

When I was diagnosed with HIV in 1989, survival was not guaranteed. Treatments were suboptimal, and I had no reason to think that I would make it while my friends were all dying around me. Little did I know that I would be here today, living, thriving, and aging with HIV some 30 years later. Programs such as Positively Aging, and other collaborations and networks of PLWH, are finally beginning to emerge to address the unique challenges facing people living and aging with HIV. I'm grateful to be a part of them, and blessed to work in a community that values the lives of *all* people living, and aging, with HIV.

Putting hopes and dreams into reality, creating real-world solutions, so that people can age positively—Positively Aging. Tell us your plan for aging positively with HIV, and we might just share it here. **Email us at** inbox@tpan.com.



VENCAVOLRAB -ISTOCK

EAT. DRINK. GIVE.

DINING OUT FOR LIFE

SUBARU Loves to Care

DINING OUT FOR LIFE CHICAGO | APRIL 25, 2019

Help TPAN deliver compassionate care and health services to Chicagoans living with and affected by HIV.
For details, go to tpan.com/diningout

Dining Out For Life is an international event involving the generous participation of restaurants, volunteers, corporate sponsors, and dining patrons in more than 60 cities—raising funds to support local lifesaving HIV/AIDS services. In Chicago, TPAN is the producer and beneficiary of Dining Out For Life.

To participate in a city near you, go to diningoutforlife.com.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